# **SUD CURRICULUM** Committee on Occupational Health John Tetzlaff, M.D. (Coordinator and Primary Author) Cleveland Clinic November 12, 2015

<u>Sections</u> Page 2: Content Outline Page 8: Model Curriculum Page 11: Syllabus Page 18: Bibliography and References

# Substance Use Disorder (SUD) – Content Outline

- I. History of chemical dependency by anesthesia providers
  - a. Scientists in the 19th century experimented on themselves
  - b. Self-administration of drugs
  - c. Non-medicinal uses
    - i. Ether
    - ii. Nitrous oxide
    - iii. Chloroform
  - d. Early anesthetic drugs
    - i. Cocaine
    - ii. Morphine
  - e. One of the most serious occupational risk of giving anesthesia
- II. Scope of the problem
  - a. Cause of death data for physician anesthesiologists
    - i. Fear of cancer and organ toxicity from working with potent drugs
    - ii. Actually, no increase in cancer, heart, lung, liver or kidney disease
    - iii. Bruce (1968) low death rate, except three times as much suicide
    - iv. Lew (1979) 6.95 accidental (higher), 6.2 percent suicide, 3.4 times greater in young males
  - b. Higher suicide rate in physicians compared to lay public (Williams, 1971)
  - c. Suicide rate higher in anesthesiologists than physicians in general (Blachy, 1963)
  - d. Incidence of SUD in Anesthesia providers
    - i. Booth (1997) 1.6 percent/year for residents, 1 percent/year for faculty
    - ii. Collins (2005) 80 percent of programs with a case, 19 percent with a death, comparable incidence in D.O. programs
    - iii. Ward (1982) 1 percent/year for first five years
    - iv. Gravenstein (1983) 1 percent/year, 7 out of 44 cases died
    - v. Berry (2000) United Kingdom, 39 percent of departments with a case within a 10-year interval
    - vi. Weeks (1993) comparable data to Berry's report within Australia, New Zealand
    - vii. Bell (1999) incidence same or greater in CRNA, SRNA
    - viii. Warner (2013) ABA database, 0.86 percent SUD in residents, 7.3 percent mortality, 43 percent 30-year relapse rate
    - ix. Warner (2015) ABA database part 2, death in 14.3 percent of SUD vs. 1.3 percent controls. 15-fold increase to not finish residency, tenfold not to become board certified, sevenfold more likely to have adverse licensure action.

- x. Rosenberg (1986) comparable incidence in oral surgery programs that provide anesthesia training, proportional to time in anesthesia
- xi. Spiegelman (1984) 10 percent mortality
- III. Causes of SUD in Anesthesia Providers
  - a. Familiarity with drugs
    - i. Access
    - ii. Repeated experience with administration and observation of effects
    - iii. Advanced parenteral administration skills
    - iv. Pre-addictive behavior during medical school
    - v. Illicit drug experiences in the past
      - 1. Drawn to anesthesia by access
      - 2. "The Candy Store"
  - b. Occupation exposure to the addictive drugs
    - i. Deliberate self-exposure (self-medication)
      - 1. High rate of SUD follows
    - ii. Contact in the workplace
      - 1. During opening of ampules
      - 2. On anesthesia work surfaces in O.R.
      - 3. From exposure to exhaled patient gasses
    - iii. Neurochemistry of addiction
      - 1. Chemical changes in brain reward centers
      - 2. Down-regulation of D-2 dopamine receptors
      - 3. Creation of reactive oxidative species creating electron transfer by addictive substances
      - 4. Quinone metabolites of propofol/fentanyl cause electron transfer
    - iv. "Start-to-Finish" controlled drug handling
      - 1. Unique to anesthesia
      - Decide to medicate, choose drug, draw up drug, administer the drug, observe the effect, chart the administration and handle waste documentation. All with minimal, if any assistance. No one else in the medical center does this.
      - 3. High level of parenteral administration skills
      - 4. Ideal training for self-medication
      - 5. Drawn to anesthesia by the "chemical solution" to problems (hemodynamics, pain, anxiety, etc.)
      - Fallacy of control "If I can do it to my patients, I can do it to myself. I can handle it". First time that an opioid is self-administered, there is addiction, the individual just doesn't know it yet.

- v. Work environment
  - 1. Work in isolation
  - 2. Long work hours
  - 3. Production pressure
  - 4. High stress environment
  - 5. Self-esteem issues
  - 6. Delayed gratification
- vi. Psychiatric co-morbidity
  - 1. Depression
    - a. Increased incidence in anesthesia
    - b. Higher in residents than staff
    - c. Seasonal
    - d. Self-medication as a symptom
    - e. Associated with suicide
    - f. Associated with increased relapse rate
    - g. Associated with addiction
  - 2. Personality disorders
    - a. Associated with SUD
  - 3. Primary psychiatric diagnosis
  - 4. High risk behavior
- IV. Chemicals associated with SUD and anesthesia
  - a. Before 1980
    - i. Meperidine
    - ii. Diazepam
    - iii. Barbiturates
  - b. After 1980
    - i. The fentanyl family
      - 1. Including intranasal remifentanil
    - ii. Nitrous oxide
    - iii. Midazolam
    - iv. Ketamine
      - 1. Associated with prior psychotropic illicit drug use
    - v. Lidocaine
      - 1. Dysphoria
    - vi. D-tubocurarine ("I just relaxed")
    - vii. Ephedrine
    - viii. Cocaine
    - ix. Antihistamines

- c. Other drugs with increasing incidence
  - i. Propofol tenfold increase over last decade
  - ii. Inhaled agents- high morbidity, mortality, relapse rate
  - iii. Less tight substance controls
- V. Risks of Diversion
  - a. Transmission of infectious diseases (Hepatitis C)
    - i. Patients
    - ii. Coworkers
  - b. Public perception of addiction within anesthesia
  - c. Violation of state, federal law
    - i. Felony
    - ii. Loss of licensure
    - iii. Denial of board certification
    - iv. Revocation of board certification
- VI. Detection of SUD
  - a. Self-reporting (rare)
  - b. Overdose, accidental death, coma
  - c. Direct observation
  - d. Investigation of suspicious behavior
  - e. Unexplained changes in performance
  - f. Random drug testing
    - i. Urine toxicology
    - ii. Hair analysis
  - g. Electronic screening of use patterns
- VII. Re-entry
  - a. Addiction as a disease
    - i. Federally protected disability
  - b. In-patient treatment, extended interval
    - i. Best at center with specialty expertise
  - c. Graded re-entry (no nights, weekends for an extended interval)
  - d. Re-entry contract
    - i. Handling of all substances by another provider
    - ii. Random drug testing strictly enforced
    - iii. Attendance at meetings with attendance documented
    - iv. Naltrexone or buprenorphine considered
    - v. Monitoring of performance, behavior
  - e. Favorable outcome
    - i. Physicians do better in rehab

- ii. Physicians do better in rehab for prescription opioids
- iii. Role of Physician Health Committees (PHC)
- iv. Risk of job change
  - 1. Loss of PHC oversight with state change
- f. Unfavorable outcome
  - i. Failure to finish training
  - ii. High relapse rate
  - iii. Death as a presentation of relapse
  - iv. 9 percent mortality (Collins, 2005)
  - v. High career relapse rate (Warner, 2015)
  - vi. Re-exposure to triggering environment

#### VIII. Prevention

- a. Healthy lifestyle
- b. Management of stress
- c. Education of trainees
- d. Prevention of diversion
  - i. Electronic dispensing
  - ii. Surveillance
  - iii. Random testing of waste solutions
  - iv. Electronic use profiles
- e. Random drug testing
  - i. Cost
  - ii. Randomization technique versus bias
  - iii. "beat the test"
  - iv. Intrusion of the clinical work flow
  - v. Medical Review Officer
  - vi. Urine versus hair versus saliva
  - vii. "One strike and you're out"
  - viii. Perception of the medical community
    - 1. "Drug testing- get used to it"
  - ix. Government position
    - 1. Suggested universal random testing of those providers with access to controlled drugs
  - x. Lay public
    - 1. "Junkie in the O.R." (Men's Health, October 2006)
    - 2. USA Today (April 2014)
    - 3. Newsweek (June 2015)
- f. Systematic detection of diversion

- i. Investigation of all discrepancies
- ii. Multi-disciplinary response team
- iii. Random chemical analysis of waste solutions
- iv. Zero tolerance for diversion

# SUD – Model Curriculum

## PGY-1

Wearing Masks 1 Annual Departmental Grand Rounds Stress Management and Personal Well-Being Orientation to hospital physician health committee Content Outline II, III

Journal Club –

- 1. Bryson EO, Silverstein JH. Addiction and substance abuse in Anesthesiology. *Anesthesiology*. 2008;109:905-17.
- 2. Gravenstein JS, Kory P, Marks RG. Drug abuse by anesthesia personnel. *Anesth Analg*. 1983:62467-72
- 3. Fitzsimons MG, Baker KH, Lowenstein E, Zapol WM. Random drug testing to reduce the incidence of addiction in anesthesia residents: Preliminary results from one program. *Anesth Analg.* 2008;107:630-5.
- Tetzlaff J, Collins GB, Brown DL, Leak BC, Pollock G, Popa D. A strategy to prevent substance abuse in an academic anesthesiology department. *J Clin Anesth*. 2010;22:143-150

### PGY-2

Wearing Masks 2 Annual Departmental Grand Rounds Impairment and Anesthesiology Residency–PowerPoint Content Outline I, II, III, IV Journal Club –

- 1. Warner DO, Berge K, Sun H, Harman A, Hanson A, Schroeder DR. Substance use disorder among anesthesiology residents, 1975-2009. *JAMA*. 2013;310:2289-2296
- 2. Warner DO, Berge K, Sun H, Harman A, Hanson A, Schroeder DR. Risks and Outcome of substance use disorder among anesthesiology residents. A matched cohort analysis. *Anesthesiology*. 2015;123:1-8.
- 3. Booth JV, Grossman D, Moore J, Linberger C, Reynolds JD, Reves JG, Sheffield D. Substance abuse among physicians: A survey of academic anesthesiology programs. *Anesth Analg.* 2002;95:1024-30.
- Collins GB, McAllister MS, Jensen M, Gooden TA. Chemical dependency treatment outcomes of residents in anesthesiology: Results of a survey. *Anesth Analg*. 2005;101:1457-62.
- McAuliffe PF, Gold MS, Bajpai L, Merves ML, Frost-Peneda K, Pomm RM, Goldberger BA, Melker RJ, Cendan JC. Second-hand exposure to aerosolized intravenous anesthetics propofol and fentanyl may cause sensitization and subsequent opiate addiction among anesthesiologists and surgeons. *Medical Hypothesis*. 2006;66:874-882
- 6. Wischmeyer PE, Johnson BR, Wilson JE, Dingmann C, Bachman HM, Roller E, Vu Tran Z, Henthorn TK. A survey of propofol abuse in academic anesthesia programs. *Anesth Analg*. 2007;105:1066-71.

 Wilson JE, Kiselanova N, Stevens Q, Lutz R, Mandler T, Vu Tran Z, Wischmeyer PE. A survey of inhalation anaesthetic abuse in anaesthesia training programs. *Anaesthesia*. 2008;63:616-20.

## PGY-3

Annual Departmental Grand Rounds Chemical Dependency and Anesthesiology–PowerPoint Risks Associated with Diversion of Controlled Substances Content Outline V, VI, VIII Journal Club –

- 1. Berge KH, Dillon KR, Sikkink KM, Taylor TK, Lanier WL. Diversion of drugs within health care facilities, a multiple-victim crime: Patterns of diversion, scope, consequences, detection, and prevention. *Mayo Clin Proc.* 2012;87:674-82
- 2. Hellinger WC, Bacalis LP, Kay RS, et al. Health care- associated hepatitis C virus infections attributed to Narcotic diversion. *Ann Int Med*. 2012;156:477-82.
- 3. Domino KB, Hornbein TF, Polissar NL, Renner G, Johnson j, Alberti S, Hankes L. Risk factors for relapse in health care professionals with substance use disorders. *JAMA*. 2005;293:1453-60.
- Skipper GE, Campbell MD, DuPont RL. Anesthesiologists with substance use disorders: A 5 year outcome study from 16 state physician health programs. *Anesth Analg*. 2009;109:891-6.

## PGY-4

Annual Departmental Grand Rounds Orientation to State Physician Health Program Content Outline I-VIII (revisited) Journal Club –

- Vigoda MM, Gencorcelli FJ, Lubarsky DA. Discrepancies in medication entries between anesthetic and pharmacy records using electronic databases. *Anesth Analg*. 2007;105:1061-5.
- 2. Chisholm AB, Harrison MJ. Opioid abuse amongst anaesthetists: a system to detect personal usage. *Anaesth Intensive Care*. 2009;37:267-71.
- 3. Epstein RH, Gratch DM, Grunwald Z. Development of a scheduled drug diversion surveillance system based on analysis of atypical drug transactions. *Anesth Analg*. 2007;105:1053-60.
- 4. Epstein RH, Gratch DM, McNulty S, Grunwald Z. Validation of a system to detect scheduled drug diversion by anesthesia care providers. *Anesth Analg*. 2011;113: 160-4.
- 5. Bryson EO, Levine A. One approach to the return to residency for anesthesia residents recovering from opioid addiction. *J Clin Anesth*. 2008;20:397-400.

#### **Chemical Dependency and Anesthesiology – Syllabus**

The discovery of anesthesia and addiction to the drugs used to provide anesthesia have a common origin. Cocaine had a social use profile before its incidental discovery as a topical anesthetic. Experiments with injection of cocaine to anesthetize plexus and peripheral nerves led to addiction of early 20th century master surgeons, such as Halsted, who performed the experiments.<sup>1</sup> Early experimentation with ether, nitrous oxide and chloroform also caused psychological and even physical addiction. It is not surprising, therefore, that addiction to anesthetic drugs and anesthesiology remain linked and that addiction remains the most prevalent, serious occupational health risk associated with anesthesia. Because of the morbidity, much is known.

#### Scope of the Problem

Although addiction to anesthetic drugs has become a prominent issue for anesthesiology in the United States, this issue is neither new nor restricted to the U.S. In an early report, Bruce<sup>2</sup> reported on the mortality and causes of death of anesthesiologists, noting lower death rates in most categories, except suicide, which was three times the rate for other physicians (1947–1966). Lew<sup>3</sup> reported similar data (1954–1976), with lower overall age-adjusted mortality, except for 6.2 percent suicide (two-times normal) and 6.9 percent "accidental." Although the suicide rate is higher in general for physicians<sup>4</sup>, suicide in anesthesia providers is highly associated with addiction.<sup>5</sup> Ward<sup>6</sup> surveyed residency and nurse anesthesia programs for 10 years prior to 1982. With a 74 percent response rate, the incidence of addiction was 1 percent per year of giving anesthesia for the first five years. Gravenstein<sup>7</sup> reported the same 1 percent addiction rate with an alarming mortality of seven providers out of 44 reported. The issue also is not restricted to the United States. Berry<sup>8</sup> surveyed 304 departments of anesthesia in the United Kingdom and Ireland and found cases in this interval (1990–99) in 39 percent of departments reporting (71.7 percent response rate) and drew the remarkable conclusion that one anesthesia provider per month in the United Kingdom was disabled by addiction. Weeks reported a comparably high incidence for Australia and New Zealand.<sup>51</sup> The risk is not limited to physician anesthesiologists, with comparable or higher rates in CRNAs, with as high as 10 percent risk for a full career.<sup>9</sup>

Even though the issues are now well known and education and prevention steps are widely in use, the incidence has not seemed to change. Booth<sup>10</sup> surveyed 133 programs in 1997, achieved a 93 percent response rate, and reported 1.6 percent addiction rate in residents and 1 percent in faculty, despite 47 percent of respondents reporting increased education and steps to prevent diversion of controlled drugs. Collins<sup>11</sup> surveyed 176 programs (M.D. and D.O.), achieving a 66 percent response rate, with 80 percent of responding programs reporting at least one incident in the interval (1991–2001) with 19 percent reporting mortality. If anything, the mortality may actually be increasing, by comparison of the Collins<sup>11</sup> data for the 1990s with the 10 percent mortality reported by Spiegelman.<sup>12</sup> Warner reviewed the ABA database between 1975 and 2009 and found the incidence to be highest after 2003 with an overall incidence of 0.86 percent incidence at some time during training and a 7.3 percent mortality of those who demonstrated substance abuse disorder.<sup>103</sup>

#### Speculation about the Cause

While there will never be absolute proof, there is a consensus that a variety of issues combine to create a high risk of addiction. These include exposure to the drugs, familiarity with their pharmacology, access, stress and the uniquely addictive properties of anesthetic drugs. Prior addictive and high-risk behaviors seem to be highly associated. Chemical experimentation in medical students has been reported<sup>13</sup> be 30 to 50 percent, and several reports have suggested that prior illicit drug use may motivate (consciously or unconsciously) the individual to choose anesthesia.<sup>11,14</sup> In a large series, high-risk behavior was found to be highly predictive of addiction.<sup>15</sup>

Occupational exposure seems to be a clear association. As previously mentioned, early experiments to create safe anesthesia techniques (nitrous oxide, ether, chloroform and cocaine) created victims of addiction in the investigators. The high incidence identified is even more remarkable when the early presentation of addiction is considered. In both physicians and CRNAs, the incidence of addiction is highest during the first five years of giving anesthesia.<sup>6,16,17,18,52</sup> There is other suggestive evidence that the risk is giving anesthesia. Oral surgery residents in some maxillofacial residency programs receive extensive training (often from physician anesthesiologists) in giving anesthesia, and they report the same incidence of addiction proportionate to time in anesthesia with the same drug profile.<sup>17</sup> The converse is equally true— physicians who do not practice anesthesia (internists) have a lower rate of addiction and suicide compared to an age and gender matched cohort of physician anesthesiologists.<sup>53</sup>

Simply experiencing clinical anesthesia alone is too simple of an explanation for the risk of addiction. Gold has presented a provocative hypothesis that aerosol contact with fentanyl during opening of fentanyl ampoules<sup>1</sup> or from exhaled breath of patients<sup>72</sup> or contact with fentanyl or propofol from working surfaces within the operating room<sup>77</sup> may cause neurochemical changes in the brain that predispose some providers to become addicted.<sup>73</sup> They confirmed this hypothesis by detecting fentanyl and propofol in the air in several locations within active operating rooms.<sup>78</sup> The American Society of Anesthesiologists (ASA) Committee on Occupational Health has responded with the observation that exposure to fentanyl as a cause is preliminary data that should be further evaluated, citing a variety of methodological issues.<sup>57</sup> The neurochemistry of addiction is becoming well understood, with chemical changes in the reward centers leading to exaggerated need for drug acquisition and exaggerated reward from experience with the drug.<sup>89</sup> Another possible explanation for addiction is a lower density of dopamine receptors in reward centers, resulting in less reward from natural reinforcers.<sup>91,92</sup> The changes in the D-2 dopamine receptor are persistent or permanent and have the same molecular morphology as brain injury.<sup>113</sup> In adults with addiction to gambling increased activity in the reward center in response to gambling prompts is detected by functional MRI, compared to controls.<sup>101</sup> Dopamine downregulation has also been implicated in eating disorders, analogous to substance-use disorder.<sup>114</sup> A molecular mechanism for the sensitization has been suggested by Kovacic, who reports that addictive substances have in common the ability to create reactive oxygen species (ROS) that result in electron transfer that activates brain reward centers.<sup>80</sup> Further work has established that metabolites of propofol and fentanyl create these ROS messengers.<sup>81</sup>

Other elements of anesthesia practice that contribute to addiction are less objective but undisputed. The anesthesia provider is unique in organized medicine in providing "start-to-finish" administration of controlled substances. Even the most junior resident physician will obtain fentanyl, draw it up, inject, observe the effect, chart the intervention and handle the accounting of waste, often without any observed assistance. No other resident physician routinely has this experience or possesses these skills. New anesthesia providers also rapidly learn the clinical pharmacology of these substances by observation, reading, and trial and error. This creates both the skill for self-medication and the more ominous skill to achieve painless suicide. Selfmedication may be an occupational hazard of the operating room related to stress and lack of positive reinforcement. New anesthesia providers get a disproportionate level of the work, their skill level is lower and, as a result, their efficiency is low. And the operating room is rough on newcomers. These factors, combined with some natural curiosity about the drugs being used, create an unfortunate propensity for anesthesia newcomers to self-mediate. They know how and what to use, but the fallacy in the highly educated provider is that these anesthesia newcomers can control the experience. Unfortunately, this initiates a cascade of use and addiction that accelerates at a very rapid rate. Gold<sup>1</sup> reports a case where a single experiment with intranasal accelerated to injection of 30 mL/day of sufentanil within 30 days. In the context of high stress, reduced self-esteem and availability of synthetic opioid, Ward<sup>18</sup> states that control is gone after the first self-medication even though the individual doesn't know it. Farley<sup>19</sup> identifies other unique element of anesthesia practice, including a "chemical solution" to solving problems and the isolated nature of anesthesia practice. Moleski<sup>20</sup> further speculates that routine use of controlled substances minimizes the importance of tight accounting, desensitizing the individual to its relevance.

Other features may be triggering events for the subset of providers. Prior experience with substance abuse or high-risk behavior has been previously identified. A prior history of psychiatric illness (contributory or coincident) can be contributory in the addicted anesthesia provider.<sup>15,16,21</sup> Personality disorders<sup>74</sup> and primary psychiatric diagnoses<sup>75</sup> are commonly found in addicted physicians, and self-medication may represent a response to these symptoms.<sup>76</sup> Burnout and depression are reported to be prevalent within anesthesiology, particularly among physician anesthesiology residents.<sup>108</sup> Depression is known to be associated with suicide, and although complicated, may be linked to self-medication and addiction.<sup>82</sup> There is strong evidence for a genetic susceptibility to addictive behavior, especially the transition from abuse to dependency.<sup>88</sup> Self-medication of psychiatric symptoms is a major cause of relapse of substance abuse disorder.<sup>109</sup>

#### **Drugs Involved in Addiction for Anesthesiologists**

From the substance abuse literature, the progression of substance (ETOH to marijuana to cocaine) is a common observation. Addiction within anesthesiology does not follow this pattern. Although the incidence of addiction to drugs used in anesthesia is alarmingly high, the incidence of abuse of illicit drugs (alcoholism, THC, cocaine) is low. Addiction within anesthesia has always focused on anesthetic drugs. Prior to 1980, the drugs involved were meperidine, diazepam and barbiturates.<sup>22,23</sup> After 1980, addiction has been heavily concentrated in the fentanyl

family.<sup>6,10,17,19</sup> Although parenteral fentanyl is the rule, severe addiction to oral fentanyl has been reported; the victim was a nursing supervisor who lacked some of the parenteral administration skills.<sup>24</sup> While rapid metabolism would seem to make parenteral remifentanil abuse seem unlikely, intranasal self-administration has been reported as the entry point to a fentanyl addiction.<sup>79</sup> Midazolam<sup>17</sup> and ketamine<sup>25</sup> have been reported in addiction cases, as has nitrous oxide<sup>54</sup> and potent inhalation agents, such as enflurane.<sup>26</sup> In a survey of academic departments, 22 percent reported at least one incident with an inhaled agent with less than half of the individuals involved entering rehabilitation, less than 30 percent return to practice and a 26 percent mortality rate.<sup>64</sup> Propofol is the newest player on the scene with one case report<sup>27</sup> involving injection to unconsciousness up to 15 times per day. In another case report, propofol replaced a benzodiazepine because of superior sedative properties for the affected physician.<sup>110</sup> In a survey of academic anesthesiology programs from 1995–2005, Wischmeyer reported 18 percent of programs had a propofol abuse incident with 28 percent of the cases detected by death.<sup>71</sup> Repeated prior exposure to propofol may be causative, with experience of the euphoria leading to intense craving and psychological dependence.<sup>94,95,96</sup>

The addiction potential with anesthetic drugs has been reviewed. Propofol has been tested in volunteers and found to have properties associated with addiction,<sup>27</sup> although the pharmacokinetics predict a difficult abuse pattern, requiring either pump infusion or frequent, intermittent injection. The addictive potential for other uncommon substance has been predicted based on the side effect profile,<sup>28</sup> including local anesthetics (dysphoria), cocaine (euphoria, stimulation), anticholinergics (psychotomimetic), antihistamines (sedation) and ephedrine (stimulant). Ketamine has an obvious role in those with prior illicit psychedelic drug use, such as LSD, or PCP.<sup>25,29</sup>

#### Detection

Self-reporting of serious addiction is uncommon. Direct observation of abuse and audits that confirm suspicion are the most common means of detection. Unfortunately, suicide, accidental death and coma combined are more common than self-reporting.<sup>19</sup> Suicide during evaluation of possible addiction is a serious issue.<sup>30</sup> Intervention must be conducted carefully, with the goal of getting the suspected addict into a safe treatment facility, using progressively increasing motivators like reporting, termination and, as a last resort, police involvement. In one case, the cause of death was determined to be propofol by hair analysis where blood and urine toxicology were negative.<sup>31</sup> In cases where suspicion is high and urine toxicology is repeatedly negative, hair analysis has detected addiction to fentanyl, sufentanil and alfentanil.<sup>55</sup> Detection of drugs with brief half-lives such as ketamine, midazolam and propofol are difficult or impossible in routine toxicology,<sup>27,32</sup> and may require either observed abuse and rapid "for-cause" screening or hair analysis.<sup>33,55</sup> The fentanyl family is especially difficult to detect because of the brief plasma halflife and non-detection of metabolites.<sup>24,34</sup> A computer profile of drug use to detect outliers might be a better approach.<sup>35</sup> Epstein has prospectively applied this computer profile and demonstrated that it detects diversion months before clinical detection, although its sensitivity needs to be refined before it becomes a first line tool, due to false positives.<sup>87</sup> Another electronic approach using run charts comparing individual use against time to identify upward trends in individuals also shows promise.<sup>90</sup> A promising opportunity for detection is a urine assay for detection of the glucuronide metabolites of propofol, which remains present in the urine for up to three days after exposure.

The urgency for detection of substance diversion has never been low, but it has increased dramatically with the disclosure that individuals involved in diversion have used techniques that have resulted in injury to patients. Clusters of hepatitis infection have been traced to diversion practices of an infected health care provider.<sup>98</sup> Irresponsible handling of diverted substances and/or equipment presents a risk to all other health care workers.<sup>99</sup> The risk is particularly relevant given the variable level of prevention of diversion from institution to institution and state to state.<sup>100</sup>

#### **Re-entry**

Addiction is a disease as well as a federally protected disability, as long as the addict remains in treatment.<sup>67</sup> Treatment only succeeds when evaluation reveals addiction and the victim is able to fully acknowledge their addiction. This is rarely, if ever, successful without in-patient treatment, graded re-entry with a contract, handling of addictive substances by other providers, and random testing, including periodic hair samples. More controversial are the pharmacotherapeutic options, including naltrexone<sup>111</sup> and buprenorphrine.<sup>112</sup>

Even with the risk, a simple majority of providers will want to re-enter anesthesia. The outcome, however, is not always promising. In general, physicians have a better outcome in rehabilitation from addiction<sup>102</sup> than non-physicians<sup>36</sup> even from opioid (prescription) abuse.<sup>60</sup> The California Physician Diversion Program's data suggests that this rehabilitation outcome also applies to addiction involving physician anesthesiologists, although their definition of recovery may be very generous.<sup>37</sup> Some other data is in agreement,<sup>38</sup> however, there is also evidence that re-entry is both ineffective and risky. Collins reports a 40 percent failure rate with re-entry of residents and 9 percent mortality. Re-entry for student nurse anesthetists has the same poor prognosis.<sup>39</sup> Menk reports 34 percent successful re-entry for residents with 16 percent having the first presentation of relapse as death.<sup>40</sup> Bryson<sup>58</sup> reported a graded re-entry of residents involving work in a simulation center for the first 12-15 months prior to re-entry. The value of this approach has been challenged<sup>59</sup> in light of the 60 percent relapse rate they report, and there remains a serious doubt that re-entry is ever the right choice for a resident.<sup>(67</sup> The failure rate, the cost to the department with attempted re-entry, and the mortality rate led Berge,<sup>(68</sup> in an editorial in the journal Anesthesiology, to advocate "one strike and you're out," a universal prohibition to reentry. Oreskovich<sup>69</sup> and others responded to this strong position with circumstances where this would be excessive and highlighted the role of the highly effective state Physician Health Committees (PHC). It may be that the resident failure rate is related to the less universal role of PHC in the re-entry of residents.

Hedberg<sup>41</sup> has attempted to quantify the process by defining criteria that predict success and failure with re-entry. He has divided anesthesia providers in rehabilitation into three categories based on specific criteria; category two requires delay and re-evaluation of individuals after one to two years, category three consists of individuals who should never practice anesthesia. Domino reports greatly increased risk of relapse when there is a coexisting psychiatric disorder,

family history of substance abuse, or in those addicted to opioid, with the increase even greater if more than one of these risk factors is present.<sup>56</sup> Re-entry may actually oppose the process of recovery by re-exposing the addict to the visual, olfactory or physical cues to the emotions that triggered self-medication and also may explain why delayed re-entry is required.<sup>65</sup> If re-entry is attempted, the focus should be on relapse prevention.<sup>84</sup> There is even risk of relapse from subsequent required medical care, if exposure to triggering substances (opioids, propofol) is required for medical or surgical care.<sup>93</sup>

#### **Prevention**

There is universal agreement that mandatory education about the risk of substance abuse, stress and fatigue management should be a part of all anesthesia training programs at the entry point and regularly thereafter. There is also general agreement that this education process should continue beyond residency, although this is less universally applied. Despite evidence that the majority of training programs have increased their education programs, Booth<sup>10</sup> reports no change in the incidence of substance abuse. Previous reports of inadequate education<sup>42</sup> have created the education but not decreased the risk. Increased effort to prevent the diversion of controlled substances has also been instituted in a majority of programs<sup>10,43</sup> including locked boxes, dispensing machines, video surveillance and satellite pharmacies. Some effect has been observed, including reduced controlled substance discrepancy.<sup>20</sup> Electronic data analysis can reveal average user profiles, and provide detection via outliers.<sup>20,35</sup>

The subject of random drug testing is controversial.<sup>83</sup> The almost infinite number of ways to tamper with urine toxicology screening must be considered.<sup>70,86</sup> The issue of false positives, even with the use of a medical review officer, remains an administrative issue with intense consequences.<sup>107</sup> Although a promising avenue in the future, detection of anesthesia drugs in oral fluid is not possible at this time.<sup>85</sup> In responses to the survey of Booth,<sup>10</sup> a majority of chairs favored random testing, although only two programs outside the military have instituted such a program. Fitzsimons<sup>61</sup> presented the first five years of one of these programs designed to prevent addiction which includes a random testing element and reported no addicted providers detected. The Department of Transportation (DOT) has had a random screening program for almost two decades for commercial drivers, railroad and airline pilots. Industry has followed, with more than 90 percent of companies with more than 5,000 employees having some kind of testing.<sup>44</sup> Random testing programs have been shown to reduce positives<sup>45</sup> and save health care dollars. Mike Scott, previous council to ASA, has written a review of random testing,<sup>46</sup> in which he identifies the AMA endorsement of "for cause" testing and discusses the unresolved legal issues with random testing. Although random testing is prohibited in 12 states, there are exceptions for industry involved in safety. The AMA expressed concerns in an editorial which discusses privacy, handling of false positives, confidential records and the approaches to randomization.<sup>47</sup> A more recent editorial in by Pham in JAMA advocated random urine testing for all physicians as a means of ensuring patient safety.<sup>104</sup> Although disputed in responding letters to the editor of JAMA based on lack of supporting evidence, <sup>105,106</sup> the same sentiment was echoed in an editorial in the New York Times ("Why Aren't Doctors Drug Tested?", March 12, 2014) which advocated universal drug testing for all health care workers with contact to controlled substances. DOT rules have created the need for the role of a Medical Review Officer, a physician with specific training to handle the

initially positive screen.<sup>48</sup> All recovering physicians are subject to random screening during recovery and any failure or absence requires action.<sup>49</sup> Collins'<sup>11</sup> data reveals a slightly higher rate of pre-employment screening (16 percent) and pre-employment toxicology screening. Based on the kind of data in Men's Health<sup>50</sup> ("The Junkie in the O.R.") and two recent cases that made headline news in the press on the East Coast, the lay public may begin to demand random screening. Media coverage of sensational issues regarding addiction of health care providers and diversion will only add to this message.<sup>115,116</sup> It is clear that detection during residency training is a responsibility of the residency program.<sup>62</sup> Failure to report provider impairment may incur legal liability for the anesthesia department, the hospital or anesthesia groups who know.<sup>63</sup> Regardless of the legal risk, protocols for handling of impairment and substance abuse should be present in every department.<sup>66</sup>

### Conclusion

Substance abuse is the most serious occupational safety hazard for anesthesiology. Causing devastating consequences to the career, morbidity, personal stress and death, it is a high-attractive target for prevention. The nature of anesthesia (working alone, production pressure, isolation) and the handling of highly addictive drugs are contributors. Up to 1 percent per year of residents may become addicted. The mortality rate of relapse may approach 9 percent. Prevention by education, tight control of controlled substance use, profiling for outliers and possibly random urine toxicology may be needed to arrest this serious hazard of providing anesthesia.

### <u>Bibliography</u>

### References

- 1. Gold MS, Byars JA, Frost-Pineda K. Occupational exposure and addictions for physicians: case studies and theoretical implications. *Psychiatr Clin N Am*. 2004;27(4):745-53.
- 2. Bruce DL, Eide KA, Linde HW, Eckenhoff JE. Cause of death among anesthesiologists. *Anesthesiology*. 1968;29(3):565-9.
- Lew EA. Mortality experience among anesthesiologists. *Anesthesiology*. 1979;51(3):195 9.
- 4. Williams SV, Munford RS, Colton T, et al. Mortality among physicians: a cohort study. *J Chronic Dis.* 1971;24(6):393-401.
- 5. Blachy PH, Osterud HT, Josslin R. Suicide in professional groups. *N Engl J Med*. 1963;268:1278-82.
- 6. Ward CF, Ward GC, Saidman LJ. Drug abuse in anesthesiology training programs. A survey: 1970 through 1980. *JAMA*. 1983;250(7):922-5.
- 7. Gravenstein JS, Kory WP, Marks RG. Drug abuse by anesthesia personnel. *Anesth Analg*. 1983;62(5):467-72.
- 8. Berry CB, Crome IB, Plant M, Plant M. substance misuse amongst anaesthetists in the United Kingdom and Ireland. The results of a study commissioned by the Association of Anaesthetists of Great Britain and Ireland. *Anaesthesia*. 2000;55(10):946-52.
- 9. Bell DM, McDonough JP, Ellison JS, et al. Controlled drug misuse by certified registered nurse anesthetists. *AANA J.* 1999;67(2):133-40.

- 10. Booth JV, Grossman D, Moore J, Lineberger C, Reynolds JD, Reeves JG, Sheffield D. Substance abuse among physicians: a survey of academic anesthesiology programs. *Anesth Analg*. 2002;95(4):1024-30.
- Collins GB, McAllister MS, Jensen M, Gooden TA. Chemical dependency treatment outcomes of residents in anesthesiology: results of a survey. *Anesth Analg*. 2005;101(5):1457-62.
- 12. Spiegelman WG, Saunders L, Mazze RI. Addiction and anesthesiology. *Anesthesiology*. 1984;60(4):335-41.
- 13. Epstein R, Eubanks EE. Drug use among medical students. *N Engl J Med*. 1984;311(14):923.
- 14. Gallegos KV, Browne LH, Veit FW, Talbott GD. Addiction in anesthesiologists: drug access and patterns of substance abuse. *QRB Qual Rev Bull*. 1988;14(4):116-22.
- 15. Yarborough WH. Substance use disorders in physician training programs. *J Okla State Med Assoc*. 1999;92(10):504-7.
- 16. Talbott GD, Gallegos KV, Wilson PO, Porter JL. The Medical Association of Georgia's Impaired Physician Program. Review of the first 1000 physicians: analysis by specialty. *JAMA*. 1987;257(21):2927-30.
- 17. Rosenberg M. Drug abuse in oral and maxillofacial training programs. *J Oral Maxillofac Surg*. 1986;44(6):458-62.
- 18. Ward CF. Substance Abuse. Now, and for some time to come. *Anesthesiology*. 1992;77(4):619-22.
- 19. Farley WJ, Talbott GD. Anesthesiology and addiction. *Anesth Analg.* 1983;62(5):465-6.
- 20. Moleski RJ, Easley S, Barash PG, Primer G, Shier NQ, Schrier RI. Control and accountability of controlled substance administration in the operating room. *Anesth Analg*. 1985;64(10):989-95.
- 21. Flaherty JA, Richman JA. Substance use and addiction among medical students, residents, and physicians. *Psychiatr Clin North Am*. 1993;16(1):189-97.
- 22. Hughes PH, Brandenburg N, Baldwin DC, Storr CL, Williams KM, Anthony JC, Sheehan DV. Prevalence of substance use among US physicians. *JAMA*. 1992;267(17):2333-9.
- 23. Hughes PH, Baldwin DC, Sheehan DV, Conard S, Storr CL. Resident physician substance use, by specialty. *Am J Psychiatry*. 1992;149(10):1348-54.
- 24. Hays LR, Stillner V, Littrell R. Fentanyl dependence associated with oral ingestion. *Anesthesiology*. 1992;77(4):819-20.
- 25. Moore NN, Bostwick JM. Ketamine dependence in anesthesia providers. *Psychosomatics*. 1999;40(4):356-9.
- 26. Musshoff F, Junker H, Madea B. An unusual case of driving under the influence of enflurane. *Forensic Sci Int*. 2002;128(3):187-9.
- 27. Zacny JP, Lichtor JL, Thompson W, Apfelbaum JL. Propofol at subanesthetic dose may have abuse potential in healthy volunteers. *Anesth Analg*. 1993;77(3):544-52.
- 28. Zacny JP, Galinkin JL. Psychotropic drugs used in anesthesia practice: abuse liability and epidemiology of abuse. *Anesthesiology*. 1999;90(1):269-88.
- 29. Dalgarno PJ, Shewan D. Illicit use of ketamine in Scotland. *J Psychoactive Drug*. 1996;28(2):191-9.

- 30. Crawshaw R, Bruce JA, Eraker PL, Greenbaum M, Lindemann JE, Schmidt DE. An epidemic of suicide among physicians on probation. *JAMA*. 1980;243(19):1915-17.
- 31. Iwersen-Bergmann S, Rösner p, Kühnau HC, Judge M, Schmoldt A. Death after excessive propofol abuse. *Int J Legal Med*. 2001;114(4-5):248-51.
- 32. Scientific issues in drug testing. Council on Scientific Affairs. JAMA. 1987;257(22):3110-4.
- 33. Cirimele V, Kintz P, Doray S, Ludes B. Determination of chronic abuse of the anaesthetic agents midazolam and propofol as demonstrated by hair analysis. Int J Legal Med. 2002;116(1):54-7.
- 34. Henderson GL. The fentanyls. *Am Assoc Clin Chem*. 1990;12:7-14.
- Epstein RH, Gratch DM, Grunwald Z. Development of a scheduled drug diversion surveillance system based on an analysis of atypical drug transactions. *Anesth Analg.* 2007;105(4):1053-60.
- 36. Morse RM, Martin MA, Swenson WM, Niven RG. Prognosis of physicians treated for alcoholism and drug dependence. *JAMA*. 1984;251(6):743-6.
- 37. Pelton C, Ikeda RM. The California Physician Diversion Program's experience with recovering anesthesiologists. *J Psychoactive Drugs*. 1991;23(4):427-31.
- 38. Paris RT, Canavan DI. Physician substance abuse impairment: anesthesiologists vs. other specialties. *J Addict Dis*. 1999;18(1):1-7.
- 39. Luck S, Hedrick J. The alarming trend of substance abuse in anesthesia providers. *J Perianesth Nurs*. 2004;19(5):308-11.
- 40. Menk EJ, Baumgarten RK, Kingsley CP, Culling RD, Middaugh R. Success of reentry into anesthesiology training programs by residents with a history of substance abuse. *JAMA*. 1990;263(22):3060-2.
- 41. Hedberg EB. Anesthesiologists: addicted to the drugs they administer. *ASA Newsl.* 2001;65:14-16.
- 42. Lutsky I, Abram SE, Jacobsen GR, Hopwood M, Kampine JP. Substance abuse by anesthesiology residents. *Acad Med*. 1991;66(3):164-6.
- 43. Klein RL, Stevens WC, Kingston HG. Controlled substance dispensing and accountability in United States anesthesiology residency programs. *Anesthesiology*. 1992;77(4):806-11.
- 44. Zwerling C. Current practice and experience in drug and alcohol testing in the workplace. *Bull Narc*. 1993;45(2):155-96.
- 45. Peat MA. Financial viability of screening of drugs of abuse. *Clin Chem*. 1995;41(5):805-8.
- 46. Scott M. Legal aspects of drug testing. *ASA Newsl*. 2005;69(4):25-8.
- 47. Orentlicher D. From the Office of the General Counsel. Drug testing of physicians. *JAMA*. 1990;264(8):1039-40.
- 48. Clark HW. The role of physician as medical review officers in workplace drug testing programs. In pursuit of the last nanogram. *West J Med*. 1990;152(5):514-24.
- 49. Canavan DI. Screening: urine drug tests. *Md Med J*. 1987;36(3):229-33.
- 50. McDougall CM. The Junkie in the O.R. *Men's Health*. 2006;11:186-93.
- 51. Weeks AM, Buckland MR, Morgan EB, Myles PS. Chemical dependence in anaesthetic registrars in Australia and New Zealand. *Anaesth Intensive Care*. 1993;21(2):151-5.
- 52. Roberts CA, Burke SO. Assessment of the substance abuse curriculum in schools of nurse anesthesia. *J Addiction Nursing*. 1999;11(3):112-22.

- 53. Alexander BH, Checkoway H, Nagahama SI, Domino KB. Cause-specific mortality risks of anesthesiologists. *Anesthesiology*. 2000;93(4):922-30.
- 54. Suruda AJ, McGlothlin JD. Fatal abuse of nitrous oxide in the workplace. *J Occup Med*. 1990;32(8):682-4.
- 55. Kintz P, Villain M, Dumestre V, Cirimele V. Evidence of addiction by anesthesiologists as documented by hair analysis. *Forensic Sci Int*. 2005;153(1):81-4.
- 56. Domino KB, Hornbein TF, Polissar NL, Renner G, Johnson J, Alberti S, Hankes L. Risk factors for relapse in health care professionals with substance use disorders. *JAMA*. 2005;293(12):1453-60.
- 57. Polk SL, Katz JD, Berry AJ, McGregor DG, Arnold WP. Does inhaled ambient fentanyl enhance the susceptibility of anesthesiologists to addiction? *ASA Newsl.* 2007;71(2):18-19.
- 58. Bryson EO, Levine A. One approach to return to residency for anesthesia residents recovering from opioid addiction. *J Clin Anesth.* 2008;20(5).397-400.
- 59. Tetzlaff JE, Collins GB. Reentry of anesthesiology residents after treatment of chemical dependency–is it rational? *J Clin Anesth*. 2008;20(5):325-27.
- 60. Merlo LJ, Gold MS. Prescription opioid abuse and dependency among physicians: hypotheses and treatment. *Harv Rev Psychiatry*. 2008;16(3):181-94.
- 61. Fitzsimons MG, Baker KH, Lowenstein E, Zapol WM. Random drug testing to reduce the incidence of addiction in anesthesia residents: preliminary results from one program. *Anesth Analg.* 2008;107(2):630-5.
- 62. Aach RD, Girard DE, Humphrey H, McCue JD, Reuben DB, Smith JW, Wallenstein L, Ginsburg J. Alcohol and other substance abuse and impairment among physicians in residency training. *Ann Intern Med*. 1992;116(3):245-54.
- 63. Liang BA. To tell the truth: potential liability for concealing physician impairment. *J Clin Anesth.* 2007;19(8):638-41.
- 64. Wilson JE, Kiselanova N, Stevens Q, Lutz R, Mandler T, Tran ZV, Wischmeyer PE. A survey of inhalational anaesthetic abuse in anesthesia programmes. *Anaesthesia*. 2008;63(6):616-20.
- 65. Wilson H. Environmental cues and relapse: an old idea that is new for reentry of recovering anesthesia care professionals. *Mayo Clin Proc.* 2009;84(11):1040-1.
- 66. Berge KH, Seppala MD, Schipper AM. Chemical dependency and the physician. *Mayo Clin Proc.* 2009;84(7):625-31.
- 67. Bryson EO, Silverstein JH. Addiction and substance abuse in anesthesiology. *Anesthesiology*. 2008;109(5):905-17.
- Berge KH, Seppala MD, Lanier WL. The anesthesiology community's approach to opioidand anesthetic-abusing personnel: time to change course. *Anesthesiology*. 2008;109(5):762-4.
- 69. Oreskovich MR, Caldeiro RM. Anesthesiologists recovering from chemical dependency: can they safely return to the operating room? *Mayo Clin Proc*. 2009;84(7):576-80.
- 70. Jaffee WB, Trucco E, Levy S, Weiss RD. Is this urine really negative? A systematic review of tampering methods in urine drug screening and testing. *J Subst Abuse Treat*. 2007;33(1):33-42.

- 71. Wischmeyer PE, Johnson BR, Wilson JE, et al. A survey of propofol abuse in academic anesthesia programs. *Anesth Analg*. 2007;105(4):1066-71.
- 72. Gold MS, Melker RJ, Dennis DM, Morey TE, Bajpai LK, Pomm R, Frost-Pineda K. Fentanyl abuse and dependence: further evidence for the second hand exposure hypothesis. *J Addict Dis*. 2006;25(1):15-21.
- 73. Mohn AR, Yao WD, Caron MG. Genetic and genomic approaches to reward and addiction. *Neuropharmacology*. 2004;47(Suppl 1):101-10.
- 74. Nace EP, Davis CW, Gaspari JP. Axis II comorbidity in substance abusers. *Am J Psychiatry*. 1991;148(1):118-20.
- 75. Udel MM. Chemical abuse/dependence: physicians' occupational hazard. *J Med Assoc Ga*. 1984;73(11):775-8.
- Markou A, Kosten TR, Koob GF. Neurobiological similarities in depression and drug dependence: a self-medication hypothesis. *Neuropsychopharmacology*. 1998;18(3):135-74.
- 77. Merlo LJ, Goldberger BA, Kolodner D, Fitzgerald K, Gold MS. Fentanyl and propofol exposure in the operating room: sensitization hypotheses and further data. *J Addict Dis*. 2008;27(3):67-76.
- 78. McAuliffe PF, Gold MS, Bajpai L, Merves ML, Frost-Pineda K, Pomm RM, Goldberger BA, Melker RJ, Cendán JC. Second-hand exposure to aerosolized intravenous anesthetics propofol and fentanyl may cause sensitization and subsequent opiate addiction among anesthesiologists and surgeons. *Med Hypotheses*. 2006;66(5):874-82.
- 79. Levine AI, Bryson EO. Intranasal self-administration of remiferitanil as the foray into opioid abuse by an anesthesia resident. *Anesth Analg*. 2010;110(2):524-5.
- 80. Kovacic P. Unifying mechanism for addiction and toxicity of abused drugs with application to dopamine and glutamate mediators: electron transfer and reactive oxygen species. *Med Hypotheses*. 2005;65(1):90-6.
- 81. Kovacic P. Unifying electron transfer mechanism for addiction involvement by the anesthetic propofol. *Med Hypotheses*. 2010;74(1):206.
- 82. Rose GL, Brown RE Jr. The impaired anesthesiologist: not just about drugs and alcohol anymore. *J Clin Anesth*. 2010;22(5):379-84.
- 83. Donohoe M. Urine trouble: practical, legal, and ethical issues surrounding mandated drug testing of physicians. *J Clin Ethics*. 2005;16(1):85-96.
- 84. Carinci AJ, Christo PJ. Physician impairment: is recovery feasible? *Pain Physician*. 2009;12(3):487-91.
- 85. Pil K, Verstraete A. Current developments in drug testing in oral fluids. *Ther Drug Monit*. 2008;30(2):196-202.
- 86. Dasgupta A. The effects of adulterants and selected ingested compounds on drugs-ofabuse testing in urine. *Am J Clin Pathol.* 2007;128(3):491-503.
- 87. Epstein RH, Gratch DM, McNulty S, Grunwald Z. Validation of a system to detect scheduled drug diversion by anesthesia care providers. *Anesth Analg.* 2011;113(1):160-4.
- 88. Hiroi N, Agatsuma S. Genetic susceptibility to substance dependence. *Mol Psychiatry*. 2005;10(4):336-44.

- 89. Koob GF, Volkow ND. Neurocircuitry of addiction. *Neuropsychopharmacology*. 2010;35(1):217-38.
- 90. Chisholm AB, Harrison MJ. Opioid abuse amongst anaesthetists: a system to detect personal usage. *Anaesth Intensive Care*. 2009;37(2):267-71.
- 91. Volkow ND, Fowler JS, Wang GJ. The addicted human brain: insights from imaging studies. *J Clin Invest*. 2003;111(10):1444-51.
- 92. Volkow ND, Fowler JS, Wang GJ. The addicted human brain viewed in light of imaging studies: brain circuits and treatment strategies. *Neuropharmacology*. 2004;47(Suppl 1):3-13.
- 93. Hamza H, Bryson EO. Exposure of anesthesia providers in recovery from substance abuse to potential triggering agents. *J Clin Anesth*. 2011;23(7):552-7.
- 94. Welliver M. Propofol alert! *Gastroenterol Nurs*. 2011;34(5):398-9.
- 95. Koopmann A, von der Goltz C, Hermann D, Kiefer F. Propofol addiction initiated by anesthetic use. *Am J Psychiatry*. 2011;168(2):211-2.
- 96. Mégarbane B. The tragic end of the King of Pop: An exceptional example of pharmacodependence to propofol. Réanimation. 2010;19(6):601-4.
- 97. Bryson EO, Hamza H. The drug seeking anesthesia care provider. *Int Anesthesiol Clin*. 2011;49(1):157-71.
- 98. Hellinger WC, Bacalis LP, Kay RS, Thompson ND, Xia GL, Lin Y, Khudyakov YE, Perz JF. Health care-associated hepatitis C virus infections attributed to narcotic diversion. *Ann Intern Med*. 2012;156(7):477-82.
- 99. Berge KH, Dillon KR, Sikkink KM, Taylor TK, Lanier WL. Diversion of drugs within health care facilities, a multiple-victim crime: patterns of diversion, scope, consequences, detection, and prevention. *Mayo Clin Proc.* 2012;87(7):674-82.
- 100. McClure SR, O'Neal BC, Grauer D, Couldry RJ, King AR. Compliance with recommendations for prevention and detection of controlled-substance diversion in hospitals. *Am J Health Syst Pharm*. 2011;68(8):689-94.
- 101. van Holst RJ, Veltman DJ, Büchel C, van den Brink W, Goudriaan AE. Distorted expectancy coding in problem gambling: is the addictive in the anticipation? *Biol Psychiatry*. 2012;71(8):741-8.
- 102. Carinci AJ, Christo PJ. Physician impairment: is recovery feasible? *Pain Physician*. 2009;12(3):487-91.
- 103. Warner DO, Berge K, Sun H, Harman A, Hanson A, Schroeder DR. Substance use disorder among anesthesiology residents, 1975-2009. *JAMA*. 2013;310(21):2289-96.
- 104. Pham JC, Pronovost PJ, Skipper GE. Identification of physician impairment. *JAMA*. 2013;309(20):2101-2.
- 105. Stolbach A, Nelson LS, Hoffman RS. Protection of patients from physician substance misuse. *JAMA*. 2013;310(13):1402-3.
- 106. Selzer J. Protection of patients from physician substance misuse. *JAMA*. 2013;310(13):1403.
- 107. Fitzsimons MG, Ishizawa Y, Baker KH. Drug testing physicians for substances of abuse: case report of a false-positive result. *J Clin Anesth*. 2013;25(8):669-71.
- 108. de Oliveira GS Jr, Chang R, Fitzgerald PC, Almeida MD, Castro-Alves LS, Ahmad S, McCarthy RJ. The prevalence of burnout and depression and their association with

adherence to safety and practice standards: a survey of United States anesthesiology trainees. *Anesth Analg.* 2013;117(1):182-93.

- 109. Merlo LJ, Singhakant S, Cummings SM, Cottler LB. Reasons for misuse of prescription medication among physicians undergoing monitoring by a physician health program. *J* Addict Med. 2013;7(5):349-53.
- 110. Bonnet U, Harkener J, Scherbaum N. A case report of propofol dependence in a physician. *J Psychoactive Drugs*. 2008;40(2):215-6.
- 111. Merlo LJ, Greene WM, Pomm R. Mandatory naltrexone treatment prevents relapse among opiate-dependent anesthesiologists returning to practice. *J Addict Med*. 2011;5(4):279-83.
- 112. Hamza H, Bryson EO. Buprenorphine maintenance therapy in opioid-addicted health care professionals returning to clinical practice: a hidden controversy. *Mayo Clin Proc*. 2012;87(3):260-7.
- 113. Gold MS, Kobeissy FH, Wang KK, et al. Methamphetamine- and trauma-induced brain injuries: comparative cellular and molecular neurobiological substrates. *Biol Psychiatry*. 2009;66(2):118-27.
- 114. Blumenthal DM, Gold MS. Neurobiology of food addiction. *Curr Opin Clin Nutr Metab Care*. 2010;13(4):359-65.
  - 115. Eisler P. Doctors, medical staff on drugs put patients at risk. USA Today. http://www.usatoday.com/story/news/nation/2014/04/15/doctors-addicted-drugshealth-care-diversion/7588401/. Published April 17, 2014. Accessed April 15, 2016.
  - 116. Eichenwald K. When drug addicts work in hospitals, no one is safe. *Newsweek*. http://www.newsweek.com/2015/06/26/traveler-one-junkies-harrowing-journey-across-america-344125.html. Published June 18, 2015. Accessed April 15, 2016.