Interesting Cases with Audience Response System (ARS) Edwin A. Salsitz, MD, DFASAM Associate Clinical Professor Mount Sinai Beth Israel



Financial Disclosures

The ASAM Review Course in Addiction Medicine July 2022

Edwin A. Salsitz, MD, DFASAM

No Disclosures





Name the Event



Patient 1: 64-year-old Female

- Admitted to rehab for treatment of AUD following a "detox" protocol. MMTP 60mg for many years-OUD in Remission
- Married: Spouse no SUD
- ◆ F: +EtOH M: No EtOH 4S: No EtOH 2Children: No EtOH
- HS Graduate: Employed in Sales
- Social, Occasional EtOH until age 56
- ? Event $\rightarrow \uparrow \uparrow$ EtOH one year after event \rightarrow AUD
- PE: unremarkable
- Labs: Normal CMP, CBC, Lipids
- UDT: + Methadone



Patient 2: 22-year-old Male

- Admitted to rehab for treatment of AUD, following "Detox"
- FH: neg for EtOH
- Stutter age 8—14: Physical Abuse Stepparent 8—15
- Associate Degree
- ◆ Age 16—17: Occasional EtOH
- Age 18: ?Event $\rightarrow \uparrow \uparrow$ EtOH 2yrs after event \rightarrow AUD



What was the event?







64-year-old Female with AUD

Age 56: Bariatric Surgery: 5' 4" 240lbs. BMI= 41 •? Type of Bariatric Surgery? RYBS, SG, LAGB ◆SG Current BMI: 24 2 liters Vodka day



22-year-old Male with AUD

- Age 18: Bariatric Surgery: ?RYGB, SG, LAGB
- ♦ Age 6: ↑ Weight: Teased
- Age 16: 6' 00": 300lbs: BMI= 41
- ◆ Age 18: RYGB Mother RYGB 6 mos. Earlier
- Age 20: Felt depressed: Drank EtOH : Felt much different than prior to RYGB
- One Liter Bourbon daily
- Current BMI: 37
- Thinks alcohol substituted for food



Demographics WLS

Estimate of Bariatric Surgery Numbers, 2011-2018

Published June 2018

	2011	2012	2013	2014	2015	2016	2017	2018*
Total	158,000	173,000	179,000	193,000	196,000	216,000	228,000	252,000
Sleeve	17.8%	33.0%	42.1%	51.7%	53.6%	58.1%	59.4%	61.4%
RYGB	36.7%	37.5%	34.2%	26.8%	23.0%	18.7%	17.8%	17.0%
Band	35.4%	20.2%	14.0%	9.5%	5.7%	3.4%	2.7%	1.1%
BPD-DS	0.9%	1.0%	1.0%	0.4%	0.6%	0.6%	0.7%	0.8%
Revision	6.0%	6.0%	6.0%	11.5%	13.6%	14.0%	14.1%	15.4%
Other	3.2%	2.3%	2.7%	0.1%	3.2%	2.6%	2.5%	2.3%
Balloons	-	-	-	-	0.3%	2.6%	2.8%	2.0%

The ASMBS total bariatric procedure numbers are based on the best estimation from available data (BOLD,ACS/MBSAQIP, National Inpatient Sample Data and outpatient estimations).

> Proportion of male patients who underwent bariatric surgery, 2002 to 2011.

252,000



ASAM

Journal of the American College of Surgeons Volume 222, Issue 3, March 2016, Pages 226-231



Roux-en-Y, is an end-to-side surgical anastomosis of bowel used to reconstruct the gastrointestinal tract. The name is derived from the surgeon who first described it César Roux and the stick-figure representation.



Impaired Alcohol Metabolism after Gastric Bypass Surgery: A Case-Crossover Trial

Gavitt A Woodard, BS, John Downey, MD, Tina Hernandez-Boussard, PhD, MPH, John M Morton, MD, MPH, FACS





From: Effect of Roux-en-Y Gastric Bypass Surgery: Converting 2 Alcoholic Drinks to 4

- 8 F, RYGB 1-5 years ago
- 9F, awaiting RYGB
- 2 Standard Drinks

5F, before and after RYGB
Mean time 10 months
2 Standard Drinks



JAMA Surg. 2015;150(11):1096-1098, Pepino et al



Comparison of patients screening positive for AUD between baseline and year 1 and year 1 to year 2 following surgery



Ibrahim, N., Alameddine, M., Brennan, J. et al. New onset alcohol use disorder following bariatric surgery. Surg Endosc 33, 2521–2530 (2019)



What is Special at the 2-year mark?

 "The 2-year follow-up stands out as a pivotal time point to identify patients needing additional support to achieve a positive long-term outcome after metabolic and bariatric surgery. After that point, weightloss phase is over and further improvements are unlikely."

Lancet, Child and Adolescent Health, January 21, 2020



Estimated mean frequency of substance use by category for bariatric weight loss surgery (WLS) based on Compulsive Behaviors Questionnaire (CBQ) scores of 155 participants.

Substance Use Following Bariatric Weight Loss Surgery

Alexis Conason, PsyD; Julio Teixeira, MD; Chia-Hao Hsu, PhD; Lauren Puma, MS; Danielle Knafo, PhD; Allan Geliebter, PhD



JAMA Surg. 2013;148(2):145-150



From: Mental Health Conditions Among Patients Seeking and Undergoing Bariatric Surgery: A Meta-analysis

Table 1. Prevalence of Preoperative Mental Health Conditions Among Patients Seeking and Undergoing Bariatric Surgery

Condition	Studies Reporting Data	Patients Reporting Data	Patients With Condition	Prevalence Estimate, % (95% CI)ª
Any mood disorder	10	3307	788	23 (15-31)
Depression	34	51 908	12 009	19 (14-25)
Binge eating disorder	25	13769	2400	17 (13-21)
Anxiety	22	38 459	10 515	12 (6-20)
Suicidal ideation or suicidality	6	3518	315	9 (5-13)
Personality disorders	6	3002	184	7 (1-16)
Substance abuse disorders ^b	19	40 725	1515	3 (1-4)
Posttraumatic stress disorder	10	15 039	187	1 (1-2)
Psychosis	6	3406	31	1 (0-1)

^a Pooled estimate based on random-effects meta-analysis.

^b Includes alcohol abuse, drug abuse, and unspecified substance abuse; tobacco use and abuse were excluded.



Addiction Transfer/Substitution

◆Why the ~ 2-year delay?
◆Why procedure-dependent?
◆Occurs In Patients with Gastrectomy for peptic ulcer and CA with nl BMI
◆Rodent Model: ↑EtOH after RYGB



Pharmacokinetics/Pharmacodynamics

- Explains Difference RYGB, SG, LAGB
- ◆↓ Gastric ADH (Cimetidine H2 Blocker)
- \downarrow Weight \rightarrow \uparrow Socialization
- Absorption, ↑ Cmax, earlier Tmax
- Feeling More Intoxicated
- AUD>> Other SUDs
- Cocaine Analogy: I.N. \rightarrow Smoked (Crack Cocaine)



Gastric Origin of the First-Pass Metabolism of Ethanol in Humans: Effect of Gastrectomy

J. CABALLERIA, M. FREZZA, R. HERNÁNDEZ-MUÑOZ, C. DIPADOVA, M. A. KORSTEN, E. BARAONA, and C. S. LIEBER Section of Liver Disease and Nutrition and Alcohol Research and Treatment Center, Bronx

Veterans Administration Medical Center and Mount Sinai School of Medicine, New York, New York; and Institute of Medical Pathology, University School of Medicine, Trieste, Italy



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GASTROENTEROLOGY 1989;97:1205-9

Predictors of AUD Post WLS

 Type of Weight Loss Surgery Male: Women More WLS Younger Age, FH EtOH use Pre-Op Tobacco, Illicit Drug Use ADHD Lower Sense of Belonging, Depression • More Weight Loss $\rightarrow \uparrow$ Socialization $\rightarrow \uparrow$ EtOH





Surgery for Obesity and Related Diseases 6 (2010) 615-621

Original article

Bariatric surgery history among substance abuse treatment patients: prevalence and associated features

Karen K. Saules, Ph.D.^{a,*}, Ashley Wiedemann, B.S.^a, Valentina Ivezaj, M.S.^a, John A. Hopper, M.D.^b, Joyce Foster-Hartsfield, D.O.^c, Daniel Schwarz, M.D.^d

^aDepartment of Psychology, Eastern Michigan University, Ypsilanti, Michigan ^bSt. Joseph Mercy Hospital, Ypsilanti, Michigan ^cBrighton Hospital, Brighton, Michigan ^dUniversity of Michigan, Ann Arbor, Michigan Received October 19, 2009; revised December 22, 2009; accepted December 22, 2009





Key Takeaways

- New Onset EtOH related problems occur in ~ 10% of WLS Pts.
- More likely with RYGB & SG than with LAGB.
- Some WLS patients \downarrow EtOH intake.
- EtOH problems increase over time. Usually begins ~2 years after WLS.
- Inform and Monitor all WLS patients about the risk of AUD/SUD over time.
- Special Thanks to Allan Geliebter PhD, for alerting me to the relationship between Bariatric Surgery and Alcohol



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"Rapid Sudden Death" After IV Drug Use



Sudden Death IVDU

- 26 yo male
- 8 year hx of OUD
- ◆ Prescription Opioids → IN Heroin → IV Heroin last 12 months
- 3 non-fatal ODs last 8 months
- Non compliant with Bupe Rx and Psychosocial Tx
- Argued with his Mother: Went up to his Room: Mother heard a loud thud, found him on floor, unresponsive, with syringe and needle in his arm 5 minutes later.
- Naloxone Nasal Spray 4mg administered X2—No Response
- Patient could not be resuscitated by EMS



What Happened?



Sudden Death IVDU

◆ ? Typical Opioid Induced Respiratory Depression Fatal Overdose
 ◆ Time Frame: ≥ 1 hour: Naloxone Reversal Effectiveness Evidence

 Post Mortem Toxicology: +Fentanyl, –Norfentanyl, +Heroin, –6-MAM, +Morphine

Fentanyl Induced Chest Wall Rigidity ("Wooden Chest")
 Fentanyl Induced Respiratory Muscle Rigidity & Laryngospasm



Fentanyl Chest Wall Rigidity

- First Reported in 1953 in anesthesia literature
- Skeletal Muscle Rigidity: Chest Wall Most Common
- Most common with fentanyl and its congeners (lipid solubility)
- Most common with rapid IV administration
- Activation of the coerulospinal noradrenergic pathway, following mu receptor activation in LC
- Not dose related
- Reversed with naloxone (IV route in literature)
- Ventilatory Support
- Low or Absent Norfentanyl (appears in 2 minutes: CYP3A4(Inhb)



Burns, G et al Clinical Toxicology, Vol 54, No 5, 420-23, 2016

100 Accidental OD deaths 2017: 99% + FENTANYL Only 3 cases + HEROIN





RESEARCH UPDATE ON FENTANYL OUTBREAKS IN THE DAYTON, OH AREA:

Acryl Fentanyl and Furanyl Fentanyl Commonly Found In Overdose Death Cases UPDATE 04/28/2017

DAYTON, OHIO. The Dayton area (Montgomery County, Ohio) has recently experienced dramatic increases in heroin and other opioid-related problems. Unintentional drug overdose deaths increased significantly from 127 in 2010 to 264 in 2014. In 2016, there were 349 overdose deaths in Montgomery County, and 251 of them screened positive for fentanyl. Preliminary data from 2017 indicate continuing increases in overdose deaths.

	Α.	В.	C.
Synthetic	All cases	Acryl	Furanyl
opioids/fentanyl	(N=100)	Fentanyl	Fentanyl
analogues/metabolites		Positives	Positives
		(N=56)	(N=39)
Fentanyl	99 (99%)	56 (100%)	39 (100%)
Norfentanyl	64 (64%)	39 (70%)	26 (67%)
Acryl fentanyl	56 (56%)		25 (64%)
Despropionylfentanyl	46 (46%)	26 (46%)	32 (82%)
Furanyl Fentanyl	39 (39%)	25 (45%)	
Carfentanil	3 (3%)	2 (4%)	1 (2.6%)
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Butyryl/isobutyrylfentanyl	1 (1%)	0 (0%)	0 (0%)
Furanyl Norfentanyl	1 (1%)	1 (2%)	1 (2.6%)
U47700	1 (1%)	1 (2%)	1 (2.6%)

2 min: 3A4







Morphine = 1X
Fentanyl =100X
Carfentanil =10,000X

Lethal doses of heroin compared to "synthetic" opioids. New Hampshire State Police Forensic Lab



National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2020



Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021.

'Death pill': Fentanyl disguised as other drugs linked to spike in US overdoses





By dennis thompson | healthday | August 10, 2016, 12:13 PM

Fake Xanax can be a killer





Name the Drug



24-year-old Male

- Admitted to inpatient rehab for SUD of IN X drug.
- Lives at home with father and sister. Mother died when patient was 21 yo.
- X drug use started age 20, quickly daily, episodes of not using and relapsing.
- Drug use limited to IN X drug
- Medical history is negative, except for urinary complaints: frequency, burning, gross hematuria, & suprapubic pain. Has had similar in the past. No discharge or lesions. Sexually active. Heterosexual. HIV-
- Tobacco: 1ppd since age 17


24-year-old Male

Find	lings					
Res	ult Name	Result	Abn1	Normal Range	Units	LOC.
Col	or.	Yellow		Yellow		
App	earance	Hazy	a	CLEAR		
Spe	cific Gravity	1.033		1.004-1.036		
рĤ	- UR	5.0		5.0-8.0		
Pro	otein, Urine	100	a	Negative		
Glu	icose, Urine	Negative		Negative	mg∕dL	
Ket	ones	Neĝative		Neĝative	mĝ∕dL	
Bil	irubin	Negative		Negative		
B] (od, Urine	Large	a	Negative		
Ni t	rites	Negative		Negative		
Und	bilinogen	<2.0		0.2-2.0	mg∕dL	
Lei	kocyteš Esterase	Moderate	a	Negative		
WBC	, Urine	96	н	0-5	/HPF	
RBC	., Urine	>182	н	0-3	/HPF	
Hya	aline Cast	6-10		0-5		
Cal	cium Oxalate Crystals	Rane	a	None Seen		

Urine culture negative, CMP- WNL, CBC-WNL
 UDT: negative-- opiates, cocaine, methadone, amphetamine, THC, benzo
 GC, Chlamydia, RPR all negative

4

What is the Diagnosis?

- Want to know his Ethnicity?
- Chinese American
- Which Drug?

•KETAMINE CYSTITIS



Urological Science 26 (2015) 153-157

Contents lists available at ScienceDirect



Urological Science

journal homepage: www.urol-sci.com

Review article

Ketamine cystitis: Its urological impact and management*



Yao Chou Tsai a, b, Hann-Chorng Kuo b, c, *

^a Division of Urology, Department of Surgery, Taipei Tzu Chi General Hospital, Buddhist Tzu Chi Medical Foundation, Taipei, Taiwan ^b Department of Urology, School of Medicine, Tzu Chi University, Hualien, Taiwan ^c Department of Urology, Buddhist Tzu Chi General Hospital, Hualien, Taiwan



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Urological Science

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Mini review

A murderer of young bladders: Ketamine-associated cystitis*



En Meng*, Sheng-Tang Wu, Tai-Lung Cha, Guang-Huan Sun, Dah-Shyong Yu, Sheng-Yran Chang

Division of Urology, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, ROC

Am 7 Physical Annual Physical 2010; \$148-\$7114, 2015. Freed published June 24, 2015; doi:10.11555/specied.00002.2014

Ketamine-induced ulcerative cystitis and bladder apoptosis involve oxidative stress mediated by mitochondria and the endoplasmic reticulum

Kele-Min Lin,¹ Shu-Mion Chuang,⁷ Chong-Yu Long,¹ Yi-Lun Lov,⁵⁷ Chao-Chuan Wang,¹ Mel-Chin Lu,⁵⁷ Rong-Jyh Lin,⁹ Jian-He Lu,² Mel-Yu Jang,⁹ Wen-Jeng Wu,^{5,20,27} Wan-Ting Hu,¹⁰ and Yong-Shun Jaan^{55,10,11}

¹Department of Austrein, College of Mediciae, Kardniang Medical Dalaerstip, Kardniang, Talwan: ¹Dramitational Research Contro: Cancer Control, Department of Medical Research, Kardniang Medical Dalaerstip, Kardniang, Talwan: ¹Department of Obstavies and Opserology, Kardniang Medical Dalawstip Hosphal, Kardniang, Talwan: ¹Department of Volegy, Celi Shar Boghed, Department of Medica, Decontre Faso, Kardniang, Talwan: ¹Department of Volegy, Celi Shar Medical University, Kardniang, Talwan: ¹Destimal Messam of Mexico Bology and Aquesiam, Pingtong, Talwan: ¹Department Medical University, Kardniang, Talwan: ¹Destimal Messam of Mexico Bology and Aquesiam, Pingtong, Talwan: ¹Oradeate Institute of Mexico Bology, Mathema Using, Talwan: ¹Department of Provinsiong, College of Medicine, Kardniang, Medical University, Kardniang, Talwan: ¹Department of Provinsiong, Mathema Hano-Kong Hospite, Kardniang, Talwan: ¹Department of University, College of Medicale, Kardniang, Mathema Mathematig, Kardniang, Talwan; and ¹¹Department of University, Kardniang, Medical University, Respinal, Kardniang, Talwan; ¹¹Department of University, Kardniang, Medical University, Respinal, Kardniang, Talwan;

Saturated 12 November 2018, accepted in final forts 16 June 2015

Am J Physiol Renal Physiol 309: F318-F331, 2015. First published June 24, 2015; doi:10.1152/ajprenal.00607.2014.

Ketamine-induced ulcerative cystitis and bladder apoptosis involve oxidative stress mediated by mitochondria and the endoplasmic reticulum

Keh-Min Liu,¹ Shu-Mien Chuang,² Cheng-Yu Long,³ Yi-Lun Lee,^{4,5} Chao-Chuan Wang,¹ Mei-Chin Lu,^{6,7} Rong-Jyh Lin,⁸ Jian-He Lu,⁵ Mei-Yu Jang,⁹ Wen-Jeng Wu,^{9,10,11} Wan-Ting Ho,¹⁰ and Yung-Shun Juan^{5,9,10,11}



Ketamine Cystitis (KC)

- Most common illicit drug in Taiwan. HK, Singapore, Malaysia
- Frequency, urgency, suprapubic pain, dysuria, hematuria
- Urothelial ulceration, inflammation, bladder wall fibrosis
- ~26% in regular users—dose/frequency related M:F=
- Pathophysiology: local bladder, autoimmune, vascular damage
- Sterile pyuria, \checkmark Bladder Capacity
- Treatment: D/C ketamine--most improve. Hyaluronic acid, Chondroitin sulfate, Botulinum toxin instillation.
- NSAIDS, Steroids, Anticholinergics (oxybutynin): ± efficacy
- Urinary diversion, Augmentation Cystoplasty
- Patient improved over one week: Urological f/u. D/C ketamine





Fig. 1. Intravenous pyelography in a man with ketamine cystitis reveals bilateral hydronephroureters and contracted urinary bladder.

Yao Chou Tsai, Hann-Chorng Urological Science, Volome 26, Issue 3, 2015, 153–157

NIDA Fact Sheet

Street Names	Commercial Names	Common Forms	Common Ways Taken	DEA Schedule	
Cat Valium, K, Special K, Vitamin K	Ketalar ®	Liquid, white powder	Injected, snorted, smoked (powder added to tobacco or marijuana cigarettes), swallowed	III <u>**</u>	
Possible Health Effects					
Short-termProblems with attention, learning, and memory; dreamlike states, hallucinations; sedation; confusion and problems speaking; loss of memory; problems moving, to the point of being immobile; raised blood pressure; unconsciousness; slowed breathing that can lead to death.Long-termUlcers and pain in the bladder; kidney problems; stomach pain; depression; poor memory.				ry; infusion iblems d blood g that can	
				ms;	
Other Health- related Issues	other Sometimes used as a date rape drug. lealth- elated Risk of HIV, hepatitis, and other infectious diseases ssues from shared needles.				
In Increased risk of adverse effects.					

 In
 Increased risk of adverse effects.

 Combination
 with Alcohol

 Withdrawal
 Unknown.

 Symptoms
 Treatment Options

 Medications
 There are no FDA-approved medications to treat





Two Additional Cases

- 36 yo Chinese American Female: Using IN Ketamine since age 18. Presents with dysuria and frequency—every 10 minutes. Wears diaper. +Sterile pyuria. Uses illicit Buprenorphine SL as an analgesic. Understands urinary problems are a result of ketamine use. Many friends with same issues. Left AMA after 48 hours.
- 26 yo Greek American Female: IN Ketamine initially as component of "Club Drug" cocktail at Raves starting age 18. Then IN ketamine becomes primary drug along with IN cocaine. Drug dealers primarily Columbian. Friends who are users are Caucasian and Hispanics. Has had intermittent dysuria and frequency. Normal U/A. Knows the connection between IN Ketamine and urinary symptoms.
- Cocaine + Ketamine = Calvin Klein



Ketamine : Phencyclidine(PCP) No Reports of PCP induced Cystitis No Reports of Cystitis: Pain/Depression





FDA Approves Esketamine Nasal Spray for Resistant Depression

Caroline Cassels March 05, 2019

13 Read Comments f 💟 in 🖂 🖨 🔂 Add to Email Alerts

The US Food and Drug Administration (FDA) has approved esketamine nasal spray (*Spravato*, Janssen Pharmaceuticals) for treatment-resistant depression.

"There has been a long-standing need for additional effective treatments for treatment-resistant depression, a serious and life-threatening condition," Tiffany Farchione, MD, acting director of the Division of Psychiatry Products in the FDA's Center for Drug Evaluation and Research, said in an FDA release announcing the drug's approval.

"Controlled clinical trials that studied the safety and efficacy of this drug, along with careful review through the FDA's drug approval process including a robust discussion with our external advisory committees, were important to our decision to approve this treatment. Because of safety concerns, the drug will only be available through a restricted distribution system and it must be administered in a certified medical office where the health care provider can monitor the patient," Farchione added.

The potential risk for serious adverse outcomes associated with the drug, including sedation and dissociation and the potential for abuse and misuse, means it is only available through a restricted distribution system, under a Risk Evaluation and Mitigation Strategy.



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- Tobacco: 1ppd since age 17



24-year-old Male

Find	lings					
Res	ult Name	Result	Abn1	Normal Range	Units	LOC.
Col	or.	Yellow		Yellow		
App	earance	Hazy	a	CLEAR		
Spe	cific Gravity	1.033		1.004-1.036		
рĤ	- UR	5.0		5.0-8.0		
Pro	otein, Urine	100	a	Negative		
Glu	icose, Urine	Negative		Negative	mg∕dL	
Ket	ones	Neĝative		Neĝative	mĝ∕dL	
Bil	irubin	Negative		Negative		
B] (od, Urine	Large	a	Negative		
Ni t	rites	Negative		Negative		
Und	bilinogen	<2.0		0.2-2.0	mg∕dL	
Lei	kocyteš Esterase	Moderate	a	Negative		
WBC	, Urine	96	н	0-5	/HPF	
RBC	., Urine	>182	н	0-3	/HPF	
Hya	aline Cast	6-10		0-5		
Cal	cium Oxalate Crystals	Rane	a	None Seen		

Urine culture negative, CMP- WNL, CBC-WNL
 UDT: negative-- opiates, cocaine, methadone, amphetamine, THC, benzo
 GC, Chlamydia, RPR all negative

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Ketamine cystitis: Its urological impact and management*



Yao Chou Tsai a, b, Hann-Chorng Kuo b, c, *

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Mini review

A murderer of young bladders: Ketamine-associated cystitis*



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- Most common illicit drug in Taiwan. HK, Singapore, Malaysia
- Frequency, urgency, suprapubic pain, dysuria, hematuria
- Urothelial ulceration, inflammation, bladder wall fibrosis
- ~26% in regular users—dose/frequency related M:F=
- Pathophysiology: local bladder, autoimmune, vascular damage
- Sterile pyuria, \checkmark Bladder Capacity
- Treatment: D/C ketamine--most improve. Hyaluronic acid, Chondroitin sulfate, Botulinum toxin instillation.
- NSAIDS, Steroids, Anticholinergics (oxybutynin): ± efficacy
- Urinary diversion, Augmentation Cystoplasty
- Patient improved over one week: Urological f/u. D/C ketamine





Fig. 1. Intravenous pyelography in a man with ketamine cystitis reveals bilateral hydronephroureters and contracted urinary bladder.

Yao Chou Tsai, Hann-Chorng Urological Science, Volome 26, Issue 3, 2015, 153–157

NIDA Fact Sheet

Street Names	Commercial Names	Common Forms	Common Ways Taken	DEA Schedule	
Cat Valium, K, Special K, Vitamin K	Ketalar ®	Liquid, white powder	Injected, snorted, smoked (powder added to tobacco or marijuana cigarettes), swallowed	III <u>**</u>	
Possible Health Effects					
Short-termProblems with attention, learning, and memory; dreamlike states, hallucinations; sedation; confusion and problems speaking; loss of memory; problems moving, to the point of being immobile; raised blood pressure; unconsciousness; slowed breathing that can lead to death.Long-termUlcers and pain in the bladder; kidney problems; stomach pain; depression; poor memory.				ry; infusion iblems d blood g that can	
				ms;	
Other Health- related Issues	other Sometimes used as a date rape drug. lealth- elated Risk of HIV, hepatitis, and other infectious diseases ssues from shared needles.				
In Increased risk of adverse effects.					

 In
 Increased risk of adverse effects.

 Combination
 with Alcohol

 Withdrawal
 Unknown.

 Symptoms
 Treatment Options

 Medications
 There are no FDA-approved medications to treat





Two Additional Cases

- 36 yo Chinese American Female: Using IN Ketamine since age 18. Presents with dysuria and frequency—every 10 minutes. Wears diaper. +Sterile pyuria. Uses illicit Buprenorphine SL as an analgesic. Understands urinary problems are a result of ketamine use. Many friends with same issues. Left AMA after 48 hours.
- 26 yo Greek American Female: IN Ketamine initially as component of "Club Drug" cocktail at Raves starting age 18. Then IN ketamine becomes primary drug along with IN cocaine. Drug dealers primarily Columbian. Friends who are users are Caucasian and Hispanics. Has had intermittent dysuria and frequency. Normal U/A. Knows the connection between IN Ketamine and urinary symptoms.
- Cocaine + Ketamine = Calvin Klein



Ketamine : Phencyclidine(PCP) No Reports of PCP induced Cystitis No Reports of Cystitis: Pain/Depression





FDA Approves Esketamine Nasal Spray for Resistant Depression

Caroline Cassels March 05, 2019

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The US Food and Drug Administration (FDA) has approved esketamine nasal spray (*Spravato*, Janssen Pharmaceuticals) for treatment-resistant depression.

"There has been a long-standing need for additional effective treatments for treatment-resistant depression, a serious and life-threatening condition," Tiffany Farchione, MD, acting director of the Division of Psychiatry Products in the FDA's Center for Drug Evaluation and Research, said in an FDA release announcing the drug's approval.

"Controlled clinical trials that studied the safety and efficacy of this drug, along with careful review through the FDA's drug approval process including a robust discussion with our external advisory committees, were important to our decision to approve this treatment. Because of safety concerns, the drug will only be available through a restricted distribution system and it must be administered in a certified medical office where the health care provider can monitor the patient," Farchione added.

The potential risk for serious adverse outcomes associated with the drug, including sedation and dissociation and the potential for abuse and misuse, means it is only available through a restricted distribution system, under a Risk Evaluation and Mitigation Strategy.



Interesting Cases with Audience Response System (ARS) Edwin A. Salsitz, MD, DFASAM Associate Clinical Professor Mount Sinai Beth Israel



Financial Disclosures

The ASAM Review Course in Addiction Medicine July 2022

Edwin A. Salsitz, MD, DFASAM

No Disclosures





"Rapid Sudden Death" After IV Drug Use



Sudden Death IVDU

- 26 yo male
- 8 year hx of OUD
- ◆ Prescription Opioids → IN Heroin → IV Heroin last 12 months
- 3 non-fatal ODs last 8 months
- Non compliant with Bupe Rx and Psychosocial Tx
- Argued with his Mother: Went up to his Room: Mother heard a loud thud, found him on floor, unresponsive, with syringe and needle in his arm 5 minutes later.
- Naloxone Nasal Spray 4mg administered X2—No Response
- Patient could not be resuscitated by EMS



What Happened?


Sudden Death IVDU

◆ ? Typical Opioid Induced Respiratory Depression Fatal Overdose
 ◆ Time Frame: ≥ 1 hour: Naloxone Reversal Effectiveness Evidence

 Post Mortem Toxicology: +Fentanyl, –Norfentanyl, +Heroin, –6-MAM, +Morphine

Fentanyl Induced Chest Wall Rigidity ("Wooden Chest")
 Fentanyl Induced Respiratory Muscle Rigidity & Laryngospasm



Fentanyl Chest Wall Rigidity

- First Reported in 1953 in anesthesia literature
- Skeletal Muscle Rigidity: Chest Wall Most Common
- Most common with fentanyl and its congeners (lipid solubility)
- Most common with rapid IV administration
- Activation of the coerulospinal noradrenergic pathway, following mu receptor activation in LC
- Not dose related
- Reversed with naloxone (IV route in literature)
- Ventilatory Support
- Low or Absent Norfentanyl (appears in 2 minutes: CYP3A4(Inhb)



Burns, G et al Clinical Toxicology, Vol 54, No 5, 420-23, 2016

100 Accidental OD deaths 2017: 99% + FENTANYL Only 3 cases + HEROIN





RESEARCH UPDATE ON FENTANYL OUTBREAKS IN THE DAYTON, OH AREA:

Acryl Fentanyl and Furanyl Fentanyl Commonly Found In Overdose Death Cases UPDATE 04/28/2017

DAYTON, OHIO. The Dayton area (Montgomery County, Ohio) has recently experienced dramatic increases in heroin and other opioid-related problems. Unintentional drug overdose deaths increased significantly from 127 in 2010 to 264 in 2014. In 2016, there were 349 overdose deaths in Montgomery County, and 251 of them screened positive for fentanyl. Preliminary data from 2017 indicate continuing increases in overdose deaths.

	Α.	В.	C.
Synthetic	All cases	Acryl	Furanyl
opioids/fentanyl	(N=100)	Fentanyl	Fentanyl
analogues/metabolites		Positives	Positives
		(N=56)	(N=39)
Fentanyl	99 (99%)	56 (100%)	39 (100%)
Norfentanyl	64 (64%)	39 (70%)	26 (67%)
Acryl fentanyl	56 (56%)		25 (64%)
Despropionylfentanyl	46 (46%)	26 (46%)	32 (82%)
Furanyl Fentanyl	39 (39%)	25 (45%)	
Carfentanil	3 (3%)	2 (4%)	1 (2.6%)
Acetyl Fentanyl	2 (2%)	1 (2%)	1 (2.6%)
Butyryl/isobutyrylfentanyl	1 (1%)	0 (0%)	0 (0%)
Furanyl Norfentanyl	1 (1%)	1 (2%)	1 (2.6%)
U47700	1 (1%)	1 (2%)	1 (2.6%)

2 min: 3A4







Morphine = 1X
Fentanyl =100X
Carfentanil =10,000X

Lethal doses of heroin compared to "synthetic" opioids. New Hampshire State Police Forensic Lab



National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2020



Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021.

'Death pill': Fentanyl disguised as other drugs linked to spike in US overdoses





By dennis thompson | healthday | August 10, 2016, 12:13 PM

Fake Xanax can be a killer





Name the Drug



24-year-old Male

- Admitted to inpatient rehab for SUD of IN X drug.
- Lives at home with father and sister. Mother died when patient was 21 yo.
- X drug use started age 20, quickly daily, episodes of not using and relapsing.
- Drug use limited to IN X drug
- Medical history is negative, except for urinary complaints: frequency, burning, gross hematuria, & suprapubic pain. Has had similar in the past. No discharge or lesions. Sexually active. Heterosexual. HIV-
- Tobacco: 1ppd since age 17



24-year-old Male

Find	lings					
Res	ult Name	Result	Abn1	Normal Range	Units	LOC.
Col	or.	Yellow		Yellow		
App	earance	Hazy	a	CLEAR		
Spe	cific Gravity	1.033		1.004-1.036		
рĤ	- UR	5.0		5.0-8.0		
Pro	otein, Urine	100	a	Negative		
Glu	icose, Urine	Negative		Negative	mg∕dL	
Ket	ones	Neĝative		Neĝative	mĝ∕dL	
Bil	irubin	Negative		Negative		
B] (od, Urine	Large	a	Negative		
Ni t	rites	Negative		Negative		
Und	bilinogen	<2.0		0.2-2.0	mg∕dL	
Lei	kocyteš Esterase	Moderate	a	Negative		
WBC	, Urine	96	н	0-5	/HPF	
RBC	., Urine	>182	н	0-3	/HPF	
Hya	aline Cast	6-10		0-5		
Cal	cium Oxalate Crystals	Rane	a	None Seen		

Urine culture negative, CMP- WNL, CBC-WNL
 UDT: negative-- opiates, cocaine, methadone, amphetamine, THC, benzo
 GC, Chlamydia, RPR all negative

4

What is the Diagnosis?

- Want to know his Ethnicity?
- Chinese American
- Which Drug?

•KETAMINE CYSTITIS



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Long-term	Ulcers and stomach p	Ulcers and pain in the bladder; kidney problems; stomach pain; depression; poor memory.					
Other Health- related Issues	Sometime Risk of HI from shar	Sometimes used as a date rape drug. Risk of HIV, hepatitis, and other infectious diseases from shared needles.					
In	Increased	Increased risk of adverse effects.					

In Increased risk of adverse effects. Combination with Alcohol Withdrawal Symptoms Unknown. Treatment Options Medications There are no FDA-approved medications to treat





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