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Clinical Reviews

EXCITED DELIRIUM SYNDROME (EXDS): DEFINING BASED ON A REVIEW OF THE LITERATURE

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☐ **Abstract—Background: Patients present to police, Emergency Medical Services, and the emergency department with aggressive behavior, altered sensorium, and a host of other signs that may include hyperthermia, "superhuman" strength, diaphoresis, and lack of willingness to yield to overwhelming force. A certain percentage of these individuals will go on to expire from a sudden cardiac arrest and death, despite optimal therapy. Traditionally, the forensic community would often classify these as "Excited Delirium" deaths. Objectives: This article will review selected examples of the literature on this topic to determine if it is definable as a discrete medical entity, has a recognizable history, epidemiology, clinical presentation, pathophysiology, and treatment recommendations. Discussion: Excited delirium syndrome is characterized by delirium, agitation, acidosis, and hyperadrenergic autonomic dysfunction, typically in the setting of acute-on-chronic drug abuse or serious mental illness or a combination of both. Conclusions: Based upon available evidence, it is the consensus of an American College of Emergency Physicians Task Force that Excited Delirium Syndrome is a real syndrome with uncertain, likely multiple, etiologies.** © 2011 Elsevier Inc.

☐ **Keywords—excited delirium; in-custody death; sudden death; TASER; restraint; agitated delirium**

INTRODUCTION

The term "Excited Delirium" has been used to refer to a subcategory of delirium that has primarily been described retrospectively in the forensic literature. It has also been referred to as "Agitated Delirium" and is closely associated with the "Sudden Death in Custody Syndrome." Originally, the concept of excited delirium was described in the forensic literature and has been synonymous with death, but over time the term has made its way into the emergency medicine, psychiatric, law enforcement, prehospital, and medicolegal literature. It

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has generally been used to describe patients displaying altered mental status with severe agitation and combative or assaultive behavior that has eluded a unifying, prospective clinical definition. For the remainder of this article, these kinds of cases will be referred to as the Excited Delirium Syndrome (ExDS).

The difficulty surrounding the clinical identification of ExDS is that the spectrum of behaviors and signs overlap with many other clinical disease processes. Treatment interventions targeting these alternate diagnoses (e.g., acute hypoglycemia) may potentially alleviate the clinical presentation of the ExDS. Faced with the lack of a clear definition and cause, as well as the infrequency of events such that individual practitioners are unlikely to encounter large numbers of cases, the decision to identify ExDS as a syndrome instead of a unique disease has been delayed, somewhat similar to the decades-long controversy over Sudden Infant Death Syndrome.

The problem is that a small percentage of patients with ExDS progress to sudden cardiopulmonary arrest and death. Although many of the current deaths from ExDS are likely not preventable, there may be an unidentified subset in whom death could be averted with an early directed therapeutic intervention. In fact, it is impossible at present to know how many patients with this type of clinical presentation have received a therapeutic intervention that halted a terminal progression, or whether this is a spectrum of severity to a disease state that causes death to only a few of its victims.

In response to increased reports and lay media coverage of sudden deaths in severely agitated subjects, along with lack of clarity and consistency among the medical community regarding ExDS, the American College of Emergency Physicians (ACEP) convened a Task Force of experts in the field of excited delirium. Experts included emergency physicians published in the field, forensic pathologists researching in the field, and tactical Emergency Medical Services (EMS) physicians. The expertise was extended to include researchers knowledgeable in Sudden Death in Custody Syndrome, positional asphyxia, conducted energy devices, and tactical medicine. This Task Force was charged with reviewing the body of literature available and coming to a consensus, if possible, to define two major questions:

1. Does the entity commonly referred to as "excited delirium" exist as a separate disease?
   And if it does,
2. Can it be better defined, identified, and treated?

In this article, the Task Force provides a review of the history and epidemiology of ExDS along with a discussion of the potential pathophysiology, clinical and diagnostic characteristics, differential diagnoses, and treatment. The goal is to determine if ExDS is a disease, and if so, to educate those who have to provide care for the victims, which would include medical and public organizations, including first responders, law enforcement, physicians, and other health care providers.

METHODS

ACEP convened a consensus group of experts in the field of ExDS who have conducted research on or are nationally recognized as having specific expertise in ExDS. The group was selected by assessing all ACEP members who have published significant writings beyond case reports in the areas of Sudden Death in Custody Syndrome, positional asphyxia, conducted energy devices, and tactical medicine. These individuals were invited to participate and queried for other "experts" in the field and those individuals were also invited. All but one of the invitees participated. The group met by teleconference three times and communicated electronically, and subsequently met in person on two separate occasions: a 2-day retreat dedicated to the review and drafting of a consensus paper, and a second time to finalize the working document.

The medical literature was reviewed to include key word and topic searches on excited delirium, agitated delirium, acute exhaustive mania, sudden in-custody death, in-custody death syndrome, TASER (TASER International Inc., Scottsdale, AZ), electronic control devices, conducted electrical weapons, positional restraint, restraint asphyxia, positional asphyxia, and less lethal weapons. Additionally, other special reports, text books and chapters, agency reports, and governmental reviews were evaluated. The task force reviewed these materials for appropriateness to the topic and the quality of the work. Studies included for the final review were limited to randomized controlled trials, clinical trials, prospective and retrospective cohort studies, and meta-analyses in human subjects. Case reports, case series, and general review articles were not included for the selection criteria for formal rigorous review but were utilized for the compilation of the published signs and symptoms.

DISCUSSION

ExDS 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 (1). These historical cases occurred primarily within institutions that housed mentally disturbed individuals in protective custody due to their violent and aggressive

behavior. At that time, there was lack of effective pharmacologic treatment available for these patients. The behavior seen in these cases has been called "Bell's Mania," named after Dr. Luther Bell, the primary psychiatrist at the McLean 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 may well be the case that Bell's Mania is related to the syndrome of ExDS that we witness today. The incidence of the problem behaviors and sudden death described in the 1800s seemed to decline drastically by the mid-1950s (2). This has been largely attributed to the advent of modern antipsychotic pharmaceutical therapy used for these patients with severe behavior issues.

In the 1980s, there was a dramatic increase in the number of reported cases with behavior similar to an uncontrolled psychiatric emergency. Whereas 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 (3,4). Since then, this connection between ExDS and cocaine has continued (5). Additionally, ExDS has now been recognized to occur in association with other illicit drugs of abuse, particularly cocaine, methamphetamine, and PCP, as well as with certain types of mental illness and their associated treatment medications (6–10).

Before the mid-1980s, 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 article that coined the term "excited delirium" (11). The typical patient involves an 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 that may include an electrical control device (ECD) application, sudden and unexpected death, and an autopsy that 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 law enforcement personnel when someone dies while in their custody. It has been articulated by some that ExDS is a term or concept that has been "manufactured" as a law enforcement conspiracy or cover-up for brutality (12).

This argument mainly centers on the fact that most organized medical associations, like the American Medical Association, and medical coding reference materials including the *International Classification of Disease*, Ninth Revision (ICD-9) do not recognize the exact term "excited delirium" or "excited delirium syndrome" (13). The countering argument is that there are organized medical associations, including the National Association of Medical Examiners and the American College of Emergency Physicians, that do recognize ExDS as an entity. Additionally, the ICD-9 does contain several codes that can be and are used to describe the same entity as ExDS (Table 1). This semantic issue 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 by which to identify ExDS. In addition, because ExDS is discussed mainly in the forensic literature, and is a diagnosis of exclusion established on autopsy, there is little documentation about survivors, which have led some to believe the syndrome to be near-uniformly fatal. However, some Task Force members have reported caring for multiple patients with ExDS who have survived. A published observational study suggests that the incidence of death among patients manifesting signs and symptoms that may be consistent with ExDS is < 10% (14). An exact figure is difficult to ascertain because it is believed that repetitive exposure to triggering substances, such as cocaine or mental health medications, leads to kindling events in the brain that start the patient down the progressive path of ExDS, with each subsequent presentation becoming worse until death occurs (15,16). 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 involve men at a mean age of 36 years (17–24). These subjects are hyper-aggressive with bizarre behavior, and are typically impervious to pain, combative, hyperthermic, and tachycardic. There is typically a struggle with law enforcement

Table 1. ICD-9 Codes that Describe the Same Entity as ExDS

- 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

ICD = International Classification of Diseases; ExDS = Excited Delirium Syndrome.

that involves physical, noxious chemical, or ECD use followed by a period of quiescence and sudden death. The majority of cases involve stimulant abuse, most commonly cocaine, although methamphetamine, PCP, and LSD have also been described (25,26). As more attention is drawn to ExDS as a recognized entity, it is likely that other drugs of abuse may be identified as also etiologic.

Persons with psychiatric illnesses comprise the other cohort of ExDS cases and deaths. The literature on ExDS frequently cites abrupt cessation of psychotherapeutic medications as a cause (27). 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. Health care providers should be aware that medication noncompliance in psychiatric patients is a potential cause for ExDS. Less commonly, persons with new-onset psychiatric disease, particularly with manic or psychotic features, will present with ExDS (14). In most cases, the underlying psychiatric disease will be untreated at the time of presentation, but in some cases the psychiatric illness may be partially treated or mistreated.

Over a 2-year period, the presence or absence of 10 potential clinical features of ExDS was recorded by Canadian police for cases seen in over 1 million police-public interactions (28). The features of ExDS looked for included pain tolerance, tachypnea, sweating, agitation, tactile hyperthermia, non-compliance with police, lack of tiring, unusual strength, inappropriately clothed, and mirror or glass attraction (which has been referred to in the forensic literature as a possible commonality in ExDS deaths). Of the 698 encounters involving use of force, 24 (3.4%) probable ExDS cases were identified based upon the presence of perceived abnormal behavior and at least six of the 10 potential clinical criteria for ExDS. Eighteen (2.7%) of the cohort manifested seven or more features, including tactile hyperthermia.

Pathophysiology

The actual pathophysiology of patients who have been previously identified with signs and symptoms of ExDS is complex and poorly understood. The fundamental manifestation is delirium. As described above, 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 some do not.

Although our knowledge about 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 (17,19–21,24,29). 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 "overdose" deaths, suggesting a different mechanism of death. Although some individuals have had alcohol in their system at the time of death, many cases are not associated with alcohol ingestion, intoxication, or known dependency.

Subsequent anatomic and molecular characterization of this group of fatal ExDS patients has focused primarily on postmortem brain examination findings. Results 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 (30,31).

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 (18). Postmortem studies in these patients have demonstrated elevated levels of heat shock proteins. The central dopamine hypothesis also provides a link to psychiatric etiologies of ExDS, such as schizophrenia.

Although the specific precipitants of fatal ExDS remain unclear, epidemiologic and clinical reports provide some clues to the underlying pathophysiology. When available, cardiac rhythm analysis demonstrates bradyasystole or pulseless electrical activity; ventricular dysrhythmias are rare, occurring in only a single patient in one study (19). The majority of lethal ExDS patients die during or shortly after a violent struggle. Severe acidosis seems to play a prominent role in lethal ExDS-associated cardiovascular collapse (32).

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 *Diagnostic and Statistical Manual of Mental Disorders*, 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 (33). 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.

Due to 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 have the same clinical presentation; however, all patients with ExDS present delirious with evidence of psychomotor and physiologic excitation. Lacking either of these findings eliminates ExDS as a diagnosis. Historically in ExDS, there is typically a component of illicit drug use or psychiatric illness, particularly schizophrenia. Clinical findings in subjects who die with a post-mortem diagnosis of ExDS typically have many or most of the features listed in Table 2.

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

	No. Articles
Features in history	
Male gender	16
Mean age ~30s	16
Sudden onset	4
History of mental illness	8
History of psychostimulant abuse	11
Features evident at scene	
Call for disturbance/psychomotor agitation/ excitation	18
Violent/combative/belligerent/assault call	11
Not responding to authorities/verbal commands	1
Psychosis/delusional/paranoid/fearful	13
Yelling/shouting/guttural sounds	7
Disrobing/inappropriate clothing	5
Violence toward/destruction of inanimate objects	7
Walking/running in traffic	3
Subject obese	5
Features evident on contact	
Significant resistance to physical restraint	11
Superhuman strength	8
Impervious to pain	3
Continued struggle despite restraint	7
Profuse sweating/clammy skin	3
Features with clinical assessment	
Tachypnea	1
Tachycardia	7
Hyperthermia	12
Hypertension	3
Acidosis	3
Rhabdomyolysis	5
Features of death	
Period of tranquility/"giving up"	4
Sudden collapse after restraint	12
Respiratory arrest described	5
Cardiac rhythm brady-asystole or PEA	4
Aggressive resuscitation unsuccessful	5
Features on autopsy	
Drug screen positive for psychostimulants	9
Drug levels lower than anticipated	3
No anatomic correlate for death	6
Dopamine transporter dysregulation	2

ExDS = Excited Delirium Syndrome; PEA = Pulseless electrical activity.
This table lists the features of ExDS 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 evident only with clinical assessment like vital signs, features that are described if the subject dies, and finally, features that are described on autopsy.

Differential Diagnosis

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 will not be able to readily discern the cause of an acute behavioral disturbance, or differentiate a specific organic disease from ExDS based solely on observation.

Several specific entities that 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. Heat stroke may manifest as tactile hyperthermia, rhabdomyolysis, and delirium, and may be associated with neuroleptic use and mental illness. Thyrotoxicosis may manifest a similar clinical presentation, especially during episodes of thyroid storm. 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.

Sudden unexpected death is the hallmark of fatal ExDS. The differential diagnosis for sudden death includes ischemic or drug-induced sudden cardiac death, stress, or 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).

Treatment and Protocols

In the absence of clearly stated case definitions and prospective clinical studies, treatment of ExDS remains largely speculative and individually styled, 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 the Task Force, posit the beneficial use of aggressive chemical sedation as first-line intervention, though the specific medications may vary based on individual practice. Restraint will often be necessary for safety of the staff as well as the patient, but should be done in conjunction with aggressive chemical sedation. 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. There are well-documented cases of ExDS deaths with minimal restraint such as handcuffs without ECD or maximal "hogtie" restraint use. The use of multiple personnel with training in safe physical control measures is prudent.

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 (34). Because 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.

After adequate physical control is achieved, medical assessment and treatment should be immediately initiated. Indeed, because cardiopulmonary arrest might occur suddenly, EMS should ideally be present and prepared to resuscitate before definitive law enforcement officer control measures are initiated, when possible. Although the need for control measures may initially take precedence, initial assessment should include vital signs, cardiac monitoring, intravenous (i.v.) access, glucose measurement, pulse oximetry and supplemental oxygen, and careful physical examination. Several Task Force members who have cared for witnessed ExDS sudden death patients have experienced unsuccessful resuscitations even when the cardiopulmonary arrest occurs in the setting of a well-staffed and well-equipped hospital emergency department (ED). This implies that some patients who develop ExDS and go into cardiac arrest will not be resuscitated, and that the cardiac arrest in these individuals is a terminal event despite optimal management.

Agitation. Agitation, hyperthermia, and acidosis are all major components of ExDS that should be managed with standard medical interventions. The approach to each of these components is described below. For the treatment of agitation, the i.v. route is preferred if available; however, intramuscular or intranasal transmucosal administration of sedative agents may be needed initially to facilitate i.v. placement. Commonly used agents include benzodiazepines (midazolam, lorazepam, diazepam), antipsychotics (haloperidol, droperidol, ziprasidone, olanzapine), and the dissociative agent ketamine (35–37). The Food and Drug Administration has issued "black box" warnings regarding potential serious adverse effects (QT prolongation and torsades de pointes) with the use of haloperidol and droperidol. Clinicians should use their best clinical judgment regarding the risk/benefit ratio on a case-by-case basis. The actual effective dose of all suggested medications is unknown. Because these agents have respiratory and cardiovascular effects, continuous monitoring of both heart and lungs should be performed as soon as feasible whenever parenteral sedation is administered.

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 (38). 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 i.v. 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 will present 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 (32). If suspected based on the clinical situation or physical examination, 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. Hyperventilation is the body's normal compensatory

mechanism for correcting acidosis. Control measures that might interfere with ventilation should be avoided. In some cases, patients have been treated with muscle paralytic agents in the hope of preventing further metabolic acidosis from movement when chemical sedation has proven to be insufficient. Mechanical hyperventilation is also deemed useful.

Rhabdomyolysis and Hyperkalemia. 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 standard interventions.

Future Directions

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 police actions or from ExDS, or from interplay of all these factors? Furthermore, there is no clear proof of the most effective control measures or therapy for the extremely agitated and delirious patient. Sedative or dissociative agents such as benzodiazepines, major tranquilizers, and ketamine are suggested and used regularly, 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 suspected cases, including those who survive. At a molecular level, and based upon post-mortem cocaine-associated ExDS brain tissue, there may be a genetic basis for susceptibility to ExDS.

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. For these purposes, thorough documentation of the patient's signs and symptoms along with appropriate testing should occur in suspected cases, including the presence of sweating or muscle rigidity, temperature, pulse, respiratory rate, blood pressure, venous blood gases, urine and serum toxicology, thyroid functions, and blood and (if fatal) anatomic brain specimens for genetic, heat shock proteins, and neurochemical analyses. Creating such a registry 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 subjects with ExDS. Finally, research is needed to establish field protocols and techniques that allow police, EMS, and hospital personnel to interact with these agitated, aggressive patients in a manner safe for both the patients and the providers.

CONCLUSION

Based upon available evidence, it is the consensus of the Task Force that ExDS is a real syndrome with uncertain, likely multiple, etiologies. It is characterized by delirium, agitation, acidosis, and hyperadrenergic autonomic dysfunction, 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 are insufficient data at this time to determine whether fatal ExDS is preventable, or whether there is a point of no return after which the patient will die regardless of advanced life support 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 medical intervention to attempt to reduce the risk of death.

For diagnostic and research purposes, thorough assessment and documentation of a suspected ExDS patient's signs and symptoms, along with appropriate testing, should occur. Doing so would play an important role in creating a large database of cases for study and scientific investigation.

The ante-mortem diagnosis in the prehospital or ED setting depends upon clinical characteristics and the exclusion of alternative disease processes. It is our consensus opinion that rapid and appropriate control measures, and immediate administration of supportive care and sedation, such as i.v. benzodiazepines or ketamine, intramuscular ketamine, or intranasal midazolam, may be lifesaving by preventing deterioration into sudden death.

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ARTICLE SUMMARY

1. Why is this topic important?

Excited Delirium Syndrome (ExDS) is seen all across the country in emergency departments, but is not always recognized as a syndrome with significant mortality.

2. What does this review attempt to show?

To better define ExDS as a discrete medical entity, the history, epidemiology, clinical presentation, pathophysiology, and treatment recommendations.

3. What are the key findings?

ExDS is characterized by delirium, agitation, acidosis, and hyperadrenergic autonomic dysfunction, typically in the setting of acute-on-chronic drug abuse or serious mental illness. Based upon available evidence, it is the consensus of the Task Force that ExDS is a real syndrome with uncertain, likely multiple, etiologies.

4. How is patient care impacted?

Treatment options are described and with increased awareness and knowledge, patient care can be improved.