Excited Delirium Syndrome (ExDS)

**History:**

1849: Description of cases of psychiatric patients developing acute onset of agitation, mania and fever, and suddenly collapsing and dying

1980s: “Fatal excited delirium” described in the literature, in the face of rising cocaine consumption in North America, as a combination of:

1. Acute drug intoxication (often cocaine, but also methamphetamine, PCP, LSD)
2. History of mental illness (especially paranoid schizophrenia & bipolar disorder)
3. Struggle with law enforcement (more severe than anyone anticipates, and intense even when a struggle is futile and self mutilation is a result)
4. Physical, chemical or TASER restraint
5. Sudden unexpected death, with autopsy which fails to reveal a definite cause of death (therefore diagnosis of exclusion)


**Clinical features:**

Typical scenario: obese male in mid-30’s displaying destructive/bizarre behavior leading to call to police in setting of psycho-stimulant drug or alcohol intoxication, with prior psychiatric illness

Subset of pts eventually enter a quiescent period (for less than a minute) where they suddenly stop struggling followed by a respiratory or cardiac arrest, for an overall incidence of death of 8%

This is a medical emergency necessitating cardiac monitoring and rescusitation, not seclusion in a psychiatric room

Possible **case definition** of excited delirium syndrome (based on Canadian study not yet published)

When 6 out of 10 of the following elements are present (presented in decreasing order of frequency):

1. Increased pain tolerance, (2) tachypnea, (3) sweating, (4) agitation, (5) tactile hyperthermia, (6) police non-compliance (ongoing struggle despite futility), (7) lack of tiring, (8) unusual (superhuman) strength, (9) inappropriate clothing (eg, nakedness) and (10) mirror/glass attraction
**Pathophysiology theories:**

Dopamine hypothesis: Predisposition in certain individuals to deficiency of dopamine transport in the brain, and association with dopamine-altering psychotropic drugs

This cannot explain fully the pathophysiology, however, as drugs with no dopaminergic activity (PCP, amphetamines) are also involved in many cases of ExDS

Cocaine effects: Chronic cocaine use leads to dopamine depletion in striatum and therefore affects dopaminergic balance, and also leads to cardiac hypertrophy and contraction bands, potentially making the heart more susceptible to arrest

Positional or compression asphyxia:

Probably negligible involvement of position in contribution of death in cases of excited delirium, although allowing patients to breathe effectively is obviously important

**Differential diagnosis:**

Any diagnosis leading to altered mental status, especially the following:

Serotonin syndrome, sympathomimetic syndrome, neuroleptic malignant syndrome (NMS), psychotropic drug withdrawal or acute psychiatric condition, diabetic hypoglycemia, heat stroke, thyrotoxicosis

How to differentiate Excited Delirium Syndrome from sympathomimetic syndrome:

Often present similarly but more likely to display bizarre abnormal behavior (eg, walking through traffic, being naked in public), with non-toxic amount of recent drug use.

**Management – 3 spheres:**

1. **Agitation:**

Minimize use of and time spent in physical restraints, using as many properly trained people as possible for as short of a time as possible

Benzodiazepines: first-line due to their decrease in sympathomimetic outflow by central anxiolytic effects and potential cardioprotective effects (in animal studies); a single IM dose of benzodiazepine has never been reported to be fatal

Although neuroleptics and ketamine are other choices, they have more downsides:

Dopaminergic interaction and QT prolongation in neuroleptics

Laryngospasm for IM ketamine, potentially worsening a difficult airway

2. **Hyperthermia:**

IV fluids (at least 2L NS bolus, cooled if possible), which will also help in the treatment of rhabdomyolysis and acidosis

Aggressive cooling: cooled fluids, ice packs to groin and axilla, fans with mist spray, cooling blanket
3. Acidosis:

Can be very severe (almost incompatible with life)

Consider 1-2 amp of sodium-bicarbonate IV empirically, which will also help the likely hyperkalemia

If RSI is performed, hyperventilate immediately as the respiratory drive that was blowing off the CO₂ is now gone with paralysis (potentially worsening acidosis)

**Future research and education:**

Generally accepted case definition needed for advances in understanding of condition

Education for law enforcement personnel, EMS, and EPs:

Medical, not behavioral, issue that must be promptly recognized both out-of-hospital and in-hospital, and aggressively treated