**EXCITED DELIRIUM TASK FORCE**

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PREAMBLE

The 2008 Council of the American College of Emergency Physicians (ACEP) adopted Amended Resolution 21(08), “Excited Delirium,” which was then adopted by the ACEP Board of Directors:

“RESOLVED, that ACEP study:
   1. The existence of “excited delirium” as a disease entity (or not);
   2. Characteristics that help identify the presentation and risk for death; and

And be it further RESOLVED, that ACEP develop and disseminate a white paper on findings to appropriate entities (e.g., EMS, law enforcement).”

INTRODUCTION

In response to this resolution, ACEP convened a Task Force of nineteen experts in what the Task Force has chosen to call Excited Delirium Syndrome (ExDS). Eighteen of these experts are emergency physician members of ACEP and one is a PhD researcher. The Task Force was charged to examine the available literature and existing data and use their expert experience and consensus to determine:

1. if the entity commonly referred to as “excited delirium” exists, and
2. if so, whether it could be better defined, identified, and treated.

It is the consensus of the Task Force that ExDS is a unique syndrome which may be identified by the presence of a distinctive group of clinical and behavioral characteristics that can be recognized in the pre-mortem state. ExDS, while potentially fatal, may be amenable to early therapeutic intervention in some cases.

The term “Excited Delirium” has been used to refer to a subcategory of delirium that has primarily been described retrospectively in the medical examiner literature. Over time, the concept of excited delirium has made its way into the emergency medicine, psychiatric, law enforcement, prehospital and medicolegal literature. It has generally been used to describe a small group of patients with a set of symptoms that has eluded a unifying, prospective clinical definition. The Task Force debated the merits of renaming the syndrome in a medically more descriptive way. However, it was decided that the literature and general understanding in the health care and law enforcement fields of the term “Excited Delirium” favored retention of the traditionally understood word for research and clinical purposes. It was incorporated into the described syndrome as “Excited Delirium Syndrome (ExDS).”

The difficulty surrounding the clinical identification of ExDS is that the spectrum of behaviors and signs overlap with many clinical disease processes. ExDS is not intended to include these diseases, except insofar as they might meet the definition of ExDS. Treatment interventions targeted at one of these alternate diagnoses may potentially alleviate or exacerbate ExDS, thus further confounding the diagnosis. Faced with the lack of a clear definition and cause, the decision to identify ExDS as a syndrome instead of a unique disease is similar to the dec-
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ades-long controversy over the causes of Sudden Infant Death Syndrome.

Despite increased research, the exact pathophysiology of ExDS remains unidentified. Some recent research in the area of fatal ExDS points to dopamine transporter abnormalities. Eventually, there might be found a genetic susceptibility, an enzyme excess or deficiency, an overdose or withdrawal state, or some other multifactorial trigger, including a variety of medical and psychiatric conditions.

At present, physicians and other medical and nonmedical personnel involved in personal interactions with these patients do not have a definitive diagnostic “test” for ExDS. It must be identified by its clinical features. This also makes it very difficult to ascertain the true incidence of ExDS.

While not universally fatal, it is clear that a proportion of patients with ExDS progress to cardiac arrest and death. It is impossible at present to know how many patients receive a therapeutic intervention that stops the terminal progression of this syndrome. While many of the current deaths from ExDS are likely not preventable, there may be an unidentified subset in whom death could be averted with early directed therapeutic intervention.

In this paper, the Task Force provides a review of the history and epidemiology of ExDS, clinical perspectives, and a discussion of its potential pathophysiology, diagnostic characteristics, differential diagnoses, and clinical treatment. Ultimately, the goals are to raise awareness of the existence of this syndrome to medical and public entities, to aid law enforcement, Emergency Medical Service (EMS) personnel, physicians, health care providers, corrections officers and others in the recognition of ExDS, and to identify best practices to deal with this true medical emergency.

HISTORY

For more than 150 years, there have been case reports that do not use the exact term “excited delirium,” yet describe a similar constellation of symptoms and features. These cases discuss clinical behavior and outcomes that are strikingly similar to the modern day concept of ExDS.

These historical cases occurred primarily within institutions that housed mentally disturbed individuals in protective custody largely because of the lack of effective pharmacologic treatment available during that time period. The behavior seen in these cases has been called “Bell’s Mania,” named after Dr. Luther Bell, the primary psychiatrist at the McLane Asylum for the Insane in Massachusetts. Dr. Bell was the first to describe a clinical condition that took the lives of over 75% of those suffering from it. Based on the clinical features and outcomes of the institutionalized cases from the 1800s when compared to the presently accepted criteria known to accompany ExDS, it is believed that Bell’s Mania may be related to the syndrome of ExDS that we witness today.

Historical research indicates that the worrisome behaviors and deaths following uncontrolled psychiatric illness described in the 1800s seemed to decline drastically by the mid-1950s. This is largely attributed to the advent of modern antipsychotic pharmaceutical therapy that changed psychiatric practice from one of custodial patient control to a goal of de-institutionalization and patient placement within normal community settings.

There is only one reference before 1985 known to mention the exact term “Excited Delirium.” In this reference, the words “excited” and “delirium” were combined to describe the condition of a patient just prior to death following a hemorrhoid operation by an accomplished surgeon. At the time, it was felt that the operation somehow damaged the patient’s nervous system, and lead to acute psychiatric decompensation and death.

In the 1980s, there was a dramatic increase in the number of reported cases with behavior similar to an uncontrolled psychiatric emergency. While some seemed to be unchecked psychiatric disease, most of these cases were found to be associated with the introduction and abuse of cocaine in North America. Since then, this connection between ExDS and co-
caine has continued. Additionally, ExDS has now been recognized to occur in association with other illicit drugs of abuse, as well as with certain types of mental illness and their associated treatment medications.

Before 1985, there was no single unifying term to describe the clinical pattern seen in these patients. In 1985 a subset of cocaine deaths was described by Wetli and Fishbain in a seminal paper which for the first time used the term “excited delirium.”

The typical course of a published ExDS patient involves acute drug intoxication, often a history of mental illness (especially those conditions involving paranoia), a struggle with law enforcement, physical or noxious chemical control measures or electrical control device (ECD) application, sudden and unexpected death, and an autopsy which fails to reveal a definite cause of death from trauma or natural disease.

As a consequence of the circumstances surrounding the death and the lack of a definitive cause on autopsy, there has been continued debate about the validity of the term “excited delirium.” This debate continues today. There are those who believe it to be a convenient term used to excuse and exonerate authorities when someone dies while in their custody. It is articulated by some that ExDS is a term or concept that has been “manufactured” as a law enforcement conspiracy or cover-up for brutality.

This argument mainly centers on the fact that most organized medical associations (e.g., American Medical Association) and medical coding reference materials (e.g., International Classification of Diseases, Ninth Revision, or ICD-9) do not recognize the exact term “excited delirium” or “excited delirium syndrome.” The countering argument is that there are organized medical associations that do recognize ExDS as an entity (e.g., National Association of Medical Examiners) and references such as the ICD-9 contain several codes that can be used to describe the same entity as ExDS, albeit with different wording such as:

- 296.00s Manic Excitement
- 293.1J Delirium of Mixed Origin
- 292.81Q Delirium, drug induced
- 292.81R Delirium, induced by drug
- 307.9AD Agitation
- 780.09E Delirium
- 799.2AM Psychomotor Excitement
- 799.2V Psychomotor Agitation
- 799.2X Abnormal Excitement

This issue of semantics does not indicate that ExDS does not exist, but it does mean that this exact and specific terminology may not yet be accepted within some organizations or references.

**EPIDEMIOLOGY**

The exact incidence of ExDS is impossible to determine as there is no current standardized case definition to identify ExDS. In addition, since ExDS is mainly discussed in the forensic literature and is a diagnosis of exclusion established on autopsy, there is little documentation about survivors of the syndrome. A published observational study suggests that the incidence of death among patients manifesting signs and symptoms consistent with ExDS is 8.3%. Some Task Force members have cared for multiple individual patients with ExDS who have survived.

Stimulant drug use, including cocaine, methamphetamine, and PCP, demonstrates a well established association with ExDS and is usually associated with cases of ExDS death.

A review of the literature reveals common characteristics among patients identified post-mortem as suffering from ExDS. More than 95% of all published fatal cases are males with a mean age of 36. These subjects are hyperaggressive with bizarre behavior, and are impervious to pain, combative, hyperthermic and tachycardic. There is typically a struggle with law enforcement that involves physical, noxious chemical, or ECD use followed by a period of quiet and sudden death. The majority of
cases involve stimulant abuse, most commonly cocaine, though methamphetamine, PCP, and LSD have also been described. At least in the setting of cocaine use, the episode of ExDS usually appears to occur in the context of a cocaine binge that follows a long history of cocaine abuse.

Persons with psychiatric illnesses comprise the second largest but a distinctly smaller cohort of ExDS cases and deaths. The literature on ExDS frequently cites abrupt cessation of psychotherapeutic medications as a cause. This raises the question of whether the behavioral changes seen in this context represent withdrawal syndromes characteristic of the medications involved, central nervous system adaptations to medications, or recrudescence of underlying disease. Since medication noncompliance is common in psychiatric patients, health care providers should be aware of this potential cause of delirium-like behavior. Less commonly, persons with new-onset psychiatric disease (mania or psychosis) will present with ExDS. In most cases, the underlying disease will be untreated at the time of presentation, but in some cases the disease may be partially treated or mistreated.

Over a two-year period, presence or absence of 10 potential clinical features of ExDS was recorded by Canadian police for over 1 million police-public interactions (C. Hall, personal communication).

Of the 698 encounters involving use of force, 24 probable cases were identified, based upon the presence of perceived abnormal behavior and at least 6 of 10 potential clinical criteria for ExDS. These represent 3.4% (or 2-5%) of the use of force cohort. For the individuals manifesting 7 or more features including tactile hyperthermia, Table 1 lists the occurrence of all 10 potential features with their frequencies and 95% confidence intervals. (Note that the oft-reported mirror or glass attraction is rather infrequent). These represent 2.7% (or 1-3.5%) of the use of force cohort, a not inconsequential number given the potential for sudden unexpected death.

Although no deaths occurred in this collection period, the 97.5% one sided confidence interval for the absence of death still implies that up to 14% of these individuals could experience sudden death, a number in line with the previously mentioned and published observational study.

Table 1: ExDS Prehospital Potential Features and Frequencies with 95% Confidence Intervals

<table>
<thead>
<tr>
<th>FEATURE</th>
<th>FREQUENCY % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Tolerance</td>
<td>100 (83-100)</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>100 (83-100)</td>
</tr>
<tr>
<td>Sweating</td>
<td>95 (75-100)</td>
</tr>
<tr>
<td>Agitation</td>
<td>95 (75-100)</td>
</tr>
<tr>
<td>Tactile Hyperthermia</td>
<td>95 (75-100)</td>
</tr>
<tr>
<td>Police Noncompliance</td>
<td>90 (68-99)</td>
</tr>
<tr>
<td>Lack of Tiring</td>
<td>90 (68-90)</td>
</tr>
<tr>
<td>Unusual Strength</td>
<td>90 (68-90)</td>
</tr>
<tr>
<td>Inappropriately Clothed</td>
<td>70 (45-88)</td>
</tr>
<tr>
<td>Mirror/Glass Attraction</td>
<td>10</td>
</tr>
</tbody>
</table>

PATHOPHYSIOLOGY

The pathophysiology of ExDS is complex and poorly understood. The fundamental manifestation is delirium. There are several different potential underlying associations or causes, including stimulant drug abuse, psychiatric disease, psychiatric drug withdrawal, and metabolic disorders. Unknown mechanisms lead from these conditions to the overt ExDS state. Specific manifestations vary among different cases. We do not fully understand why some cases progress to death and why some do not.

Although our knowledge concerning the etiology and pathophysiology of ExDS is limited, basic science and clinical studies have provided some insight. Stimulant drug use, especially cocaine, is associated with ExDS. Of note, post-mortem toxicological analysis of fatal cocaine-associated ExDS patients demonstrates cocaine concentrations similar to those found in recreational drug users and less
than those noted in acute cocaine intoxication deaths, suggesting a different mechanism of death.

Subsequent anatomic and molecular characterization of this group of fatal ExDS patients has focused primarily on postmortem brain examination. Results from this increasingly robust body of work demonstrate a characteristic loss of the dopamine transporter in the striatum of chronic cocaine abusers who die in police custody from apparent ExDS. This suggests that one potential pathway for the development of ExDS is excessive dopamine stimulation in the striatum, but the significance of this in the larger context of ExDS unrelated to chronic cocaine abuse remains unknown.

Making a central dopamine hypothesis more appealing is the fact that hypothalamic dopamine receptors are responsible for thermoregulation. Disturbances of dopamine neurotransmission may help explain the profound hyperthermia noted in many ExDS patients. Post-mortem studies in these patients have demonstrated elevated levels of heat shock proteins (HSP). The central dopamine hypothesis also provides a link to psychiatric etiologies of ExDS.

While the specific precipitants of fatal ExDS remain unclear, epidemiologic and clinical reports provide some understanding of the underlying pathophysiology. When available, cardiac rhythm analysis demonstrates bradycardia; ventricular dysrythmias are rare, occurring in only a single patient in one study. The majority of lethal ExDS patients die shortly after a violent struggle. Severe acidosis appears to play a prominent role in lethal ExDS-associated cardiovascular collapse.

While attention has focused largely upon cases of fatal ExDS in humans, it must be noted that a similar syndrome, termed capture myopathy, has been reported in the veterinary literature. Clinically, it is characterized by prolonged neuromuscular activity, acidosis, and rhabdomyolysis.

**Clinical Perspectives**

**Law Enforcement**

In modern times, a law enforcement officer (LEO) is often present with a person suffering from ExDS because the situation at hand has degenerated to such a degree that someone has deemed it necessary to contact a person of authority to deal with it. LEOS are in the difficult and sometimes impossible position of having to recognize this as a medical emergency, attempting to control an irrational and physically resistive person, and minding the safety of all involved.

Given the irrational and potentially violent, dangerous, and lethal behavior of an ExDS subject, any LEO interaction with a person in this situation risks significant injury or death to either the LEO or the ExDS subject who has a potentially lethal medical syndrome. This already challenging situation has the potential for intense public scrutiny coupled with the expectation of a perfect outcome. Anything less creates a situation of potential public outrage. Unfortunately, this dangerous medical situation makes perfect outcomes difficult in many circumstances.

It is important for LEOS to recognize that ExDS subjects are persons with an acute, potentially life-threatening medical condition. LEOS must also be aware that remorse, normal fear and understanding of surroundings, and rational thoughts for safety are absent in such subjects.

ExDS subjects are known to be irrational, often violent and relatively impervious to pain. Unfortunately, almost everything taught to LEOS about control of subjects relies on a suspect to either be rational, appropriate, or to comply with painful stimuli. Tools and tactics available to LEOS (such as pepper spray, impact batons, joint lock maneuvers, punches and kicks, and ECD’s, especially when used for pain compliance) that are traditionally effective in controlling resisting subjects, are likely to be less effective on ExDS subjects.

When methods such as pain compliance maneuvers or tools of force fail, the LEO is left with few op-
tions. It is not feasible for them to wait for the ExDS subject to calm down, as this may take hours in a potentially medically unstable situation fraught with scene safety concerns.

Some of the goals of LEOs in these situations should be to 1) recognize possible ExDS, contain the subject, and call for EMS; 2) take the subject into custody quickly, safely, and efficiently if necessary; and 3) then immediately turn the care of the subject over to EMS personnel when they arrive for treatment and transport to definitive medical care.

LEOs should be trained to recognize and manage subjects with ExDS. Officers should attempt to ensure that the tactile temperature of these subjects is documented and request EMS to measure it. In fatal cases, a significantly elevated temperature may suggest that a life-threatening disease or condition was present, and that the death was independent of the police intervention.

Emergency Medical Services

EMS dispatch personnel need to recognize clues from calls or radio traffic that personnel may be responding to a case of ExDS. This should trigger multiple law enforcement personnel responding in addition to EMS.

EMS personnel need to be trained in the recognition of the signs and symptoms of ExDS. They are in a difficult position because they need to recognize the heightened personal safety risks that ExDS subjects represent to them but they also have a duty to provide timely care. They need to understand and practice their expected interaction with LEOs.

It is the role of LEOs to control the person with potential ExDS. However, as soon as control has been obtained, it is the role of EMS to recognize that this is a medical emergency and to assume responsibility for assessment and care of the patient.

Emergency Department (ED)

Emergency Physicians (EP’s) should be educated about the clinical features of ExDS and should include this in the differential diagnosis of any patient with altered mental status and agitation (either at the time of presentation or by history). There should be an increased index of suspicion for ExDS in agitated patients that present in the custody of law enforcement; however, this is a clinical entity that can enter the ED from any source (EMS, Law Enforcement, ED triage, etc).

EP’s should recognize that this syndrome seems to be a multifactorial interaction of delirium and agitation, leading to hyperthermia and profound acidaemia, often in the setting of stimulant drug abuse. Regardless of etiology, ExDS may be fatal in some patients. EP’s should consider the possibility of ExDS in the evaluation of younger patients that present in cardiac arrest, especially in the setting of profound metabolic acidosis and hyperthermia. The physician should also initiate the documentation of clinical signs and the collection of specimens for research and diagnosis.

Medical Examiners

Medical Examiners are often required to render a decision as to the cause of death in cases that involve patients in police custody with multiple confounding variables such as pre-existing health conditions, concomitant illicit substance use, and underlying psychiatric conditions. Lack of complete prior medical information, especially underlying cardiac and metabolic pathology, hampers the ascertainment of the actual cause of death when only autopsy results are interpreted.

For example, an unknown case of Brugada syndrome (a genetic abnormality of sodium ion channels leading to sudden death from ventricular fibrillation) may be the actual cause of cardiac arrest in an individual under the influence of cocaine, even absent excessive LEO force. Without prior electrocardiograms, this condition would be entirely missed. Likewise, premortem potassium and glucose levels, and even basic vital signs (temperature and blood pressure) cannot possibly be investigated via autopsy.

The importance of a skilled investigation of the
scene of death cannot be overestimated. Crucial information such as subject behavior, drug use history, a history or presence of psychosis, or the presence of hyperthermia, can facilitate the determination of whether the clinical features of ExDS were present.

The time, quantity, and chronicity of drug ingestion cannot always be reliably determined by toxicology alone. Significant postmortem redistribution of drugs makes interpretation of blood levels found at autopsy fraught with speculation. Tolerance to many drugs of abuse can confound interpretation of blood or tissue levels. Specific drug levels may not correlate with acute drug toxicity or poisoning. While the majority of cases of ExDS appear to occur in the presence of or with a history of cocaine or other stimulants, their presence is not required for this syndrome to occur. Psychiatric cases not involving drugs of abuse have been reported. There is no current gold standard test for the diagnosis of ExDS. The presence of the hallmark clinical findings along with the presence of some type of centrally acting stimulant strongly suggests the diagnosis. Current understanding of pathophysiology suggests that the collection of various specimens (particularly brain tissue in fatal cases) is beneficial both for potential diagnosis confirmation and research.

**CLINICAL CHARACTERISTICS**

Because ExDS resulting in death does not currently have a known specific etiology or a consistent single anatomic feature, it can only be described by its epidemiology, commonly described clinical presentation, and usual course. The minimum features for ExDS to be considered include the presence of both delirium and an excited or agitated state. As described in the DSM-IV-R, the features of delirium are constant and defined by a disturbance of consciousness (reduced clarity of the awareness of the environment) with reduced ability to focus, sustain or shift attention. The perceptual disturbance develops over a short period of time (usually hours to days), may fluctuate during the course of a day, and is not accounted for by underlying dementia.

Because of varied underlying medical conditions that may generate ExDS, there is also variation in the specific symptom cluster. As in any disorder that affects mental status, there is no assumption that each subject’s presentation will occur as a completely discrete entity with absolute boundaries. The consistency lies with subjects who are delirious with evidence of psychomotor and physiologic excitation.

The combination of delirium, psychomotor agitation, and physiologic excitation differentiates ExDS from other processes that induce delirium only. Similarly, subjects who are agitated or violent but who do not also demonstrate features of delirium simply do not meet the definition of ExDS.

Until wider recognition of ExDS began, most publications about it were found in the forensic pathology literature and there was little publication interest in cases of ExDS that did not end catastrophically. The high reported frequency of death is likely increased by measurement and reporting bias since pathologists who first identified the unifying syndrome of ExDS that leads to sudden unexpected death necessarily encountered only those subjects who died. At least one author (a forensic pathologist) describes the combination of a syndrome of excited delirium plus unanticipated sudden death as “excited delirium syndrome,” with invocation of the term syndrome only if the subject died.

When death occurs, it occurs suddenly, typically following physical control measures (physical, noxious chemical, or electrical), and there is no clear anatomic cause of death at autopsy. In cases in which a subject dies following the application of control measures, many or most of the following features are found:

- male subjects, average age 36
- destructive or bizarre behavior generating calls to police,
- suspected or known psychostimulant drug or alcohol intoxication,
- suspected or known psychiatric illness,
- nudity or inappropriate clothing for the environment,
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- failure to recognize or respond to police presence at the scene (reflecting delirium),
- erratic or violent behavior,
- unusual physical strength and stamina,
- ongoing struggle despite futility,
- cardiopulmonary collapse immediately following a struggle or very shortly after quiescence,
- inability to be resuscitated at the scene, and
- inability for a pathologist to determine a specific organic cause of death,
- attraction to glass or reflective surfaces (less frequent than all others per the Canadian data).

Subjects are incoherent and combative, and the struggle is more severe than anyone anticipates. Many have already sustained traumatic injuries before the arrival of law enforcement and still exhibit intense struggling even when a struggle is futile and self mutilation is a result.

Table 2 lists the features of excited delirium syndrome based on a review of the medical literature including 18 articles. The table is divided to indicate features based on the medical history of the subject, features that are observed in the company of the subject, features that are evident upon physical contact, features that are only evident with clinical assessment (i.e. vital signs), features that are described if the subject dies, and finally, features that are described on autopsy. A limitation of this analysis is that not all of these publications are observational studies and there is significant overlap of publications that reference each other to derive the most common clinical presentation.

### Table 2: ExDS Features by Literature Review (n=18)

<table>
<thead>
<tr>
<th>Features in History</th>
<th># Articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>16</td>
</tr>
<tr>
<td>Mean age ~30’s</td>
<td>16</td>
</tr>
<tr>
<td>Sudden onset</td>
<td>4</td>
</tr>
<tr>
<td>History of Mental Illness</td>
<td>8</td>
</tr>
<tr>
<td>History of Psychostimulant abuse</td>
<td>11</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Features evident at scene</th>
<th># Articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Call for disturbance/psychomotor agitation/excitation</td>
<td>18</td>
</tr>
<tr>
<td>Violent/combative/belligerent/assault call</td>
<td>11</td>
</tr>
<tr>
<td>Not responding to authorities/verbal commands</td>
<td>1</td>
</tr>
<tr>
<td>Psychosis/delusional/paranoid/fearful</td>
<td>13</td>
</tr>
<tr>
<td>Yelling/shouting/guttural sounds</td>
<td>7</td>
</tr>
<tr>
<td>Disrobing/inappropriate clothing</td>
<td>5</td>
</tr>
<tr>
<td>Violence toward/destruction of inanimate objects</td>
<td>7</td>
</tr>
<tr>
<td>Walking/running in traffic</td>
<td>3</td>
</tr>
<tr>
<td>Subject Obese</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Features evident on contact</th>
<th># Articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant resistance to physical restraint</td>
<td>11</td>
</tr>
<tr>
<td>Superhuman strength</td>
<td>8</td>
</tr>
<tr>
<td>Impervious to pain</td>
<td>3</td>
</tr>
<tr>
<td>Continued struggle despite restraint</td>
<td>7</td>
</tr>
<tr>
<td>Profuse sweating/clammy skin</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Features with clinical assessment</th>
<th># Articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachypnea</td>
<td>1</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>7</td>
</tr>
<tr>
<td>Hyperthermia</td>
<td>12</td>
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<tr>
<td>Hypertension</td>
<td>3</td>
</tr>
<tr>
<td>Acidosis</td>
<td>3</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>5</td>
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</table>
Emergency clinicians and prehospital care providers are anecdotally aware that not all ExDS cases end in death. However, publication of nonfatal case reports or cohort studies remains infrequent. There is currently a paucity of literature to describe the epidemiology of ExDS if it is not accompanied by sudden death.

In the previously described Canadian data, 24 individuals demonstrated 6 or more of the clinical features found in Table 1. Prehospital ExDS may be reasonably presumed in subjects displaying 6 or more features of excited delirium (perhaps excluding attraction to reflective surfaces), thereby providing a potential case definition for future investigations. It is particularly likely if the subject displays constant or near constant physical activity, pain tolerance, superhuman strength, sweating, rapid breathing, tactile hyperthermia, and a failure to respond to police presence.

In summary, the clinical picture is one of an agitated and delirious state with autonomic dysregulation. It manifests through sympathetic hyper-arousal with frequent hyperthermia, vital sign abnormalities, and metabolic acidosis. For some, the clinical syndrome progresses to death.

### Features of death

<table>
<thead>
<tr>
<th>Features of death</th>
<th># Articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period of tranquility/“giving up”</td>
<td>4</td>
</tr>
<tr>
<td>Sudden collapse after restraint</td>
<td>12</td>
</tr>
<tr>
<td>Respiratory Arrest described</td>
<td>5</td>
</tr>
<tr>
<td>Cardiac rhythm brady-asystole or PEA</td>
<td>4</td>
</tr>
<tr>
<td>Aggressive Resuscitation unsuccessful</td>
<td>5</td>
</tr>
</tbody>
</table>

### Features on autopsy

<table>
<thead>
<tr>
<th>Features on autopsy</th>
<th># Articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug screen Positive for psychostimulants</td>
<td>9</td>
</tr>
<tr>
<td>Drug levels lower than anticipated</td>
<td>3</td>
</tr>
<tr>
<td>No anatomic correlate for death</td>
<td>6</td>
</tr>
<tr>
<td>Dopamine transporter disregulation</td>
<td>2</td>
</tr>
</tbody>
</table>

### Differential Diagnosis

**Overview of delirium and altered mental status**

Almost any drug, toxin, extraneous substance, psychiatric or medical condition, or biochemical or physiologic alteration in the body can cause acute changes in behavior or mental status. The general public, law enforcement, EMS, and even highly trained medical personnel may not be able to readily discern the cause of an acute behavioral disturbance, or differentiate a specific organic disease from ExDS.

**Conditions that cause altered mental status**

Altered mental status may be associated with a wide range of clinical signs and symptoms. The condition can range from coma to mild or profound confusion to uncontrolled agitation and delirium. A limited differential diagnosis of altered mental status is provided by the mnemonics AEI0U TIPS (Table 3), or SMASHED 2 (Table 4). Some etiologies may be suggested by clinical observation, obvious toxidromes, past medical history, patient age, or circumstances surrounding the acute event. Extensive testing and protracted evaluation and observation are often required to fully unravel the etiology of the acutely altered sensorium. As such, lifesaving interventions should be initiated prior to obtaining a specific diagnosis.

**Table 3: AEIOU TIPS Mnemonic for Abbreviated Differential Diagnosis of Altered Mental Status**

<table>
<thead>
<tr>
<th>Letter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Alcohol</td>
</tr>
<tr>
<td>E</td>
<td>Endocrine, Encephalopathy, Electrolytes</td>
</tr>
<tr>
<td>I</td>
<td>Insulin (hypoglycemia)</td>
</tr>
<tr>
<td>O</td>
<td>Oxygen (hypoxia), Opiates (drugs of abuse)</td>
</tr>
<tr>
<td>U</td>
<td>Uremia</td>
</tr>
<tr>
<td>T</td>
<td>Toxins, Trauma, Temperature</td>
</tr>
<tr>
<td>I</td>
<td>Infection</td>
</tr>
<tr>
<td>P</td>
<td>Psychiatric, Porphyria</td>
</tr>
<tr>
<td>S</td>
<td>Stroke, Shock, Subarachnoid Hemorrhage, Space-Occupying CNS Lesion</td>
</tr>
</tbody>
</table>
Several specific entities which cause altered mental status and may mimic ExDS deserve specific mention:

- Diabetic hypoglycemic reactions have been associated with outbursts of violent behavior and an appearance of intoxication. Diagnosis may be rapidly and conclusively made by determination of blood glucose and response to glucose administration.

- Heat stroke may manifest as tactile hyperthermia, rhabdomyolysis, and delirium, and may be associated with neuroleptic use and mental illness. A profound acidosis is often not present.

- Serotonin syndrome and neuroleptic malignant syndrome (NMS) may share some clinical characteristics with ExDS. However, they usually do not share the aggressive violent behavior manifested by patients with ExDS.

- Psychiatric issues may mimic ExDS. Some patients experience behavioral disturbances directly due to psychotropic drug withdrawal or noncompliance. Substance abuse is also very common in psychiatric patients. Many psychiatric conditions themselves, including acute paranoid schizophrenia, bipolar disorder, and even emotional rage from acute stressful social circumstances, may mimic an ExDS-like state. Untreated or poorly controlled psychiatric illness may also result in poor compliance with management of acute or chronic medical conditions. In Phillips v Milwaukee, a man who died in police custody of apparent ExDS was found at autopsy to have untreated thyrotoxicosis, as well as being noncompliant with his psychiatric medications.

### Conditions that cause sudden death

Sudden unexpected death is the hallmark of fatal ExDS. The differential diagnosis for sudden death includes ischemic or drug induced sudden cardiac death, stress (Takotsubo) cardiomyopathy, inherited or acquired Long QT Syndrome, Brugada syndrome, and less common entities such as Cannon’s Voodoo Death, Lethal Catatonia, and sudden unexplained death in epilepsy (SUDEP).

<table>
<thead>
<tr>
<th>Letter</th>
<th>Title</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S</strong></td>
<td>Substrates</td>
<td>glucose (high/low), thiamine deficiency</td>
</tr>
<tr>
<td></td>
<td>Sepsis</td>
<td>all CNS infections, AIDS dementia, encephalitis, brain abscess or toxoplasmosis</td>
</tr>
<tr>
<td><strong>M</strong></td>
<td>Meningitis</td>
<td>acute psychosis, medication noncompliance, mania, depression, malinger, rage, suicide intent (via police)</td>
</tr>
<tr>
<td><strong>A</strong></td>
<td>Alcohol</td>
<td>Intoxication, withdrawal</td>
</tr>
<tr>
<td><strong>A</strong></td>
<td>Accident</td>
<td>head trauma, CVA, cerebral contusion, subdural or epidural hematoma</td>
</tr>
<tr>
<td><strong>S</strong></td>
<td>Seizing</td>
<td>or postictal</td>
</tr>
<tr>
<td><strong>S</strong></td>
<td>Stimulants, hallucinogens, anticholinergics</td>
<td>Cocaine, amphetamines, caffeine, PCP, LSD, ketamine, psilocybin, antihistamines, atropine, scopalamine, jimson weed</td>
</tr>
<tr>
<td><strong>H</strong></td>
<td>Hyper</td>
<td>hypertension, hyperthyroidism, hypercarbia, hyperthermia</td>
</tr>
<tr>
<td><strong>H</strong></td>
<td>Hypo</td>
<td>hypotension, hypothyroidism, hypoxia, hypothermia</td>
</tr>
<tr>
<td><strong>E</strong></td>
<td>Electrolytes</td>
<td>hyper/hyponatremia, hypercalcemia</td>
</tr>
<tr>
<td><strong>E</strong></td>
<td>Encephalopathy</td>
<td>hepatic, HIV, uremic, hypertensive, lead, Reye’s syndrome, CNS tumor</td>
</tr>
<tr>
<td><strong>D</strong></td>
<td>Drugs</td>
<td>Intoxication or withdrawal</td>
</tr>
<tr>
<td><strong>D</strong></td>
<td>Don’t forget other drugs</td>
<td>carbon monoxide, lithium, steroids, salicylates, designer/street drugs, theophylline, MDMA, antipsychotics, toxins not on routine drug screen, others</td>
</tr>
</tbody>
</table>
**Treatment and Protocols**

In the absence of clearly stated case definitions and prospective clinical studies, treatment of ExDS remains largely speculative and consensus-driven, directed towards supportive care and reversal of obvious clinical and laboratory abnormalities. The specific circumstances under which medical interventions will provide benefit are currently unclear. Nonetheless, there are current medical approaches that have consensus support. Most authorities, including this Task Force, posit the beneficial use of aggressive chemical sedation as first line intervention. As with any critically ill patient, treatment should proceed concurrently with evaluation for precipitating causes or additional pathology.

In subjects who do not respond to verbal calming and de-escalation techniques, control measures are a prerequisite for medical assessment and intervention. When necessary, this should be accomplished as rapidly and safely as possible. Recent research indicates that physical struggle is a much greater contributor to catecholamine surge and metabolic acidosis than other causes of exertion or noxious stimuli. Since these parameters are thought to contribute to poor outcomes in ExDS, the specific physical control methods employed should optimally minimize the time spent struggling, while safely achieving physical control. The use of multiple personnel with training in safe physical control measures is encouraged.

After adequate physical control is achieved, medical assessment and treatment should be immediately initiated. Indeed, because death might occur suddenly, EMS should ideally be present and prepared to resuscitate before definitive LEO control measures are initiated.

Initial assessment should include assessment of vital signs, cardiac monitoring, IV access, glucose measurement, pulse oximetry and supplemental oxygen, and careful physical examination. While the need for LEO control measures may initially preclude some or all of these interventions, they should be performed as soon as safely possible.

Agitation, hyperthermia, and acidosis are all major components of ExDS which can be effectively managed using traditional medical interventions. The approach to each of these components is described below.

**Agitation**

LEO control measures should be rapidly supplemented with sedation in the setting of acutely agitated, combative patients displaying signs of ExDS. While the intravenous (IV) route is preferred if available, intramuscular (IM) or intranasal (IN) transmucosal administration of sedative agents may be needed initially in order to facilitate IV placement. Commonly used agents and their doses are listed in Table 5 and include benzodiazepines, antipsychotics, and the dissociative agent ketamine. Suggested doses are based upon consensus opinion. The actual effective dose of all suggested medications is unknown due to a paucity of research.

Because these agents have respiratory and cardiovascular effects, continuous monitoring of both should be performed as soon as feasible whenever parenteral sedation is administered. When appropriate safety systems are in place, one should be aware of manufacturers suggested dosing recommendations for other uses, but be prepared to use clinically effective doses for the management of this condition.
Benzodiazepines are familiar, commonly available sedative agents which can be administered by the IM or IV routes. Midazolam is also available and rapidly absorbed by the intranasal route, making it attractive for use in situations such as ExDS when rapid treatment is essential but IV access may not be available. Benzodiazepines are often preferred if stimulant drug overdose is suspected. Potential disadvantages include relatively slow onset and unpredictability of action if not given IV, the need for repeat doses in many cases to achieve adequate sedation, and the potential for respiratory suppression. Often benzodiazepine doses many times the traditional suggested dose for sedation are required, and there is likely no maximum dose limit for benzodiazepines when facilities for respiratory and blood pressure support are available.

Antipsychotic agents are commonly used for sedation of agitated psychiatric patients, and can be administered by the IV or IM route. There is some concern for potential rare cardiac conduction effects such as QT prolongation with all of these agents, which may result in ventricular dysrhythmias such as torsades de pointes. These concerns, combined with a preexisting risk for sudden death among ExDS patients, official “black box” warnings from the FDA regarding QT prolongation with haloperidol and droperidol, and a slower onset of action than benzodiazepines by the IV or IM route, have led some clinicians to avoid this class of agents in suspected ExDS. Others have noted the potential for anticholinergic effects producing hyperthermia, and a mechanism of action involving central neurotransmitter systems (which may be markedly abnormal in some patients presenting with ExDS) as reasons to consider other agents.

The dissociative agent ketamine can also be administered by the IV or IM route and appears advantageous due to very rapid onset (especially by the IM route when compared to other medications), and lack of significant respiratory and cardiovascular effects. Case reports have indicated excellent results and safety when used in ExDS patients. Potential disadvantages include rare side effects such as increased oral secretions, laryngospasm, hypertension, and distress from emergence phenomena.

In some circumstances, sedation and paralysis with rapid sequence intubation and respiratory support may be necessary to control agitation in patients with ExDS. In these cases, standard techniques and medications may be utilized at the clinician’s discretion.

Table 5. Sedation Agents for ExDS-type symptoms

<table>
<thead>
<tr>
<th>Class</th>
<th>Agent (Trade Name)</th>
<th>Available Routes</th>
<th>Dosing (mg)*</th>
<th>Onset (min)</th>
<th>Duration (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam (Versed)</td>
<td>IN</td>
<td>5</td>
<td>3-5</td>
<td>30-60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IM</td>
<td>5</td>
<td>10-15</td>
<td>120-360</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>2-5</td>
<td>3-5</td>
<td>30-60</td>
<td></td>
</tr>
<tr>
<td>Lorazepam (Ativan)</td>
<td>IM</td>
<td>4</td>
<td>15-30</td>
<td>60-120</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>2-4</td>
<td>2-5</td>
<td>60-120</td>
<td></td>
</tr>
<tr>
<td>Diazepam (Valium)</td>
<td>IM</td>
<td>10</td>
<td>15-30</td>
<td>15-60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>5-10</td>
<td>2-5</td>
<td>15-60</td>
<td></td>
</tr>
<tr>
<td>†Haloperidol (Haldol)</td>
<td>IM</td>
<td>10 – 20</td>
<td>15</td>
<td>180-360</td>
<td></td>
</tr>
<tr>
<td>†Droperidol (Inapine)</td>
<td>IM</td>
<td>5</td>
<td>20</td>
<td>120-240</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>2.5</td>
<td>10</td>
<td>120-240</td>
<td></td>
</tr>
<tr>
<td>Ziprasidone (Geodon)</td>
<td>IM</td>
<td>10 – 20</td>
<td>10</td>
<td>240</td>
<td></td>
</tr>
<tr>
<td>Olanzapine (Zyprexa)</td>
<td>IM</td>
<td>10</td>
<td>15-30</td>
<td>24 hrs</td>
<td></td>
</tr>
<tr>
<td>Ketamine (Ketaset, Ketalar)</td>
<td>IM</td>
<td>4-5 mg/kg</td>
<td>3-5</td>
<td>60-90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>2 mg/kg</td>
<td>1</td>
<td>20-30</td>
<td></td>
</tr>
</tbody>
</table>

IN: Intranasal; IM: Intramuscular; IV: Intravenous
* Typical adult dosing for severe agitation.
† The Food and Drug Administration has issued “Black Box” warnings regarding potential serious adverse effects (QT prolongation and torsades de pointes) with these agents. Clinicians should use their clinical judgment regarding the risk / benefit ratio on a case by case basis.
†† Though widely used in clinical practice, Haloperidol is not FDA approved for intravenous administration.
(For adequate control of ExDS, the above doses are conservative and describe a reasonable starting point. Clinical effect in ExDS may require doses greatly in excess of those for traditional medical use in other conditions).
**Hyperthermia**

Empiric treatment for hyperthermia may be initiated based on qualitative assessment (i.e. tactile hyperthermia) when needed, though core temperature measurement is preferred when available and practical. Basic cooling methods include removal of clothing and placement in a cool environment. Active external cooling may be initiated, with misting of water on exposed skin, providing air flow to enhance evaporative cooling, and placement of ice packs at the neck, axillae, and groin. Rapid cooling by infusion of cold saline IV has been shown to be effective in a number of other settings and can also be used. Care must be taken to avoid treatment “overshoot” leading to hypothermia.

Once the patient is stabilized in the ED or hospital setting, additional measures may be considered. In refractory or severe cases, immersion in cool water can rapidly reduce core body temperature, though this may present some difficulty with monitoring and treatment. A variety of external and internal temperature control devices are now available and may also be considered. If NMS or malignant hyperthermia is suspected, dantrolene may be indicated.

**Acidosis**

Metabolic acidosis and hypovolemia are thought to be common in ExDS. If suspected based on the clinical situation or physical exam, fluid resuscitation with intravenous fluids is prudent. In severe cases, sodium bicarbonate may be used either empirically or based on laboratory results revealing significant acidosis. Controversy exists regarding empiric use of sodium bicarbonate; the efficacy of supplemental sodium bicarbonate is unknown, and has not been supported as routine therapy for the metabolic acidosis of cardiac arrest. It is approved by some EMS agencies, but not by others (Table 6). Sodium bicarbonate may be administered by bolus injections or as a continuous infusion. Hyperventilation is the body’s normal compensatory mechanism for correcting acidosis. Control measures that might interfere with ventilation should be avoided.

**Other**

Other components of ExDS may include rhabdomyolysis and hyperkalemia. Rhabdomyolysis is initially managed by fluid administration and urine alkalinization with sodium bicarbonate. These interventions may have already been initiated empirically for other components of ExDS before laboratory results allow confirmation of rhabdomyolysis. Hyperkalemia may also be treated with traditional ACLS interventions based on characteristic EKG changes and laboratory results.

Many EMS systems already have protocols in place that incorporate these recommendations, allowing treatment of the clinical signs and symptoms of ExDS in the prehospital setting. While some agencies have adopted specific ExDS protocols, others place the interventions within traditional headings such as agitation and hyperthermia. Several prehospital protocols are summarized in Table 6.
### Table 6. Sample EMS Protocols for ExDS symptoms

<table>
<thead>
<tr>
<th>City, State</th>
<th>Sedation</th>
<th>Fluids</th>
<th>Hyperthermia</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miami, FL</td>
<td>Midazolam (Versed) 5mg IN</td>
<td>Normal Saline 1 liter bolus IV</td>
<td>Cold (&lt;60°F) IV fluid Cold packs</td>
<td>Sodium Bicarb. 1 amp (50 mEq) per liter of Normal Saline</td>
</tr>
<tr>
<td></td>
<td>[max 20mg]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nashville, TN</td>
<td>Midazolam (Versed) 2mg IV or</td>
<td>Normal Saline @ 500 cc/hr IV</td>
<td>Evaporative Cooling Cold packs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5mg IM [may repeat]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clark County (Las Vegas), NV</td>
<td>Midazolam (Versed) 2mg IV or 5mg IM / IN [may repeat]</td>
<td>Normal Saline</td>
<td>Evaporative Cooling Cold packs</td>
<td></td>
</tr>
<tr>
<td>Columbus, OH</td>
<td>Midazolam (Versed) 2-5mg IN, IV, pr [max 10 mg]</td>
<td>Normal Saline 500cc over 20 min</td>
<td>Evaporative Cooling Cold packs</td>
<td>Sodium Bicarb. ¼ amp (25 mEq) per liter of Normal Saline</td>
</tr>
<tr>
<td>Minneapolis, MN</td>
<td>Ketamine 5 mg/kg IM or 2 mg/kg IV</td>
<td>Normal Saline up to 2 liter bolus IV</td>
<td>Evaporative Cooling Cold packs</td>
<td>Sodium Bicarb. 2 amps (100 mEq) IV push</td>
</tr>
<tr>
<td>Rochester, MN</td>
<td>Lorazepam (Ativan) 1-4 mg IV/IM or midazolam (Versed) 1-5 mg IV/IM</td>
<td>Normal Saline</td>
<td>Evaporative Cooling Cold Packs</td>
<td>Sodium Bicarbonate 1mEq/kg IV push in cardiac arrest</td>
</tr>
</tbody>
</table>

IV: Intravenous; IM: Intramuscular; IN: Intranasal; pr: per rectum; Normal Saline: 0.9% Sodium Chloride

### LIMITATIONS OF CURRENT KNOWLEDGE AND RECOMMENDATIONS FOR FUTURE RESEARCH

The primary issues surrounding identifying and studying ExDS and subsequent therapeutic interventions are the lack of well-defined, consistent epidemiological case definition and overlap with other established diseases.

In those cases where a death occurs while in custody, there is the additional difficulty of separating any potential contribution of control measures from the underlying pathology. For example, was death due to the police control tool, or to positional asphyxiation, or from ExDS, or from interplay of all these factors? Even in the situation where all caregivers agree that a patient is in an active delirious state, there is no proof of the most safe and effective control measure or therapy for what is most likely an extremely agitated patient. However, the existence of multiple EMS protocols as well as expert consensus suggests that there are practical and agreed-upon methods of therapy that are believed to lower morbidity or mortality. Sedative or dissociative agents such as benzodiazepines, major tranquilizers, and ketamine are suggested but there is no evidence yet to prove that these will result in a lower morbidity or mortality.

Future research should focus on several areas. Animal models should be developed to begin to better understand the pathophysiology of ExDS.

In humans, a consistent case definition should be developed and applied in a large epidemiologic prospective study or from a national or international database of all suspected cases, including those who survive. At a molecular level, and based upon post-mortem cocaine-associated ExDS brain tissue, a Genome Wide Association Scan may be performed to identify susceptibility genes.

Development of a national orphan case report registry is recommended. This registry would be important in beginning to define the course of ExDS, and might eventually provide for earlier recognition of individuals at risk. It would also allow the scientific community to begin the process of identifying common characteristics on a large scale as well as comparing therapies. Without including suspected cases and survivors, no meaningful conclusions can be reached that would allow the development of case definitions, etiologies, and treatments.

Studies should address the role of law enforcement control techniques and devices in the death of sub-
jacts with ExDS. Finally, research is needed to es-
tablish field protocols and techniques that allow
police, EMS and hospital personnel to interact with
these agitated, aggressive patients in a manner safe
both for the patients and the providers.

SUMMARY

Based upon available evidence, it is the consensus
of the Task Force that ExDS is a real syndrome of
uncertain etiology. It is characterized by delirium,
agitation, and hyperadrenergic autonomic dysfunc-
tion, typically in the setting of acute on chronic drug
abuse or serious mental illness.

Research suggests the pathophysiology may include
genetic susceptibility and chronic stimulant-induced
abnormalities of dopamine transporter pathways,
along with elevation of heat shock proteins in fatal
cases. There is insufficient data at this time to de-
terminate whether fatal ExDS is preventable, or
whether there is a point of no return after which
the patient will die regardless of advanced life sup-
port interventions.

The risk of death is likely increased with physiologic
stress. Attempts to minimize such stress are needed
in the management of these patients. Ideally, any
necessary law enforcement control measures
should be combined with immediate sedative medi-
cal intervention to attempt to reduce the risk of
death.

There are well-documented cases of ExDS deaths
with minimal restraint such as handcuffs without
ECD use. This underscores that this is a potentially
fatal syndrome in and of itself, sometimes reversible
when expert medical treatment is immediately
available.

For research and diagnostic purposes, thorough do-
cumentation of the patient’s signs and symptoms
along with appropriate testing should occur. This
includes the presence of sweating or muscle rigidi-
ty, temperature, pulse, respiratory rate, blood pres-
sure, venous blood gases, urine and serum toxicolo-
gy, thyroid functions, and blood and (if fatal) ana-
tomic brain specimens for genetic, heat shock pro-
teins, and neurochemical analyses.

The ante-mortem diagnosis in the prehospital or
emergency department setting depends upon clin-
ical characteristics and the exclusion of alternative
disease processes. It is our consensus that rapid and
appropriate but limited control measures, and im-
mediate administration of IV benzodiazepines or
ketamine, IM ketamine, or intranasal midazolam,
can be lifesaving.
EXCITED DELIRIUM TASK FORCE

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Excited Delirium

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Excited (or agitated) delirium is characterized by agitation, aggression, acute distress and sudden death, often in the pre-hospital care setting. It is typically associated with the use of drugs that alter dopamine processing, hyperthermia, and, most notably, sometimes with death of the affected person in the custody of law enforcement. Subjects typically die from cardiopulmonary arrest, although the cause is debated. Unfortunately an adequate treatment plan has yet to be established, in part due to the fact that most patients die before hospital arrival. While there is still much to be discovered about the pathophysiology and treatment, it is hoped that this extensive review will provide both police and medical personnel with the information necessary to recognize and respond appropriately to excited delirium. [West J Emerg Med. 2011;12(1):77-83.]

INTRODUCTION

Excited delirium (EXD), first described in the mid 1800’s, has been referred to by many other names – Bell’s mania, lethal catatonia, acute exhaustive mania and agitated delirium. Regardless of the label used, all accounts describe almost the exact same sequence of events: delirium with agitation (fear, panic, shouting, violence and hyperactivity), sudden cessation of struggle, respiratory arrest and death. In the majority of cases unexpected strength and signs of hyperthermia are described as well. While the incidence of EXD is not known, the purpose of this review is to identify what is known or suspected about the pathophysiology, outcomes and management options associated with EXD to assist medical professionals in the future.

Issues Regarding EXD

EXD has gained increasing public attention recently due to the number of post-mortem explanations offered by medical examiners regarding the death of individuals being restrained by police or being taken into custody. This diagnosis has caused concern because EXD is not a currently recognized medical or psychiatric diagnosis according to either the Diagnostic and Statistical Manual of Mental Disorders (DSM-IVTR) of the American Psychiatric Association or the International Classification of Diseases (ICD-9) of the World Health Organization. Likewise, the authors of one review article found enough evidence in the literature to suggest that excited delirium, rhabdomyolysis and neuroleptic malignant syndrome might represent the clinical spectrum of a single disease. Although more research is needed to elucidate cause and effect, it is important to note that a lack of recognition of the condition in the context of law enforcement activities does not negate the significance of the behavioral and physical signs referred to as EXD. For instance, one important study found that only 18 of 214 individuals identified as having EXD died while being restrained or taken into custody. If anything, the possible association with other life-threatening syndromes only gives impetus to the need for critical emergency medical intervention when encountering a person thought to be in a state of excited delirium.

Background

Although reports of patients with similar symptoms first appeared in the 19th century, the first modern mention of EXD was in 1985. The presentation of excited delirium occurs with a sudden onset, with symptoms of bizarre and/or aggressive behavior, shouting, paranoia, panic, violence toward others, unexpected physical strength and hyperthermia. An extensive review of reported case series reveals that in a majority of cases EXD was precipitated by stimulant drug use and in much fewer cases psychiatric illness (such as mania, depression, or schizophrenia) or systemic illness.
Methamphetamine, PCP and LSD have been reported in a few series, but by far the most prevalent drug of abuse found on toxicology screening was cocaine.\textsuperscript{19} Since the victims frequently die while being restrained or in the custody of law enforcement, there has been speculation over the years of police brutality being the underlying cause. However, it is important to note that the vast majority of deaths occur suddenly prior to capture, in the emergency department (ED), or unattended at home.

Prior to 1985 most reported cases of sudden death from cocaine intoxication involved “body stuffers” who died secondary to massively high exposure to the drug after packets they were carrying burst. A report published by Wetli and Fishbain \textsuperscript{3} in 1985 was one of the first case series to examine recreational cocaine users who died following episodes of excited delirium. They noticed that these deaths differed in both presentation and average blood cocaine concentrations from typical cocaine overdose fatalities. In fact, cases of agitated delirium were often associated with lower blood levels of cocaine. Explorations by Pollanen et al\textsuperscript{10} and Ruttenber et al\textsuperscript{11} showed blood levels of cocaine in EXD cases to be similar to levels found in recreational cocaine users and much lower than levels found in people who died from cocaine associated intoxication. Moreover, the reports found that the blood levels of benzoylecgonine, the primary metabolite of cocaine, in the cocaine-associated EXD cases were higher than in recreational users, suggesting the cocaine use prior to death was consistent with recent “binge” use. More recently, Stephens et al.,\textsuperscript{12} in an analysis of the significance of cocaine upon a specific death, confirmed that a pattern of chronic cocaine use characterized by repeated binges is associated with the development of fatal EXD.

**PATHOPHYSIOLOGY**

Cocaine has many neurotransmitter affects on the brain, including the blockade of all monamine neurotransmitters via its interaction with the various transporters. The reinforcing or addictive properties of cocaine are primarily attributed to increased dopamine levels. Dopamine is an essential neurotransmitter in several neural pathways regulating movement, hypothalamic function, positive behavioral reinforcement and higher cognitive function. The mesolimbic pathway, which connects the nucleus accumbens and tegmentum, is most critical for reinforcement and addiction to psycho-stimulants. Several researchers have suggested that cocaine use may cause aberrant dopamine processing in the mesolimbic pathway and elsewhere in the brain, resulting in hyperactivity and hyperthermia.\textsuperscript{13,14} Additionally, in cases of EXD, dopamine processing has been shown to be further altered compared to non-psychotic cocaine users. Recent research has identified several possible explanations for this critical difference.

First, Mash et al\textsuperscript{14} discovered evidence of increased alpha α-synuclein, a native protein and major component of Lewy bodies in Parkinson’s disease, in midbrain dopamine neurons of chronic non-psychotic cocaine users.\textsuperscript{2} In vivo, increased binding of α-synuclein to dopamine transporters has been shown to increase dopamine uptake and dopamine mediated apoptosis, leading to irreversible neuroadaptive changes. The authors suggested that the increased α-synuclein deposition might occur as a protective response due to high dopamine recycling and oxidative stress from cocaine abuse. Their postmortem research demonstrated that chronic non-psychotic cocaine users, compared to control non-drug users, had markedly elevated presynaptic α-synuclein levels in the substantia nigra and ventral tegmental area of the midbrain. However, compared to the same control group, victims of fatal EXD showed decreased levels of α-synuclein in the substantia nigra and only slightly increased levels in the ventral tegmental area. This discovery suggests that EXD victims might have a different pattern of α-synuclein regulation and perhaps lack normal compensatory measures for dealing with rapidly elevating dopamine levels.

Second, multiple studies have documented dopamine transporter binding sites that are increased in human chronic cocaine users.\textsuperscript{15-17} Mash et al\textsuperscript{18} used in vitro autoradiography and ligand binding studies to map and measure D3 dopamine and kappa 2 opioid receptors in brain tissue from postmortem cocaine overdose victims and compared them to fatal EXD victims. The D3 receptor subtype has a distinctive neuroanatomy pattern in the normal human brain, with high densities in areas associated with the pattern-building, euphoric effects of cocaine, such as, the nucleus accumbens and limbic sectors of caudate and putamen. The authors found that chronic cocaine abuse lead to an adaptive elevation of D3 dopamine receptors (2-3 times vs. control) and kappa 2 opioid receptors (2 times vs. control) in the nucleus accumbens and associated limbic regions. By contrast, cocaine abusing EXD victims did not demonstrate increased density for D3 receptor binding. This finding mirrored similar results by Staley et al\textsuperscript{19} that failed to demonstrate an elevation in dopamine transporters in the striatum of EXD victims versus aged-matched drug-free control patients. Mash et al\textsuperscript{18} suggested that the lack of compensatory changes in the EXD victims could be related to concurrent psychiatric co-morbidity, recent “binge” cocaine use, or aberrant molecular processing of D3 receptor mRNA. Interestingly, different mRNA species have been found in the cerebral cortices of chronic schizophrenia patients, which raise the possibility that similar alterations in D3 receptor processing could be involved in EXD victims.\textsuperscript{20}

Third, further investigation by Mash et al\textsuperscript{22} focused on the functional activity of dopamine transporters, which were previously found to be elevated in the limbic system of chronic cocaine abusers.\textsuperscript{18,21} Using cryopreserved tissue samples from aged-matched chronic cocaine users (n=10), EXD victims (n=8) and control subjects (n=10), the authors quantified the number of dopamine transporters in parallel to dopamine uptake and discovered dopamine uptake was
twofold in the ventral striatum from chronic cocaine users versus aged-matched controls. Victims of fatal EXD failed to demonstrate an increase in dopamine transport function, despite having a history of cocaine use and post-mortem blood elevations of cocaine and benzoylecgonine. Based on the results, chronic cocaine use seems to cause a compensatory increase in dopamine transporters, which would decrease the amount of dopamine available to potentially over stimulate the post-synaptic receptors. This effect, which may be neuron protective, is lacking in fatal EXD victims.

In addition to altering dopamine reuptake directly, cocaine has been shown to potently inhibit serotonin reuptake, thus elevating synaptic levels of the neurotransmitter. Despite the relative certainty that dopamine is the primary substrate mediating the reinforcing and addictive properties of cocaine, a study by Rocha et al. of dopamine transporter knockout mice suggests the involvement of serotonergic brain regions in the initiation and maintenance of cocaine self-administration and withdrawal symptoms. Meanwhile, serotonin has been implicated as an independent modulator of dopaminergic neurotransmission. Mash et al. compared serotonin transporter density in brain tissue from cocaine overdose victims and cocaine-associated EXD victims, finding that the transporters localized to the dopamine rich substantia nigra and striatum in response to chronic cocaine use. Once again, EXD victims failed to display an up regulation of serotonin transporters within aforementioned brain regions.

Lastly, in a 2009 case series of an unprecedented ninety fatal EXD victims, Mash et al. conducted a post-mortem quantitative analysis of dopamine transporters and heat shock protein 70. Incident circumstances, force measures, autopsy and toxicology results were determined and controlled in the analysis. Mean core body temperature among the ninety victims was 40.7°Celsius and, although the majority tested positive for cocaine, four had no licit or illicit drugs or alcohol found at autopsy. The authors discovered heat shock proteins were elevated 1.8-4 fold in postmortem brain tissue, confirming that hyperthermia is an associated symptom and indication of fatal autonomic dysfunction in the victims. In addition, dopamine transporter levels were decreased compared to age-matched controls, which correlate with the findings by previous authors of aberrant dopamine signaling in EXD.

These observations demonstrate that cocaine affects a number of different neurochemical substrates in the brain and suggest that chronic exposure may lead to complex neuroadaptations within discrete brain loci. Furthermore, compared to non-psychotic cocaine overdose victims, fatal EXD victims have been shown to possess alterations in neuroanatomy and neurophysiology that may represent a subtype of patient with an altogether unusual genotype and/or phenotype; one characterized by high dopamine levels and a hyperactive autonomic nervous system. This understanding may lead to changes in the recognition, handling and acute treatment of EXD by first responders and emergency physicians.

OUTCOMES

Approximately two thirds of EXD victims die at the scene or during transport by paramedics or police. Victims who do not immediately come to police attention are often found dead in the bathroom surrounded by wet towels and/or clothing and empty ice trays, apparently succumbing during failed attempts to rapidly cool down. It appears that in all cases, victims died of either respiratory arrest or fatal cardiac dysrrhythmia. Diagnoses were supported by postmortem exams showing pulmonary and cerebral edema with nonlethal self-inflicted injuries. The few who live long enough to be hospitalized often succumb to disseminated intravascular coagulation, rhabdomyolysis and renal failure. These fatal cardiopulmonary changes are thought to be the result of increased catecholamine stress on the heart, myocardial hypertrophy, microangiopathy and fatal arrhythmias. The proposed cause of these changes is debated.

Since the victims sometimes die in police custody, the most widely publicized proposed causes of death in EXD are asphyxia and positional asphyxia. No study thus far has been able to demonstrate a causal relationship between Taser use and subsequent individuals’ deaths. In one study of 32 healthy police volunteers, a 12-lead electrocardiogram was performed at baseline and then repeated within 60 seconds post-exposure to a one to five second shock by the Taser X26. The authors reported no instances of dysrhythmia nor ectopy among the subjects. Furthermore, no statistically significant changes were noted in the QRS duration, QT and QTc intervals. These results corroborate with previous reports using single-lead monitoring to assess cardiac changes before, during, and after Taser activation.

As mentioned before, people experiencing EXD are highly agitated, violent, and show signs of unexpected strength so it is not surprising that most require physical restraint. The prone maximal restraint position (PRMP, also known as “hobble” or “hottie”), where the person’s ankles and wrists are bound together behind their back, has been used extensively by field personnel. In far fewer cases, persons have been tied to a hospital gurney or manually held prone with knee pressure on the back or neck. Supporters of the positional asphyxia hypothesis postulate that an anoxic death results from the combination of increased oxygen demand with a failure to maintain a patent airway and/or inhibition of chest wall and diaphragmatic movement. This explanation has been further supported by coroners’ reports of “positional asphyxia” as the cause of death in multiple fatal EXD cases.

The positional asphyxia theory has been refuted by a series of articles by Chan et al. exploring the effect of PRMP on ventilatory capacity and arterial blood gases. In one study of fifteen healthy male volunteers, the authors found a small, but statistically significant decline in forced vital capacity.
Excited Delirium

(FVC), forced expiratory volume in one second (FEV1) and maximal minute ventilation (MVV) comparing sitting to restrained positions. However, there was no evidence of hypoxia (mean oxygen tension [PO2] less than 95 mmHg or co-oximetry less than 96%) in either position, nor was there a significant difference in PCO2, heart rate recovery or oxygen saturation. In another study, the authors sought to determine the effect of adding 25 and 50 pounds weight force on respiratory function of healthy volunteers in the PRMP.33 Validating earlier results, they found FVC/FEV1 was significantly lower in restrained positions versus sitting, but not significantly different between restrained positions with and without weight force. Furthermore, they found mean oxygen saturation levels were above 95% and mean end-tidal CO2 levels were below 45 mmHg for all positions, regardless of weight force. Based on these findings, PMRP may result in a transient pattern of restricted pulmonary function, but the lack of evidence for hypoxia or hypoventilation suggests that factors other than body positioning appear to be more important determinants for sudden, unexpected death. Nonetheless, respiratory muscle fatigue resulting from exertion and struggle against restraints (exertion vs. position asphyxia) cannot be excluded nor can potentially fatal pre-existing problems with central cardiac output, oxygen saturation, or oxygen use.6,20,28,34

Another potential cause of death is cardio toxicity due to chronic cocaine abuse. Preexisting coronary artery disease appears to account for many of the deaths, as does the contribution of cocaine acting as a potent adrenergic agonist, but the mechanism is likely more complex.27 A larger case series published in 2006 noted that more than half of EXD fatalities were found to have some degree of cardiovascular disease.28 Since the majority of deaths occur after prolonged drug use, it is thought that cocaine initiates a series of detrimental changes to the heart that might take years to express. These changes may be due to long-term catecholamine toxicity and include cardiac hypertrophy, microangiopathy and myocardial fibrosis.35 Electrocardiographic and autopsy studies confirm that the heart weight of cocaine users, is, on average, ten percent greater than expected values.36,37 It is not clear how cocaine initiates the process of hypertrophy, but it could be due to the direct oxidant effect of cocaine or cocaine-induced hypertension. Either way, research using rats injected with cocaine demonstrated increases in levels of mRNA coding for atrial naturetic factor, collagen and alpha/beta myosin.38

Small intramyocardial arteries are often thickened in cocaine users. It is hypothesized that cocaine-induced apoptosis damages the muscular layer of the small vessels or that the damage is once again due to the direct oxidant effect of cocaine.39 The smaller artery lumen may lead to a mismatch in blood flow supply-demand, and ultimately under perfusion whereby the myocardium is not receiving enough blood and becomes ischemic. Lastly, cocaine users’ hearts often resemble those of patients with heart failure secondary to pheochromocytoma. The high levels of catecholamine, particularly norepinephrine, seem to induce a diffuse pattern of discrete fibrotic lesions, which tend to favor reentry and the induction of arrhythmias.40 Hypertrophied hearts with diffuse fibrosis and microangiopathy utilize oxygen less efficiently and are more likely to have disordered electrical conduction. During times of increased stress, the myocardium becomes ischemic and should have a lower threshold for fibrillation. Unfortunately, few case series have been able to publish the initial cardiac rhythms found at the scene of cocaine-associated EXD fatalities. One report documents 18 fatal EXD cases with 13 primary cardiac rhythms confirmed by emergency personnel.4 Only one victim was confirmed to have ventricular tachycardia and none were found to have ventricular fibrillation. If primary arrest was strongly associated with sudden death in excited delirium, it would be expected that more victims would have presented with the above-mentioned abnormal rhythms. However, this case series was limited because the exact time delays in determining initial cardiac rhythms on arrival of emergency medical services to the scene was not available; thus, it is impossible to calculate how many of the patients might have progressed from ventricular tachycardia/fibrillation to asystole. Nevertheless, the molecular, cellular and anatomic alterations induced by chronic higher-dose cocaine use might explain why very low cocaine levels can be lethal in EXD victims.

MANAGEMENT

While our understanding of EXD is expanding, the disorder still presents significant challenges to emergency first responders and physicians. Recent research has demonstrated unique cellular and neurochemical alterations in EXD victims, leading to dopamine excess and autonomic hyperactivity. EXD victims display extreme agitation, aggression, unexpected physical strength and florid psychosis. Emergency physicians must recognize the danger posed by these patients and should act in an expeditious and aggressive manner to avoid medical complications including metabolic acidosis, rhabdomyolysis, hyperthermia, multisystem failure and/or death. To address these clinical findings, we propose a treatment protocol that includes rapid sedation, followed closely by external cooling, intravenous (IV) fluids, monitoring, and treatment of potential medical complications.

Given the violent and unpredictable nature of EXD victims, rapid sedation is likely essential to positive outcomes. Furthermore, if autonomic hyperactivity and aberrant dopamine processing is to blame for the clinical presentation of EXD, then the ideal drug(s) needs to “turn off” the catecholamine cascade and rapidly sedate the patient. Several types of drugs could fulfill these requirements. Neuroleptics, benzodiazepines, or both in combination are commonly used in the management of agitated patients; however, to date, there
are no published double-blind, randomized, placebo-controlled trials to confirm the efficacy and safety of antipsychotic medications to manage acute delirium.\textsuperscript{41} One study of 111 violent and agitated patients by Nobay et al\textsuperscript{42} compared efficacy and side effect profiles of intramuscular (IM) midazolam (5mg), lorazepam (2mg) and haloperidol (5mg) randomly assigned to the study participants. They concluded that midazolam had a significantly shorter onset (18.3 +/- 14 minutes) and more rapid time to arousal. Several studies found a significant advantage in combining two or more drugs to achieve maximal sedation. For instance, Battaglia et al\textsuperscript{43} and Bieniek et al\textsuperscript{44} documented superior efficacy and similar side effect profile for a combination haloperidol and lorazepam versus either drug alone.

Despite the proven efficacy and safety record of neuroleptics and benzodiazepines, they require at least 10-15 minutes for sedation. EXD victims may not have minutes to spare as they continue to struggle against law enforcement or physical restraints in a state of hyperthermia and metabolic acidosis. With the particulars of EXD in mind, we propose intramuscular ketamine as an alternative sedating agent worthy of consideration. It is a drug that can be administered IM (4-5 mg/kg/dose; onset of action: 3-4 minutes) or IV (1-2 mg/kg/dose; onset of action: 30 seconds), does not require endotracheal intubation, and reliably produces rapid analgesia, sedation, and amnesia via direct action on the cortex and limbic system. The use of ketamine for procedural sedation in the pediatric ED and rural operating rooms is popular and has a proven record of efficacy and safety.\textsuperscript{45} With 25 years surgical experience in the South Pacific, Reich et al\textsuperscript{46} documented that ketamine was effectively used to sedate 866 unmonitored patients without serious complications.

Adult data on ketamine use in the ED is sparse, but one recent literature review by Strayer et al\textsuperscript{47} attempted to determine ketamine’s adverse effect profile when used for procedural sedation. The analysis revealed that IM ketamine reliably produced adequate sedation to facilitate painful procedures with few side effects. Emergence phenomenon was documented in 10-20% of patients; but if ketamine was administered with a rapidly metabolized benzodiazepine (i.e. midazolam), then the effects were reduced significantly. In a unique retrospective study of 11 combative trauma patients, Melamed et al\textsuperscript{48} found that sedation with ketamine, with or without midazolam, was effective in all cases. Ketamine was administered intravenously for sedation by prehospital providers during an average transport time of 114 minutes. Although this report is based on a very small sample size, the authors reported no adverse events and suggest that ketamine might be an ideal intervention for the combative patient.

Although concerns about ketamine causing increased intracranial pressure and/or laryngospasm and subsequent airway obstruction have lessened, the agitated EXD victim represents a unique patient group for future analysis of the drug.\textsuperscript{49} Furthermore, if a catecholamine surge is at least partially responsible for the medical and psychiatric symptoms of EXD victims, then ketamine might actually exacerbate the underlying problem by acting as a mild stimulant of the cardiovascular system.\textsuperscript{46} Therefore, ketamine’s most lauded characteristic of having no cardiovascular, respiratory or airway protective reflex depression, might also be cause for concern. One could imagine a scenario in which ketamine’s rapid and superior sedation might lure the emergency physician into a false sense of security while the EXD patient is quietly decompensating. Perhaps the potential cardiovascular stimulation could be averted by using a β-adrenoreceptor blocker immediately after sedation with ketamine, as suggested by the results of a recent in vitro study using human atrial myocardium.\textsuperscript{50} Despite the promise of ketamine, more structured research is needed to establish its safety and efficacy for emergent sedation of the agitated patient.

In addition to adequate sedation, several protective measures must be taken to increase the chances of survival in persons presenting with EXD. Proper management should arrest the catecholamine cascade quickly. Medical evaluation should begin promptly and include basic monitoring (IV access, pulse oximetry and oxygen), radiographs, blood tests and a focused physical exam. As mentioned previously, EXD victims present with autonomic hyperactivity, which often leads to metabolic acidosis, hyperthermia, and rhabdomyolysis. This clinical picture is similar enough to that of malignant hyperthermia (MH) and neuroleptic malignant syndrome (NMS) that dantrolene could be considered as another useful adjunctive therapy. One informative case report described a 25 year old patient with cocaine-excited delirium and severe acidosis who was treated with hyperventilation, passive cooling, sodium bicarbonate and dantrolene.\textsuperscript{51} This intervention lead to a swift correction of the acidosis and the patient survived. Dantrolene is a hydantoin derivative that abolishes excitation-contraction coupling of muscle cells by blocking calcium release from intracellular storage in the sarcoplasmic reticulum. It has been used successfully for years by anesthesiologists to treat MH and NMS; however, its use in emergent situations is limited by poor water solubility and difficulties in rapidly preparing a suitable solution for IV administration.\textsuperscript{52,53}

CONCLUSION

EXD is a unique medical issue characterized by the acute onset of agitation, aggression, distress, and possibly sudden death. While the contribution of restraint, struggle and the use of electrical conduction devices to the cause of death raises controversy, recent research points toward central nervous system dysfunction of dopamine signaling as a cause of the delirium and fatal autonomic dysfunction. Victims of EXD usually die from cardiopulmonary arrest, although the exact cause of such arrest is likely multifactorial and chronic. Unfortunately, an adequate treatment plan has yet
to be established, although rapid sedation, followed closely by external cooling, IV fluids, monitoring, and treatment of potential medical complications is likely critical to decrease morbidity and mortality. Neuroleptics, benzodiazepines and ketamine are among the potent sedating agents that have been proposed to stabilize EXD victims. While there is still much to be discovered about the pathophysiology and treatment, it is hoped that this extensive review will provide both police and medical personnel with the information necessary to recognize and appropriately respond to EXD.

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Failed Takeover Spawns Federal Inquiry

By Ruth SoRelle, MPH

A failed hostile takeover and a lawsuit filed with it spotlight the ambiguities that exist between admission to an inpatient unit and admission to an observation unit, a topic of particular interest to emergency physicians. All this occurs at a time when the federal Centers for Medicare & Medicaid Services are scrutinizing inpatient admissions to determine whether they should have been classified as observations instead.

As one federal official admitted, “This is a complicated issue.” It is so thorny, in fact, that CMS has published a pamphlet titled: “Are You a Hospital Inpatient or Outpatient? If You Have Medicare – Ask!” The cost of treating patients in inpatient units is usually much higher than those in observation units, and that is at the heart of the dispute between two hospital systems.

The facts in the failed hostile takeover of Dallas-based Tenet Healthcare by Community Health Systems, Inc., of Franklin, TN, are made even more knotty by the fact that company officials are constrained in what they can say by the pending litigation, and federal officials cannot comment on ongoing investigations. But the effects of the lawsuit may affect hospitals across the country, something Community Health Systems (CHS) noted in a first quarter earnings call in April: “We believe that Tenet’s lawsuit against CHS in this proxy contest has negatively affected the entire health care sector.”

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Failed Takeover Spawns Federal Inquiry

Special Report

Waiting for the Deluge

Health care reform, experts say, will bring emergency departments a short-term flood but long-term change.

By Anne Scheck

It was brief — only a few lines of text — but the plea for more research on Excited Delirium Syndrome (ExDS) obviously was written by a grieving family member, and that’s probably why it made headlines in a British newspaper this past summer.

“We fully recognize that drug toxicity played a key role in Jason’s death,” wrote the deceased’s uncle after a coroner’s report attributed the fatality to cardiac arrest in police custody. So, he asked, shouldn’t his nephew’s lost life put more focus on the “potential of this condition” to help prevent future tragedies? (http://bit.ly/p0dTGZ.)

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care is essential to saving lives from ExDS, and “many cases of fatality probably could be prevented with treatment,” said Mark DeBard, MD, an emergency physician who served on the task force instrumental in ExDS’ acceptance as a distinct syndrome two years ago from the American College of Emergency Physicians. (EMN 2009;31[11]:4; http://bit.ly/ory9ec)

Following that acceptance, the task force worked to define the condition, looking at its epidemiology, pathophysiology, and clinical characteristics. That consensus paper, to be published in an upcoming issue of the Journal of Emergency Medicine, concludes that ExDS has uncertain but multiple etiologies, but is characterized by delirium, agitation, acidosis, and hyperadrenergic autonomic dysfunction. The group, led by Gary Vilke, MD, and Dr. DeBard, said the risk of death is likely increased with physiologic stress, and called for immediate sedation to reduce the chance of death.

Research so far has shown that most of those who die are noncompliant and exhibit severe aggression. (Ann J Forensic Med Pathol 2009;30[1]:23.) And a stressful encounter increases the chemical imbalance in the brain that is characteristic of ExDS. The hyper-responsive neurotransmitter system aggravates an already acidoic state, which can progress rapidly and fatally, explained Dr. DeBard, a clinical professor of emergency medicine at Ohio State University in Columbus.

Because certain drug use and physical resistance to intervention are signs of ExDS, restraint by TASER is more frequently used by law enforcement. But this year, after ExDS was pronounced the cause of death for a Connecticut man following a reported 34 stuns by police, lawmakers there drafted a bill that will mandate a study on the use of such electronic jolts (SB 6615), in part to answer the question: Does the way these devices are employed affect outcome? (The Hartford Courant May 3, 2011; http://bit.ly/mPsjqa.)

Previous studies have, in fact, found that less injury occurs among police departments with policies that place TASER use alongside deadly force. (Law & Order 2008;56[3]:50.)

Only a few years ago, “positional asphyxiation” was the claim often made when suspected criminals died after being placed in restraints. “We refuted that,” said Gary Vilke, MD, a professor of clinical medicine at the University of California, San Diego, and the director of clinical research in emergency medicine at UCSD Medical Center. In fact, the circumstances of such arrests often included hallmarks of ExDS — profound sweating, high body temperature, delusional behavior, but such symptoms were not taken into account until the syndrome was actually studied.

“We asked: ‘Well, if that is not what is killing them, what is?’ The answer, said Dr. Vilke, turned out to be a delirium first described in psychiatric patients around the late 1800s, but which all but disappeared from medical journals by the 1950s following the utilization of antipsychotic medication. Thirty years later, it was rediscovered in individuals using cocaine, among other stimulants.

Police departments that learn to recognize the signs, that have a protocol in place for managing it, and that institute a training program for officers are helping to reduce risk, said Dr. DeBard, adding: “I’m concerned that it [diagnosis of ExDS] be used appropriately.” In a metropolitan city of a million people, there probably should be only one to three cases of ExDS annually, he said. “There needs to be an understanding of the difference between bad behavior, drunken behavior, and excited delirium,” Dr. DeBard said.

An increase in deaths linked to ExDS has been occurring “as TASER use seems to be raising questions about such fatalities, particularly with the American Civil Liberties Union. A few months ago, the ACLU published an investigative survey on TASER use by 20 Arizona law enforcement agencies. One conclusion: Though dispersive an electrical charge is largely regarded as an alternative to lethal force, it may be applied in situations in which compliance can be achieved in other ways.

And, in an opinion similarly expressed by Dr. DeBard, the ACLU called on law enforcement agencies to “make sure that officers have enough training and preparation to deal with intoxicated or emotionally disturbed individuals, so that they are able to de-escalate a situation without resorting to force.” (A Force To Be Reckoned With, ACLU of Arizona, 2011; http://bit.ly/nI1pjk.)

A previous ACLU examination of the issue, which looked at cases in California, found that deaths in custody had increased along with the utilization of allegedly nonlethal electronic weapon. (Stun Gun Fallacy: How the Lack of TASER Regulation Endangers Lives, ACLU of Northern California, 2005; http://bit.ly/ghlth.)

The idea that there is physical risk imposed by TASER use isn’t the sole source of the debate; one suggestion is that it might contribute to ExDS death. But is there more risk from the TASER than from the syndrome itself? Not likely, said Michael Wilson, PhD, MD, a clinical research fellow of emergency medicine at UCSF. The very act of resisting custody exacerbates the life-threatening cardiac stress, he explained. “These are people who might walk — even run — right into traffic,” he said.

“It is important to note that some people, even those who haven’t been TASERed, die unexpectedly while in custody,” said David Murphy, PhD, an associate professor of criminal justice at Western Oregon University, who has studied restraint alternatives and consulted on them with police. “TASER use is by no means the only type of law enforcement response with the potential to cause or exacerbate symptoms of excited delirium,” he said.

Cuffing the individual with hands behind the back or forcing a suspect to the ground could also be dangerous. So could any force used to achieve compliance in a person at risk for death due to ExDS, he said.

There is reason to believe TASER use saves lives. About the same time as the ACLU published its results, the U.S. Department of Justice issued its own research findings on the issue, noting that the injury rates in two cities — Orlando, FL, and Austin, TX — had dropped substantially for suspects and police officers after the devices were adopted.

In a white paper published by the ACEP task force, the association between cocaine use and ExDS is emphasized, and so is the threat of dying at levels similar to those of death due to ExDS. So what is the “different mechanism of death” alluded to in the ACEP paper? And can that mechanism be adversely influenced by TASER?

Data from the U.S. Justice Department — the same data that found lower injury rates with TASER use — also indicate that when TASER injuries do occur, the application sometimes had been repetitive, and carried in ways such as pressing against flesh rather than release of a dart from a distance. (Police Use of Force, TASERS and Other Lethal Weapons, Research in Brief by the National Institute of Justice, 2011; http://us.gov/ojp/nij.)

TASER has an exceptional profile of safety, said Steve Tuttle, the vice president of communications for TASER International, Inc., in Scottsdale, AZ. News accounts about these electronic-control devices often fail to distinguish between the two ways in which they can be used: discharging an electrical stun directly in contact with a subject, an approach that causes pain but is unlikely to cause incapacitation, or by deploying probes that confer a low-level current that usually subdues the subject.

Adding to the potential for confusion, discussions of “firings” can be too general. “The number of deployments does not necessarily reflect the number of probes that have reached the intended target or the number of stuns. Even when the firings are successful, the electrical impact can be reduced or avoided by clothing,” Mr. Tuttle said.

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ACEP Recognizes Excited Delirium Syndrome

By Lisa Hoffman

The American College of Emergency Physicians formally recognized excited delirium as a unique syndrome on Sunday, taking an initial step toward identifying its causes and preventing the deaths that can occur in these patients.

Excited Delirium Syndrome (ExDS) has long been the sole purview of medical examiners, largely because the syndrome is often only diagnosed on autopsy. But as Mark L. DeBard, MD, the chairman of the ExDS Task Force, said, ACEP’s approval of the task force white paper allows emergency physicians not only to recognize the syndrome and save lives, but to force it into the consciousness of law enforcement and emergency medical services.

“I want emergency physicians around the country to know that most of the time they’re treating these cases successfully, but this allows the medical community to call it by name,” he said. “That’s the first step, and we need case reports to identify its characteristics.”

Patients with excited delirium are challenging to everyone involved in their care, often leaving police and health care providers struggling to control their aggressive behavior rather than treating their medical condition, one that could suddenly end in death. The task force members found themselves facing a dilemma much like the decades-long one over sudden infant death syndrome: Researchers and clinicians argued whether ExDS was even a syndrome, essentially because no clear definition or cause exists.

The exact pathophysiology remains unidentified, the task force noted in a white paper it presented to the ACEP Council and Board of Directors during this year’s Scientific Assembly. And although the syndrome is not always fatal, many patients experience cardiac arrest and death. About 250 patients die in the United States each year from ExDS, an estimated eight to 14 percent of those who experience the syndrome, said Dr. DeBard, a professor of emergency medicine at Ohio State University College of Medicine and a past ACEP speaker and board member.

The task force called for identifying those whose deaths might be averted with early intervention. And that starts with identifying the triad of conditions that are the hallmark of ExDS: delirium, psychomotor agitation, and physiological excitation.

A typical ExDS patient usually has acute drug intoxication, usually from cocaine, or less often has a serious history of mental illness on multiple medications. Because the syndrome is marked by aggressive and erratic behavior — being extremely combative and ripping off their clothes, for instance — the police often become involved and use physical or chemical control measures, sometimes a conducted electrical weapon (CEW). Mainstream media have often pointed to CEWs, commonly called TASERS, as the cause of these deaths while emergency physicians often think the syndrome is acute cocaine intoxication. But Dr. DeBard, also an attending at Ohio State University Hospital East, said

Potential Clinical Features of ExDS

- Pain tolerance
- Tachypnea
- Sweating
- Agitation
- Tactile hyperthermia
- Police noncompliance
- Lack of tiring
- Unusual strength
- Inappropriately clothed
something more is going on in these cases.

More than 95 percent of all published fatal cases were in men, with a mean age of 36. Besides being disoriented and hyperaggressive, patients tend to be impervious to pain, hyperthermic, and tachycardiac. In more than one million interactions with the public over two years, a yet-to-be-published Canadian study identified potential clinical features for ExDS. (See table.) Some 698 encounters involved the use of force, and of those, 24 probable cases of ExDS were identified. All of those patients also exhibited tolerance to pain and tachypnea, according to the white paper.

ExDS, the white paper task force noted, is poorly understood, and although they suspect stimulant drug abuse, psychiatric disease, psychiatric drug withdrawal, and metabolic disorders to be the underlying culprits, no one knows how those lead to ExDS or why some cases but not others end in death.

Postmortem brain examination suggests that the “loss of the dopamine transporter in the striatum of chronic cocaine abusers may cause excessive dopamine stimulation,” but the precipitants remain unclear, according to the white paper. “Making a central dopamine hypothesis more appealing is the fact that hypothalamic dopamine receptors are responsible for thermoregulation,” which may explain the hyperthermia in ExDS patients, the white paper noted. Autopsy also has revealed elevated levels of heat shock proteins.

A large component of treating patients is helping law enforcement and EMS recognize possible ExDS patients, starting with behavior reported in 9-1-1 calls. Prehospital ExDS should be presumed, the task force said, if a patient is disoriented or not making sense, constantly physically active, impervious to pain, has superhuman strength, is sweating and breathing rapidly, has tactile hyperthermia, and fails to respond to a police presence.

Many experts advocate chemical sedation as a first-line treatment, and the task force concurred, recommending immediate medical assessment and treatment once physical control is obtained. “Initial assessment should include...vital signs, cardiac monitoring, IV access, glucose measurement, pulse oximetry, supplement oxygen, and careful physical examination,” the white paper noted.

Dr. DeBard said his drug of choice is ketamine, which is far faster-acting than the benzodiazepines and antipsychotics usually used. “These drugs buy you time,” he said.

Behind the Story

EMN asked Dr. Mark DeBard what about ExDS excited him, if you’ll pardon the pun. He estimates that 250 people a year die from the syndrome, which in the overall scheme of things, doesn’t come close to those who die from coronary heart disease (almost half a million) or even the seasonal flu (36,000). So why ExDS? His answer: He saw a video of an ExDS patient on YouTube, and thought he could have saved the patient. Watch one case of many available online at http://www.youtube.com/watch?v=kckeEVAxsJM&feature=related.

Only in EMN

Read an editorial about the ACEP ExDS White Paper by Task Force Chairman Mark L. DeBard, MD, in the November issue of EMN.
ExDS Emergency Room Workup Suggestions

- Continuous pulse oximetry
- Continuous cardiac monitoring
- Initial vital signs including a rectal temperature
- VBG
- Serum Lactate
- CBC, CMP
- Total CK, CKMB, and Troponin
- EtOH
- TSH
- 10 drug urine, urine HCG
- EKG
- Portable chest x-ray
- Head CT without contrast

Suggested by Dr. William Weir, MD, Carle Hospital, Urbana, IL
Protocol: Excited Delirium:

**Signs and symptoms:** Sudden onset of the following signs: Extreme agitation and restlessness, aggressive/combative behavior, paranoia or delirium, incoherent and rambling speech, extraordinary strength, numbness to pain profuse sweating.

**This will be a three step protocol to be executed as follows:**

**Step 1.** Do not confront patient. Coordinate restraint of the patient with law enforcement using the minimal amount of force required to safely subdue the individual.

**Step 2.** Sedate patient with use of IM injection of Ketamine @ 4 mg/kg. May repeat 1 time at 2 mg/kg Ketamine; (Ketalar) Dosage form 50 mg/ml (10 ml)

- **Mechanism of action:** produces a cataleptic-like state in which the patient is dissociated from the surrounding environment by direct action on the cortex and limbic system. Ketamine is a noncompetitive NMDA receptor antagonist that blocks glutamate. Low doses produce analgesia, and modulate central sensitization, hyperalgesia and opioid tolerance. Reduces polysynaptic spinal reflexes

- **Onset of action:** IM injection anesthetic effect: 3-4 minutes.

- **Duration:** Anesthetic effect IM 12-25 minutes

- **Half-life:** Alpha 10-15 minutes; Beta 2.5 hours

- **Contraindications:** Hypersensitivity to Ketamine or any component of the formulation: conditions in which increase of blood pressure would be hazardous.

**Step 3.** Restrain patient in supine position. After patient is secured begin procedures for lowering patient’s body temperature with use of cold packs, wet towels, and unit A/C, initiate transport as soon as possible. Establish IV’s X2 with normal saline @ wide open up to 1 liter, then KVO. Apply oxygen by mask at 10 to 15 L. Assess patient vitals, connect cardiac monitor, and obtain 12 lead if possible. Monitor lung sounds for fluid overload. Consider albuterol neb and/or administration of 2 to 5 mg midazolam IV based on patient presentation and vitals.
SEDATION FOR THE EXTREMELY AGITATED PATIENT

NOTE:
1. Primary consideration should be given to EMS provider safety.
2. Notify police. Approach patient only when safe to do so.
3. Talk in an even, reassuring tone; only one provider should speak.
4. Restrain as needed if patient has a life-threatening emergency or suicidal/homicidal behavior. (see Region 6 Restraint Care Guideline)
5. Patient must be 14 years of age or older.

CRITERIA: Any may be present
1. Extreme psychological and physiological excitement/agitation
2. Aggressive or hostile combative behavior marked by incoherence
3. Superhuman strength with near complete tolerance to pain
4. Impaired thinking and perception, paranoia
5. Relative inability to “talk down”

TREATMENT:
1. Initial Medical Care. Sedate patient as necessary (as per #5 or #6 below) based on patient’s presentation and potential for self-harm. Contact medical control prior to sedation if questions/concerns exist regarding care.
2. Airway and OXYGEN 15 L NRB.
3. Assessment and history:
   a. Look for medical or traumatic causes of the patient’s behavior.
   b. Note (and later document) behavior and mental status in detail.
   c. Obtain medical history, alcohol and psychiatric history if able.
4. IV of NS or saline lock if able.
5. Administer KETAMINE 5 mg/kg IM or 1.5 mg/kg IV.
6. Alternative chemical sedative: VERSED 0.05mg/kg IVP Q3-5 minutes up to a total of 3 doses as needed or maximum 10mg.
7. Treat any potential allergic complications as per Region 6 “Allergic Reaction” protocol. Manage airway as necessary.
8. Determine blood glucose.
9. If glucose <60 mg/dl, administer DEXTROSE 50% 25g IV. If no IV access, administer GLUCAGON 1 mg IM.
10. If history of alcoholism or alcoholism is suspected, administer THIAMINE 100 mg IV/IM.
11. Transport. If restrained, have police accompany patient.
12. Contact Medical Control.

________________________________________
December 2008
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4. IV of NS or saline lock if able.
5. Administer VERSED 0.1 mg/kg IM. May repeat up to a maximum dose of 10 mg.
6. Determine blood glucose.
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May 2011

ALS
EXCITED DELIRIUM

INFORMATION

“Excited Delirium” presents as bizarre, aggressive behavior which may be associated with cocaine or “crack”, PCP or “angel dust”, methamphetamine or amphetamine use.

ADULT

PROCEDURE

- Law enforcement must first gain physical control of the patient.
- **KETAMINE:** 4mg/kg IV/IM. Max single dose 400mg.
- District Captain must accompany patient during transport with the exclusion of trauma hawk if Ketamine is administered.
- Allow patient to hyperventilate.
- Do not hold the patient in a prone position.
- Once calm, physical restraints may be unnecessary, but may be used as an added precaution.

ADVERSE REACTION TO KETAMINE

- Hypersalivation: Administer **ATROPINE** 0.5mg IV/IM/IO.
- Laryngospasm (Stridor): Try the following interventions in the order of: High flow O2, BVM, rapid sequence intubation.
  - Laryngospasm is uncommon and is usually self-limiting. It almost always resolves with high flow O2 or brief ventilation via BVM.

AFTER KETAMINE ADMINISTRATION

- Continuously monitor and maintain patient’s SpO2 at 95% and EtCO2 between 35-45mmHg.
- Obtain IV access.
- **VERSED:** Upon arrival at ED: 2.5mg IV/IO slowly over 2 minutes.
- **VERSED:** Upon arrival at ED: 5 mg IN/IM
  - Be prepared for respiratory depression and hypotension.
- Obtain a temperature.

RAPID COOLING FOR A TEMPERATURE OF GREATER THAN 103 DEGREES F

- Apply ice packs to axilla and groin area.
- **COLD NORMAL SALINE:** (If available) 30mL/kg (wide open), assess lung sounds and blood pressure every 500mL. Maximum 2L.
- **SODIUM BICARBONATE 8.4%:** 50 mEq slow IV/IO.
ADULT

CARDIAC ARREST

- Cardiac arrest shall be treated as a secondary cardiac arrest.
- SODIUM BICARBONATE: 100 mEq IV/IO, each amp given over two minutes, in addition to any Sodium Bicarbonate given prior to arrest, so long as the patient does not exceed a total dose of 150meq.
- COLD NORMAL SALINE: (if available) 30mL/kg IV/IO wide open, maximum of 2L, even if the patient’s temperature was not checked prior to arrest. Assess lung sounds every 500mL.
- Follow appropriate ACLS protocol. Medications cannot be administered in the same IV line as the cold saline.
- Once there is a ROSC, do not begin ICE protocol if patient has already received the cold normal saline during resuscitation. Follow the ACLS standard post arrest protocol for correcting the rate, rhythm and blood pressure.

PEDIATRIC

- N/A
INFORMATION

Indicated for violent, agitated patients who place themselves and/or crew in danger.

ADULT

PROCEDURE

- If possible, Law enforcement must first gain physical control of the patient.
- KETAMINE: 4mg/kg IV/IM. Max dose 400mg.
- District Captain must accompany patient during transport with the exclusion of trauma hawk if Ketamine is administered.
- Allow patient to hyperventilate.
- Do not hold the patient in a prone position.
- Once calm, physical restraints may be unnecessary, but may be used as an added precaution.

IF KETAMINE IS NOT AVAILABLE AND THERE IS NO CHANCE OF KETAMINE BEING ADMINISTERED DURING PATIENT CARE AND PATIENT IS NOT HYPOTENSIVE

- VERSED: 2.5mg IV/IO slowly over 2 minutes. May repeat 1x prn. Max dose 5mg.
- VERSED: 5 mg IN/IM. May repeat 1x prn. Max does 10mg.
  - Be prepared for respiratory depression and hypotension.
  - DO NOT ADMINISTER VERSED PRIOR TO KETAMINE.

ADVERSE REACTION TO KETAMINE

- Hypersalivation: Administer ATROPINE 0.5mg IV/IM/IO.
- Laryngospasm (Stridor): Try the following interventions in the order of: High flow O2, BVM, rapid sequence intubation.
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- VERSED: Upon arrival at ED: 5 mg IN/IM
  - Be prepared for respiratory depression and hypotension.

PEDIATRIC

- N/A
Once paralytics are administered, the District Captain shall be responsible for ensuring an airway is obtained & accompany the patient to the emergency room (excluding air rescue transport). In the event of multiple patients, the District Captain should accompany the most critical patient and turn over the additional patients to the next most experienced paramedic.

**INFORMATION**

**INDICATIONS FOR PARALYTICS**
- Status Epilepticus
- Multi-System Trauma
- Head Injury / GCS 8 or Less
- Trismus (Lock-Jaw) or clenched teeth
- Burn injuries to the upper airway
- District Captain Discretion

**CONTRAINDICATIONS FOR SUCCINYLCHOLINE**
- Predicted difficult intubation: obesity, short neck, small mouth
- Thyromental distance of less than 3 finger widths
- Major facial or laryngeal trauma
- Patient who cannot be assisted with a BVM
- Penetrating eye injuries, Glaucoma
- Organophosphate poisoning
- Renal failure (dialysis / hyperkalemia)
- Known hypersensitivity or history of malignant hyperthermia
- Preexisting neuromuscular disease
- Chronic paralysis

**ADULT**

**SEDATION FOR AIRWAY CONTROL / PRE-SEDATION FOR PARALYTICS**

- **ETOMIDATE**: 20mg IV/IO over 30-60 seconds. May repeat 1x prn.
  
  **OR**

- For Severe Asthma, **KETAMINE**: 2mg/kg IV/IO/IM. May repeat x1 prn. Max single dose 400mg.

**IF UNABLE TO OBTAIN IV/IO ACCESS**

- **VERSED**: 5mg IN/IM. May repeat 1x prn for adequate sedation. Max of 10mg.
  - *Contraindicated in hypotension.*
  - *Monitor for respiratory depression.*

**NASAL CANNULA @15 Lpm SHOULD BE APPLIED TO ALL PATIENTS**

**PARALYTIC**

- **District Captain and Flight Crew ONLY**

  - **SUCCINYLCHOLINE**: 100mg IV/IO

**ONCE PATIENT IS SUCCESSFULLY INTUBATED**

- **NORCURON**: 0.1mg/kg IV/IO. Max dose 10mg

- **VERSED**: 2.5 mg IV/IO as needed to maintain sedation. May repeat 1x prn.
  
  **OR**

- If patient is hypotensive, **KETAMINE**: 2mg/kg IV/IO/IM. May repeat 1x prn. Max single dose 400mg.
INDICATIONS

• Violent Agitated Patient
• Suspected Excited Delirium
• Advanced Airway Management
• District Captain must accompany patient during transport with the exclusion of trauma hawk if Ketamine is administered.

CONTRAINDICATIONS

• Allergy
• Penetrating Eye Injury

ADVERSE REACTIONS

• Hypertension and tachycardia, generally self limited
• Laryngospasm may produce mild stridor. Correct in the order of:
  1. High Flow \( \text{O}_2 \)
  2. Ventilation with a BVM
  3. Advanced Airway (RSI)
• Hypersalivation
• Nausea and vomiting
• Tonic and clonic muscle movements
• Transient respiratory depression occasionally occurs
• Roving eye movements and nystagmus

PSYCHOLOGICAL ADVERSE REACTIONS

• Visual Hallucinations
• Emergence Delirium
• Sensation of detachment from the body

ADMINISTRATION

☐ Adult

• For suspected excited delirium or violent patients: 4mg/kg IV/IM. Max single dose 400mg.
• Advanced Airway Management: 2mg/kg IV/IO/IM. May repeat 1x prn. Max single dose 400mg.

☐ Pediatric

• Advanced Airway Management: 1mg/kg IV/IO/IM. May repeat 1x prn. Max single dose 400mg.
EXCITED DELIRIUM

INFORMATION

“Excited Delirium” presents as bizarre, aggressive behavior which may be associated with cocaine or “crack”, PCP or “angel dust”, methamphetamine or amphetamine use.

ADULT

PROCEDURE

- Law enforcement must first gain physical control of the patient.
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- Allow patient to hyperventilate.
- Do not hold the patient in a prone position.
- Once calm, physical restraints may be unnecessary, but may be used as an added precaution.

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- Hypersalivation: Administer ATROPINE 0.5mg IV/IM/IO.
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  - Laryngospasm is uncommon and is usually self-limiting. It almost always resolves with high flow O2 or brief ventilation via BVM.

AFTER KETAMINE ADMINISTRATION

- Continuously monitor and maintain patient’s SpO2 at 95% or greater and EtCO2 between 35-45mmHg.
- Obtain IV access.
- VERSED: 2.5mg IV slowly over 2 minutes. Administer IM, if unable to obtain IV access.
  - Be prepared for respiratory depression and hypotension.
  - Withhold Versed with suspected ETOH Intoxication
- Obtain a temperature.

RAPID COOLING FOR A TEMPERATURE OF GREATER THAN 103 DEGREES F

- Apply ice packs to axilla and groin area.
- COLD NORMAL SALINE: 30mL/kg (wide open), assess lung sounds and blood pressure every 500mL. Maximum 2 liters.
- SODIUM BICARBONATE: 1 amp slow IV/IO.

Continued....
ADULT

CARDIAC ARREST

- Cardiac arrest shall be treated as a secondary cardiac arrest.

- **SODIUM BICARBONATE**: 2 amps IV/IO, each amp given over two minutes, in addition to any Sodium Bicarbonate given prior to arrest, so long as the patient does not exceed a total dose of 3 amps.

- **COLD NORMAL SALINE**: 30mL/kg IV/IO wide open, maximum of 2 liters, even if the patient’s temperature was not checked prior to arrest. Assess lung sounds every 500mL.

- Follow appropriate ACLS protocol. Medications cannot be administered in the same IV line as the cold saline.

- Once there is an ROSC, do not begin ICE protocol if patient has already received the cold normal saline during resuscitation. Follow the ACLS standard post arrest protocol for correcting the rate, rhythm and blood pressure.

PEDIATRIC

- N/A
VIOLENT / COMBATIVE PATIENT

INFORMATION

Indicated for violent, agitated patients who place themselves and crew in danger.

ADULT

PROCEDURE

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- Obtain IV access.
- **VERSED:** 2.5mg IV slowly over 2 minutes. Administer IM, if unable to obtain IV access.
  - *Be prepared for respiratory depression and hypotension.*
  - *Withhold Versed with suspected ETOH Intoxication*

PEDIATRIC

- N/A
**Excited Delirium Checklist**

Excited delirium or excited delirium syndrome is only one form of potential sudden death that law enforcement officers may encounter. Other potential causes of unexpected arrest-related deaths include, but are not limited to: SUDEP\(^1,2\) (sudden unexpected death in epilepsy), sickle cell sudden death,\(^3\) various cardiomyopathies,\(^4\) drug induced arrhythmias (including those caused by alcohol\(^5,6\) and marijuana\(^7-10\)), psychiatric arrhythmias (whether due to schizophrenia\(^11\) or medications\(^12\)), and severe coronary artery disease.

<table>
<thead>
<tr>
<th>Present?</th>
<th>Criterion</th>
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<tbody>
<tr>
<td><strong>911 Call – Emergency Contact for Assistance</strong></td>
<td></td>
</tr>
<tr>
<td>1. Critical call phrases include, “He just freaked out,” “just snapped,” “flipped out,” or a person is “running around naked.”(^13)</td>
<td></td>
</tr>
<tr>
<td><strong>Law Enforcement</strong></td>
<td></td>
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<tr>
<td>2. Agitation, screaming, extreme fear response or panic(^14-18)</td>
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<tr>
<td>3. Violence, assault, or aggression towards others(^18-21)</td>
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<tr>
<td>4. Suspicion of impending death. Typical comments include, “I’m dying,” “Please save me,” or “Don’t kill me”(^22)</td>
<td></td>
</tr>
<tr>
<td>5. Incoherence or disorganized speech. Grunting or animal sounds(^21,23)</td>
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<tr>
<td>6. Clothing removal inappropriate for ambient temperature or complete nudity.(^18,24-26)</td>
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<td>7. Disorientation or hallucinations(^18,27-30)</td>
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<tr>
<td>8. Mania, paranoia, anxiety, or avoidance behavior(^14,18,31-34)</td>
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<td>9. Constant motion or hyperactivity(^14,30,35-37)</td>
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<tr>
<td><strong>Capture, Control and Restraint of Subject</strong></td>
<td></td>
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<tr>
<td>10. Extreme or “super human” strength(^21,33)</td>
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<tr>
<td>11. High threshold of or imperviousness to pain(^23,26)</td>
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<tr>
<td>12. Extreme stamina(^36,23)</td>
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<tr>
<td>13. Brief quiet period before collapse likely corresponding with respiratory arrest(^14,17,23,39)</td>
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</tr>
</tbody>
</table>
### Emergency Medical Services Contact and Intervention

| 14. Presenting rhythm of PEA (pulseless electrical activity) or asystole.\(^{38,40-42}\)  
  Also documented by “No shock advised” with automatic external defibrillator\(^{42}\) |

### Emergency Department

| 15. High core body temperature.\(^{15,16,21,31,43,44}\) |
| 16. Acidosis (acidic blood)\(^ {23,45,46}\) |
| 17. Rhabdomyolysis (if suspect is resuscitated).\(^ {15,44,47}\) |

### Law Enforcement/Forensic Investigator Death Investigation

| 18. History of chronic stimulant abuse or mental illness\(^ {14,19,27,32,37,40,48-51}\)  
  History of violence or drug related arrests, mental health histories and treatments, and drug rehabilitation interventions, etc. |
| 19. Damage to shiny objects such as glass, mirrors and lights.\(^ {23}\) Reported behaviors may include attacking a squad car light bar or charging oncoming traffic at night. Occasionally generalized vandalism. |

### Pathologist – Medical Examiner Investigation

| 20. Minor injuries from fighting against restraints (e.g. handcuffs, hobbles). |
| 21. Positive Mash (central nervous system biomarkers) test for dopamine transporter assay and heat shock protein.\(^ {15,31,32,52-56}\) |
| 22. Positive brain and hair toxicology screen for chronic stimulant abuse.\(^ {52,57}\) Post-incident drug levels may be low to negative. |

Contributors: Mark Kroll, PhD; Charles Wetli, MD; Deborah Mash, PhD; Steven Karch, MD; Michael Graham, MD; Jeffrey Ho, MD.
Notes:

A syndrome is an aggregate of signs and symptoms that define a medical condition. Not all persons with a certain syndrome have all the same signs and symptoms. Not all cases of a syndrome result from the same cause. For example, some persons with carpal tunnel syndrome will have numbness and tingling, while others will have weakness and pain. Also, some persons with carpal tunnel syndrome will have it because of trauma, while others will have the syndrome because of pregnancy, diabetes, rheumatoid arthritis or thyroid disease.

Persons with the excited delirium syndrome will have various combinations of some of the signs and symptoms listed above. The cause (etiology) of the excited delirium syndrome in any individual may be due to one or more of a number of conditions. The most common conditions are mental illness and illegal stimulant abuse (especially cocaine and methamphetamine).  

Because the term "excited delirium syndrome" has not been widely used until recent years, many physicians do not recognize the term even though they may be very familiar with agitation and deaths due to drugs and other conditions. It is important to avoid the distraction of the various terms that have been applied to this syndrome. For example, what is now referred to as excited delirium or agitated delirium has also been called: Bell's mania, acute exhaustive mania, acute delirious mania, delirium grave, typhoma, acute delirium, manic-depressive exhaustion, excited catatonia, lethal catatonia, and neuroleptic malignant syndrome.
Statistical Confidence:

There must be at least 5 positive criteria to diagnose excite delirium syndrome. For 12 or more positive criteria the confidence level is at least 99.9%. For less than 12 positive criteria the confidence depends on the number of criteria for which information is available.

For example, the brain and hair tests are, unfortunately, typically not done. Often the blood tests for rhabdomyolysis is not done. In this case there will only be information on 19 criteria. If 8 of these 19 criteria were positive then the confidence in the diagnosis would be 93%.

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References:

17. Stefan H. Sudden death of psychiatric patients following great excitation and exhaustion which has no actual anatomic basis. *Dtsch Med Wehnschr* 1934;60:1550-1558.
20. Bell L. On a form of disease resembling some advanced stages of mania and fever, but so contradistinguished from any ordinary observed or described combination of symptoms as to render it probable that it may be overlooked.


