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AANA Peer Assistance Advisory Committee
State Peer Advisor, Texas

**History of Propofol**
- Originally developed in UK as ICI 35868 by Imperial Chemical Industries
  - Clinical trials 1977 in Belgium
  - Solubilized in cremophor → anaphylactic reactions
  - Reformulated as an emulsion of a soya oil/propofol mixture in water
  - Relaunched in 1986 as Diprivan (diisopropyl intravenous anesthetic)
  - 1% propofol, 10% soybean oil, 1.2% purified egg phospholipid as an emulsifier, with 2.25% glycerol and sodium hydroxide to adjust the pH

**Definitions**
- **Misuse** - Use of a substance for a purpose not consistent with legal or medical guidelines, as in the non-medical use of prescription medications.
- **Abuse** - The continued use of a substance despite physical or psychological harm.
- **Addiction** - a strong desire, persistent use, and impaired control over despite harmful consequences; to use a substance which is given a higher priority to other activities and obligations; increased tolerance, and a physical withdrawal reaction when substance use is discontinued.
  - (ICD-10 3 of 6 above = Dependence syndrome)
Problem:
- Does propofol have addictive or dependence potential?
- Abuse + Misuse = Addiction/Dependence?

Addiction/Dependence (WHO)
1. "a strong desire to take the drug,
2. impaired control over its use,
3. persistent use despite harmful consequences,
4. higher priority given to drug use than to other activities and obligations,
5. increased tolerance,
6. physical withdrawal reaction when drug use is discontinued".

Addiction/Dependence (ICD-10)
- √ Strong desire to use,
- √ Persistent use,
- √ Impaired control to stop, despite harmful consequences
- √ Higher priority to substance than other activities and obligations
- Increased tolerance
- ? Physical withdrawal reaction when substance use is discontinued

Case #1
Source: Powerful Sedative Propofol Found at Michael Jackson's Mansion

Public Awareness
- Survey: Since the death of Michael Jackson, have your patients expressed greater concern about the use of propofol?
  Yes- 47%  No- 55%


Profession’s Awareness
- Survey: 126 academic anesthesiology residency programs (100% response rate)
  18% program incidence (n=25)
  No propofol accounting program in 71% of incidences

**Case #1**

- Michael Jackson has shed light on an under addressed concern

**AANA Statement RE: propofol**

“At subanesthetic doses, feelings of elation and euphoria have been reported. Unfortunately, too often the first sign of propofol misuse or addiction is the practitioner’s death.”

**1987**

- Female patients 5 separate incidents
- Anesthetic
- Expressed amorous thoughts
- Assumed anesthetic recovery and discharge

**1992**

- 30+ yo Physician anesthesiologist.
- Hospital Drug diversion (midazolam, fentanyl, propofol) for stress treatment.
- 100 mg IV bolus x 10-15 daily
- Desired clear headedness after 10 minute induced sleep.
- Intense craving,
- Long-term drug rehabilitation program.
1992
- Male lay person
- 9 day binge
- 50 mg IV x 3 doses daily (150 mg total daily). 9 day binge
- Relief of anxiety, inner tension, restlessness.
- Abstinent alcoholic


1992
- 29 yo female radiologist
- Apparent suicide
- First reported death by overdose
- 400 mg suspected


1994
- 37 yo male physician
- Assumed diversion
- Overdose. Infusion. Found empty:
  - 8 propofol, 6 Ca gluconate, 5 KCL vials.
  - Emotionally upset related to failed relationship
  - Death, overdose, ruled suicide


1997
- 31 yo physician
- Hospital Drug diversion
- Propofol 50mg injections (up to 100x/day)
- Mild euphoria, relaxation, relieved boredom, tension, depression x 10 months
- Craving, tolerance to euphoria, no withdrawl, intense craving


1999
- 3 male medical technicians
- Hospital Drug diversion
- Police apprehension injecting propofol while driving an automobile


2001
- 26 male nurse
- Propofol abuse for years. Poly substance abuse.
- Death, overdose. likely due to resp. arrest. Prior treatment for depression x 6mos

2001
- 25 yo male lay person
- Tx Tension H/A by anesthesiologist.
- Hx Ritalin as child x 1yr
- Propofol 200 mg IV boluses x 10-15 daily
- Relaxation, mild euphoria, relieved tension x 6months.
- Intense craving, no withdrawal symptoms
- Outpatient Psychotherapy. ICD-10 criteria met for propofol addiction, ADHD likely.

2002
- 44 yo female nurse anesthetist
- Assumed diversion
- Overdose. Found empty midazolam vial (5mg/5ml) and syringe
- Known anesthetic abuser for years. Serum Propofol, midazolam, and ethanol detected. Propofol and midazolam abuse x6 months detected by hair analysis

2002
- 31 yo lay person
- Tx Tension H/A by anesthesiologist. Veterinarian obtained.
- Hx Ritalin as child x 1yr
- 50 mg IV bolus x 12-20 daily
- No withdrawal,
- 7 day in-patient treatment. Refused further treatment. ADHD hx

2006
- 27 yo male nurse anesthetist
- Overdose. 3 empty propofol vials present, unused vials found in car
- Previous abuse suspected d/t multiple venipuncture sites

2006
- 21 yo male medical layman
- Overdose.
- Permanent IV catheter in place
- Propofol purchased through online eBay auction

2007
- 38 yo female anesthesiologist
- Assumed diversion
- Overdose.
- Found empty: 3 propofol, 1 lidocaine vials
- Known propofol abuser for several months
- Hospital 'dormitory' locked from inside
2009

- 40 yo male Nurse Anesthetist
- Found in hospital call room
- Empty propofol vial bedside
- Empty syringe with propofol residue in antecubital vein
- Death, ruled suicide
- Married with children

2009

- 42 yo female Nurse Anesthetist
- Assumed diversion
- Overdose. Found 14 empty vials ampoules propofol and two full syringes of propofol.
- Family reported daily propofol abuse

2009

- 38 yo male Physician surgeon
- False prescription
- 1 empty propofol ampule present diluted in IV infusion of LR
- Previous abuse with alcohol suspected
- Death d/t apnea

2009

- 24 yo female Lay person
- Hospital diversion by male RN
- Death, Murder by propofol injection.

2009 (cont)

Human case of abuse/dependency – 38
- 1992 to 2007
- 14 cases fatal
- 12 medical professionals
- 9 anesthesia providers

2009

- 30 yr old female Nurse Anesthetist
- Found unconscious in hospital prep bath room
- propofol vial, syringe with propofol residue in PICC line (relapse)
- Prior hx treatment, enrolled in state monitoring program x 3 yrs
- Employed while awaiting BON investigation of being released under monitoring program
- License suspended


Kirby RR. Death from Propofol: Accident, suicide, or murder. Anesthesia Analgesia. 2009.108:1182-4
2012
- 30 yr old male anesthesia resident
- Repeated dosing 100-200mg to induce sleep for over 1 year,
- 20-40 injections/day
- Failed self-detox d/t intense craving (cue=access)
- No prior use of addictive substances


2013
- Repeated dosing 100-200mg to induce sleep for over 1 year,
- 20-40 injections/day
- Failed self-detox d/t intense craving (cue=access)
- No prior use of addictive substances


2013
- Study of prevalence of abuse and deaths due to propofol
- 131 cases of propofol detection over 6 years (14,673 autopsies)
- Propofol alone detected in 49 cases; 16 cases accidental death after self-administration


Two New Case Reports of Propofol Abuse and a Pattern Analysis of the Literature (n=21)

- Welliver M, et al. Two New Case Reports of Propofol Abuse and a Pattern Analysis of the Literature. IJANS, 1(1);2012

Two New Case Reports of Propofol Abuse and a Pattern Analysis of the Literature (n=21)
- Healthcare providers are the most frequent propofol abusers (n = 14, 67%). Nurses (n=7, 33%) Physicians (n=7, 33%) Anesthesia providers (MD, CRNAs) (n = 6, 28%)

Welliver M, et al. Two New Case Reports of Propofol Abuse and a Pattern Analysis of the Literature. IJANS, 1(1);2012

Two New Case Reports of Propofol Abuse and a Pattern Analysis of the Literature (n=21)
- Primary access is hospital drug diversion (n = 15, 71%). False prescription is another mode of access (n = 2, 10%).

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Two New Case Reports of Propofol Abuse and a Pattern Analysis of the Literature (n=21)

- Healthcare providers are the most frequent propofol abusers (n=14, 67%). Nurses (n=7, 33%) Physicians (n=3, 33%) Anesthesia providers (MD, CRNA) (n = 6, 28%)
- Prior access is hospital drug diversion (n = 15, 71%). False prescription is another mode of access (n = 2, 10%).

**Regimen of abuse: Frequent, repetitive injections (n = 10, 48%) Punctuated by unconsciousness/awake cycles**

Underlying psychological unrest (n = 11, 52%) Anxiety, stress (n = 7, 33%) Depression, insomnia (n = 4, 19%)

Prior substance use (n = 11, 52%) Yes (n = 11, 52%) No (n = 3, 14%) Unknown (n = 2, 10%)

Narcotics (n = 3, 14%) Alcohol (n = 4, 19%) Other or poly-substance (n = 7, 33%)

Subjective effects (disclosed) (n = 11, 61%)
- Relief of anxiety, stress, or depression (n = 8, 38%)
- Induced, restful sleep (n = 3, 14%)
- Euphoria (n = 5, 24%)
- Craving (n = 5, 24%)
- Withdrawal (n = 2, 10%)

Welliver M, et al. Two New Case Reports of Propofol Abuse and a Pattern Analysis of the Literature. IJANS, 1(1); 2012
Addiction to Propofol: A Study of 22 Treatment Cases


A Study of 22 Treatment Cases

- History and clinical presentation of a cohort of health care professionals (HCPs) who have abused the drug propofol

- More likely to work in the operating theater, be female, and have training as an anesthesiologist or certified registered nurse anesthetist.

- Acute injuries from propofol intoxication uncovered abuse and initiated inpatient tx

- Depressive illness present

- History of earlier life trauma.
A Study of 22 Treatment Cases

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> High frequency of biological relatives with substance dependence.

10.1097/ADM.0b013e3182872901

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> Acute injuries from propofol intoxication uncovered abuse and initiated in-patient tx
> Depressive illness present
> History of earlier life trauma.
> High frequency of biological relatives with substance dependence.
> Subjective reason for why they began using propofol was to induce sleep.

2011

> 39 yo female Nurse Anesthetist
> Hospital diversion after vicodan Rx for ankle injury
> MSO4 x 6 months followed by propofol x 2 months
> Daily propofol injections for escape & stress reduction. Denies euphoria
> Daily propofol 5 cc (50 mg) IV bolus q 10-15 minutes until supply gone or interruption
> Withdrawal symptoms: emotional distress, anxiety, insomnia
> In-patient Tx x 28 days, out-patient x 6 wks. Relapse at 4 months (1 night binge). Readmitted
> Abstinent x 5 years

2011

> 41 yo female Nurse Anesthetist
> Hospital diversion after epidural fentanyl OD
> MVA x 2 driving during/after propofol inj./use
> 7 months fentanyl abuse followed by 2 months propofol use.
> Daily propofol 50 mg IV followed by 150 mg IV
> Euphoria, escape, induced restful sleep
> 14 weeks in-patient intensive therapy, immediate relapse, return to in-patient tx
> Abstinent x 4 yrs → 6 1/2

Propofol Has Addiction Potential!

> Increasing awareness of propofol’s actual Addiction/Dependence potential
> Greater understanding of propofol’s addictive effects
> Psychological (euphoric/sexual sensations)
> Physical (VTA/reward center dopamine receptor excitability)
Psychology Propofol Addiction

- Relief of stress, anxiety
- Desire to escape
- Euphoria
- Pro-naps
- Pharmacologic knowledge rationale
  - Short duration
  - No routine drug testing
  - Thought “non-addictive”

Problem Restated

Does propofol have addictive or dependence potential?

- a strong desire to take the drug,
- impaired control over its use,
- persistent use despite harmful consequences,
- higher priority given to drug use than to other activities and obligations,
- increased tolerance,
- physical withdrawal reaction when drug use is discontinued.

Substance Abuse and Addiction in Anesthesia

The Disease Model

(a CAUSAL model)

Exposure

- Anesthesia personnel risks
- Sensitization to propofol and opiates by aerosolized operating room environments
- Anesthesia addiction rate 15%²

Problem Restated

- Limit access to propofol
- DEA schedule control
- Maintain accountability
  - Propofol scheduling?
  - Support this policy
- Awareness
- Supportive policies
  - Peer support
- Zero tolerance
- Wellness initiatives

Welliver M, et al. IJANS, 1(1);2012

Addiction is NOT
- A lack of will power
- A moral issue
- A matter of intelligence

Addiction is a DISEASE

Addiction is a BRAIN disease
The brain’s a HARD organ - very complex and difficult to study
- There are no good tests for brain diseases (yet)
- So people with brain diseases start out at a disadvantage
- The symptoms of brain diseases are more likely to be labeled as “badness”

Risk factors in Anesthetists
- Irregular work hours, Sleep deprivation, need to be vigilant during long hours of surgery
- Stress
- Sensation/excitement seeking personality
- Desire to self-medicate
- Increased knowledge of drug pharmacodynamics
- Achievement oriented (67% with SA in the upper third of the class)

Addictive Behavior = Survival Behavior Gone Awry
- Over the course of evolution, we have developed circuitry in our brains that have promoted our survival
- Drugs of addiction activate this “survival circuitry” and with chronic use, essentially take it over
- In the late stages of addiction, an individual is basically a “survivalist” doing whatever it takes to acquire and use drugs regardless of the costs
The Neuron
- Communicates with neurotransmitters
- Example neurotransmitter: Dopamine (important in addiction)
- “Plastic” wiring – can change and adapt

“Survival Circuits” of the Brain
- Over our evolutionary history, circuits in the brain have evolved to accomplish the following:
  1. Identify things that promote survival (e.g. food, sex) = REWARD CIRCUITRY
  2. Record information that will help us find those things again = MEMORY CIRCUITRY
  3. Continue to remind us to keep getting those things that are important = MOTIVATIONAL CIRCUITRY
- THIS IS THE BASIC SURVIVAL CIRCUITRY, Some call this the “GO CIRCUITRY”

Survival Scenario -- INITIAL LEARNING
1. Reward: Liking of the Banana
2. Memory: Remembering aspects of banana
3. Motivation: Wanting more banana

Reward circuitry releases DOPAMINE; Facilitates learning – strengthens the connections between these structures; with many encounters, strong learning

Survival Scenario – REPEAT ENCOUNTER
Memory: BANANA RECOGNIZED
Previous learning allows the very sight of the BANANA to lead to banana-obtaining behavior
Motivation: MOTIVATION TO GET/CONSUME BANANA
**Survival Circuitry is Modulated**
- survival circuitry, a.k.a. the “GO” circuitry
- As humans evolved and human society became more complex, needed a means to moderate this circuitry
- Further development of cerebral cortex, particularly frontal cortex, allowed humans to keep survival circuitry in check

**Survival Scenario: DELAYING GRATIFICATION**
- Memory: BANANA RECOGNIZED
- Motivation: MOTIVATION TO GET/CONSUME BANANA
- Cognitive control/inhibition/thinking: PREVENTS IMMEDIATE EATING FOR LONG TERM GOAL (e.g. USING BANANA FOR SEED)

**Summary**
- Survival (“GO”) circuitry:
  - Identifies rewards
  - Records information about rewards
  - Initiates motivation to get more reward
- Inhibitory cortical areas (“STOP”) circuitry
  - Inhibits survival circuitry
  - Allows for long-term planning, thinking (and morality!)

**EXPOSURE TO DRUGS**
- HEIGHTENED DOPAMINE RELEASE AND REWARD – 'EUPHORIA'
- HEIGHTENED MOTIVATION – 'GO' MODE
- IMPAIRED COGNITIVE CONTROL – JUDGMENT, PLANNING IMPAIRED
- CHANGES IN NEURONS (LEARNING) ARE ALMOST IMMEDIATE;

**HIJACKING THE SURVIVAL CIRCUITRY**
- All drugs of abuse cause release of dopamine – in greater quantities than natural rewards

11/2/2013
Long Term Consequences

- With repeated and frequent use, a series of neuroadaptations occur (example: down regulation of receptors)

- In reward circuits, reduced sensitivity to natural rewards
- Less "euphoria" from the drug itself
- Motivational circuitry hypoactive when it comes to seeking natural rewards...
- ...but in a drug-withdrawn state, it can become hyperactive when the addict is stressed or presented with drug-related cues
- Frontal areas become less active in general, but can also become hyperactive when presented with drug-related information

Survival Encounter: DIMINISHED NATURAL REWARD

- Memory: BANANA RECOGNIZED
- Reward: Little response
- Motivation: Little motivation
- Inhibition: Less inhibition, less planful

DRUG ENCOUNTER AFTER YEARS OF USE

- Seeing the drug, activates memories
- Very strong, near permanent learning, connecting memories to motivational circuit
- Go mode activated
- Previously hypoactive cortex is now hyperactive, instead of stopping the go mode, it may be "helping out"...

Hijack is complete

- After chronic use, “Survival Circuitry” becomes less and less sensitive to natural rewards, only responding to drug of abuse
- Less and less cortical activity; less planning, less thinking of the future, the past. Only active when thinking about drugs of abuse
- The person becomes completely focused on drugs, as if survival depends on it
- That person will lie, cheat, steal and do whatever it takes to “survive”
- Leads to baffling and confusing behavior...

“Survivalist Behavior” of the Addict

- For a person in “survivalist mode,” the only guiding moral principle is survival – what’s best for #1
- Long term goals give way to short term immediate gratification – e.g. they want everything and want it now
- Self-centered thinking – e.g. Addicts early in recovery can be very demanding and entitled – don’t understand why family is not supportive of them
- Deceit is rampant – e.g. “conning behavior,” a person will deny use, even when you have a UDS that is clearly positive
- All of this behavior is totally justified if you’re doing it for your survival (reality television has demonstrated this repeatedly)
Further “baffling” behavior: amazing lack of insight

- Despite compromised cortical function, the universal self-perception is that the person is still in control – the addict is often the last person to realize there is a problem
- The hardest part is getting addicts to accept this loss of control
- Society’s view: addictive behavior is “moral failing” – people should be “in control”
- In fact, those areas that are responsible for self-control are compromised at a basic neurobiological level (i.e. it’s a biological failing, not a moral one)

Is the “Hijacking” permanent...

- It is possible that if one uses enough over sufficiently long enough time, many changes in the brain are long-lasting and possibly permanent
- As such, science generally thinks of addiction as chronic disease, not unlike asthma, diabetes
- Relapse rates for addiction similar to that of these other diseases, about 40-60%
- There is hope, however, because despite the lack of a “cure”, there are effective treatments
NEVER, EVER, EVER, EVER, EVER DO AN INTERVENTION ALONE!!!!

What is Intervention?
- Action(s) taken based on the desire of family, friends and other concerned persons to take an active role in assisting another person to change unacceptable or self-destructive behavior

Goals
- Immediate admission into a comprehensive treatment facility with a health care professionals program
- Evaluation for physical co-morbidities

Goals
- Evaluation for detoxification issues
- Evaluation for psychiatric co-morbidities

Goals
- Evaluation for disability
- Beginning of long term treatment process
**Pre intervention Checklist**
(Remember the A's)
- Attendance
- Appearance
- Attitude
- Affect
- Anger (out of proportion)

**Data Collation**
- All personnel files
- Time line clear chronography
- Clinical records

**Data Collation**
- Objective observations (never interpretive or judgmental)
- On 5-9-09 you asked me to sign your waste for 15 cc of fentanyl and I never saw you waste it.

**Plan A & B**
- Make sure HR and family are on board!
- A professionally trained interventionist leading the team is best.

**Plan A & B**
- Make sure of immediate bed availability at an inpatient CD treatment facility with an addictionologist, addictions psychiatrist and a well established health care professionals program. Preferably a program with extensive experience with anesthesia folks.
Plan A & B

• Be clear about consequences of non compliance

The PAAC recommend that all chemically dependent anesthesia professionals and students receive:

• Inpatient Treatment at a Substance Abuse and Mental Health Services Administration (SAMHSA) certified Inpatient Comprehensive Addiction Treatment Center experienced in treating health care professionals.

The PAAC recommend that all chemically dependent anesthesia professionals and students receive:

• Completion of a minimum of 28 days (also termed “short term”) of inpatient treatment is recommended, with 90 days of treatment (also termed “long term”) being most desirable and offering the highest success rate.

The treatment center chosen should at a minimum include:

• Comprehensive evaluation and treatment recommendations by an American Society of Addiction Medicine (ASAM) board certified addictionologist in all cases.

• Evaluation by an American Academy of Addiction Psychiatry (AAAP) boarded Addiction Psychiatrist where appropriate.

The treatment center chosen should at a minimum include:

• Appropriate neuro-psychiatric and or psychometric testing where appropriate.

• When detoxification is medically indicated, inpatient medically supervised detoxification.

The treatment center chosen should at a minimum include:

• Emphasis on a long term 12 step model of abstinence based recovery.

• Evaluation of suitability for, and timing of, the return to anesthesia practice.
Texas Peer Assistance Program for Nurses

non-punitive, confidential and voluntary alternative to reporting RNs and LVNs to the Texas Board of Nursing.

In Summary....
• Addiction is a chronic progressive fatal disease, affecting all aspects of society
• Anesthesia providers have an inherent risk and susceptibility due to the nature of our work
• Getting treatment right the first time is imperative!

In Summary.....
• We must, as a profession, help each other to help one another

Experience from the “Trenches”
• No one wants to think they have a problem that they can’t control
• Addicts of all stripes will direct attention away from themselves (e.g. someone else is worse off, people trying to help have never “been there”)
• Addicts new to recovery will be in a hurry to get “back on track” – but exposure to risks too early can lead to relapse

Experience from the “Trenches”
• Addicts will use initial successes as evidence that they are “cured”
• All of the above will lead to resistance to continued follow-up and after care
• Reminding a scientifically/medically minded person about the neurobiology of addiction may help curb these typical addict tendencies

Resources for Anesthetists
Anesthetists in Recovery (AIR)
• AIR’s recommendations (per AANA website)
• Re-entry must be structured
• Back-to-work contracts should be used
• Medication: Naltrexone (a narcotic antagonist), Antabuse®, (perhaps Suboxone should be added?)
• Random drug screens
PEER ASSISTANCE AND ADVOCACY

Peer Assistance Hotline
800-654-5167

Anesthetists in Recovery (AIR)
215-635-0183

Partners in Recovery (PAIR)