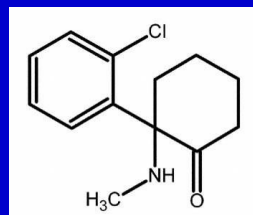


# Ketamine Cystitis

Dr Peggy CHU  
Tuen Mun Hospital

Ketamine ( $C_{13}H_{16}ClNO$ )  
(2-(*o*-Chlorophenyl)-2-(methylamino) cyclohexan-1-one

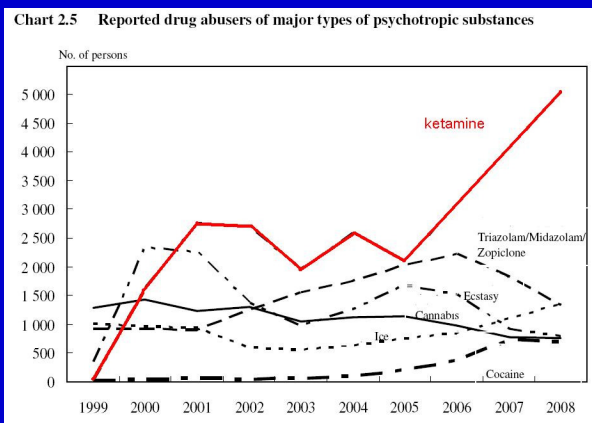


- N-methyl-D-aspartate (NMDA) receptor antagonist
- 1965, first used in humans
- analgesia & dissociative anaesthesia, provides amnesia to pain
- Rapid onset, short duration of action & titratable
- Does not depress cardiovascular and respiratory sys

## Ketamine

- onset
  - 3 – 5 min (IMI)
  - 60 s (IVI)
- duration of action
  - 20 – 30 min (IMI)
  - 10 – 15 min (IVI)
- N-dealkylated in liver, metabolized and excreted in urine (>90%)

## Hong Kong Statistics



# HK's first 10 cases of ketamine cystitis

M E D I C A L  
P R A C T I C E

## 'Street ketamine'—associated bladder dysfunction: a report of 10 cases

Peggy SK Chu 朱秀群  
SC Kwok 郭善淳  
KM Lam 林建文  
TY Chu 朱天僊  
Steve WH Chan 陳偉希  
CW Man 文志衛  
WK Ma 馬偉傑  
KL Chui 崔家倫  
MK Yiu 姚焜熿  
YC Chan 陳耀祥  
ML Tse 謝萬里  
FL Lau 劉飛龍

Ten young ketamine abusers presented with lower urinary tract symptoms to two regional hospitals in Hong Kong. Investigations demonstrated contracted bladders and other urinary tract abnormalities. These types of findings have never been reported before in ketamine abusers. The possible aetiology is also discussed.

### Introduction

Ketamine, an *N*-Methyl-D-aspartate receptor antagonist, is an anaesthetic agent characterised by a rapid onset and short duration of action. It has been used for the induction and maintenance of anaesthesia for more than 30 years<sup>1</sup> but has increasingly been abused as a 'club-drug' at dance and rave parties since the late 1980s.<sup>2</sup> This is an increasing problem in Hong Kong<sup>3</sup> and ketamine is now second only to heroin among psychotropic substances being abused.<sup>4</sup> Ten ketamine abusers (seven from Tuen Mun Hospital and three from Princess Margaret Hospital) were found to have severe bladder dysfunction—with markedly diminished functional bladder capacities of around 30 to 50 mL.

*Hong Kong Med J* 2007; 13: 311–3

## Introduction

TABLE. Physical characteristics, clinical and radiological features of the 10 patients

Patient No.	Sex/age (years)	Date of presentation	Duration of taking ketamine (years)	ALP/ALT* (U/L)	Serum creatinine (μmol/L)	USG† kidney
1	F/25	Nov 2000	1	382/129	400	B hydro
2	M/30	Jun 2006	2	142/27	220	B hydro
3	M/30	Sep 2006	4	413/83	177	B hydro
4‡	M/25	Jan 2007	Unknown	558/407	99	B hydro
5‡	F/22	Jan 2007	Unknown	164/74	46	B hydro
6	M/25	Feb 2007	2	114/114	85	Normal
7	M/26	Mar 2007	Unknown	124/242	95	B hydro
8§	M/20	Mar 2007	Unknown	107/40	75	Normal
9§	M/21	Mar 2007	1	624/1141	237	B hydro
10	F/26	Apr 2007	1	229/48	100	B hydro

\* ALP denotes alkaline phosphatase (reference range, 46–127 U/L); and ALT alanine aminotransferase (reference range, 10–57 U/L)

† USG denotes ultrasonography, and B hydro bilateral hydronephrosis

‡ Patients 4 and 5 are a couple; patient 5 became a ketamine abuser after marrying patient 4

§ Patient 8 was prescribed cimetidine while patient 9 was prescribed omeprazole for epigastric pain

*Hong Kong Med J* 2007; 13: 311–3

## Patients

- TMH
- Sep 2006 - Jun 2010
- 113 patients
- M: F = 90: 43
- mean age 25.6 yrs (14 – 42)
- years of ketamine abuse: 3/12 to 11 years
- referred by A&E, GP, psychiatrist
- C/O: LUTS+ve

## Lower Urinary Tract Symptomatology

- frequency, urgency, dysuria, urge incontinence, painful haematuria
- urine culture –ve
- no response to multiple courses of oral antibiotics

日期		23/6		24/6											
星期		日		日											
		飲水	排尿	飲水	排尿	飲水	排尿	飲水	排尿	飲水	排尿	飲水	排尿	飲水	排尿
上午 6am															
7				100	30ml	100	30								
8				100	30ml	100	30								
9				100	30ml										
10					30ml										
11															
正午 12N															
下午 1pm				300	60ml										
2				100	40ml										
3				100	30ml										
4															
5				100	30ml										
6															
7			30	100	20ml										
8			10	100	30ml										
9				100	30ml										
10			30	100	40ml										
11			10	100	30ml										
午夜 12		150	10												
凌晨 1am			30	100	30										
2		100	10	100	30										
3			30	100	30										
4		100	10	100	30										
5				100	30										

## Urodynamic evaluation

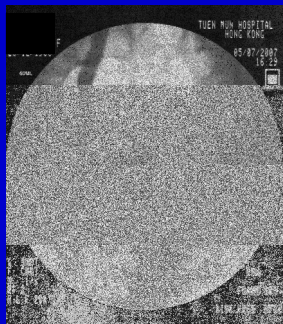
- 56/113
- Cystometric capacity 14 – 600 ml
  - 42/56  $\leq$  150 ml
  - 30/56  $\leq$  100 ml
- 6/56      bilateral vur

# Urodynamic



# Urodynamic

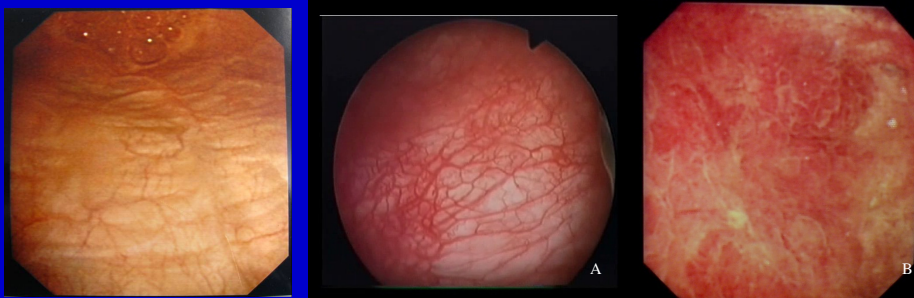
- uni/bilateral vur



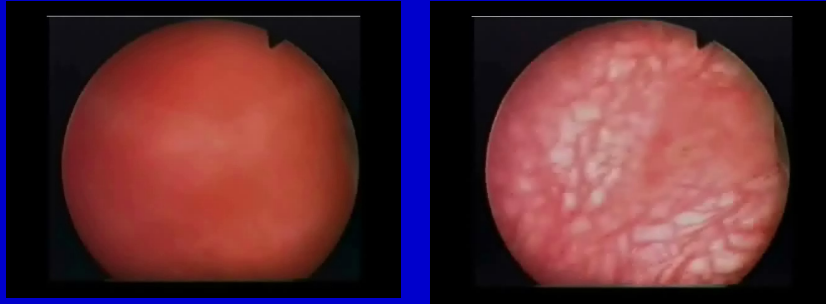
## Cystoscopic Findings

- 65/113 had cystoscopy
- 25/65
  - various degrees of mucosal inflammation
  - glomerulations

## Cystoscopic findings



## Cystoscopic findings



## Upper Urinary Tract

- blood creatinine
- +/- hydronephrosis
  
- papillary necrosis
- ureteric stricture



## Blood Creatinine

- 10/113
  - Creatinine 126 - 1069
  - 2 required PCN



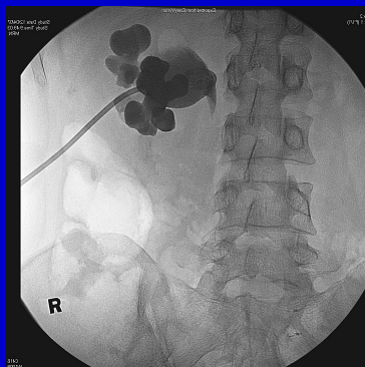
## Upper Tract Radiology

- all have renal USG
  - 30% bilateral hydronephrosis
  - 10% unilateral hydronephrosis



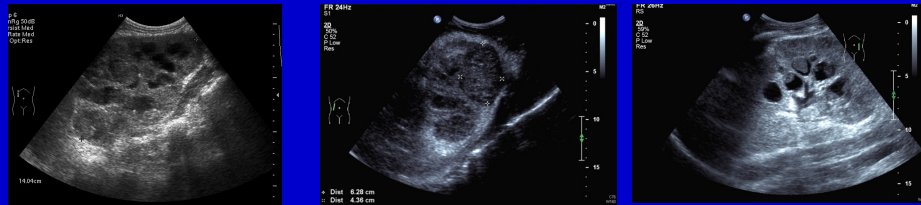
## Upper Tract Radiology

- 2 bilat PCN x ARF



## Upper Tract Radiology

- all have renal USG
  - 4/113 sonographic evidence papillary necrosis



## Upper Tract Radiology

- CT scan
  - acute papillary necrosis
  - Paraaortic lymphadenopathy
  - thickened ureteric wall suggestive of marked ongoing transmural inflammatory changes



## Aetiology

- ? ketamine
- ? cutting agent (?impurities)

## Evidence for ketamine

- HK  
only pure ketamine identified in the  
“ketamine” provided by patient &  
government lab
- Canada

**A Pediatric Case of Ketamine-associated Cystitis (Letter-to-the-Editor RE: Shahani R, Streutker C, Dickson B, et al: Ketamine-associated Ulcerative Cystitis: A New Clinical Entity. Urology 69: 810–812, 2007)**

## Pathophysiology

- ? chronic submucosal inflammatory response resulting from chemical cystitis
- ? microvascular changes
- ? autoimmune (raised ESR & C3/4)
- ? bacteriuria

## Treatment

- × Antibiotics
- × Antimuscarinic agent (oxybutynin, detrusitol)
- × Hyaluronic acid (oral elmeron /intravesical cystistat)
- √ ? Cystoplasty
- √ √ √ *ABSTINENCE*

## Guidelines (before Jun 2008)

$\leq 25$ g	within discretion of sentencer
25 – 400 g	2 - 4 yrs' imprisonment
400 - 800 g	4 - 8 yrs
$\geq 800$ g	$\geq 8$ yrs

## Guideline (after Jun 2008)

$\leq 1$ g	within discretion of sentencer
1 - 10 g	2 - 4 yrs' imprisonment
10 - 50 g	4 - 6 yrs
50 - 300 g	6 - 9 yrs
300 - 600 g	9 - 12 yrs
600 - 1000 g	12 - 14 yrs
$\geq 1000$ g	$\geq 14$ yrs

# Asia

- China

中华泌尿外科杂志 2008 年 7 月第 29 卷第 7 期 Chin J Urol, July 2008, Vol. 29, No. 7

## 氯胺酮相关性泌尿系统损害

吴芃 朱秀群 姚铭广 郑少斌 谭万龙  
文志卫 韦安阳 程伟 吴威武

**【摘要】** 目的 探讨滥用氯胺酮(K粉)所引发的泌尿系损害及其诊治方法。方法 因吸食K粉导致泌尿系统损害患者20例,男14例,女6例。平均年龄22岁。吸食K粉1~4年。均有严重的尿频、尿急、尿痛和(或)血尿症状。尿培养阴性。B超提示双侧上尿路积水16例,14例行IVU及10例行CT检查均提示上尿路积水扩张、膀胱挛缩,1例肾乳头坏死,合并不同程度肝肾功能损害。治疗时要求患者戒断毒品并实验性用药。结果 6例活检病理提示膀胱黏膜炎性改变,在停止或减少滥用K粉后,12例症状逆转,皮质激素及透明质酸钠治疗6例症状缓解。结论 K粉相关性泌尿系统损害可能是一种以下尿路刺激症状为主要表现的全尿路炎性损害,其发生机制及治疗方法有待进一步研究。

**【关键词】** 氯胺酮; 药物滥用; 泌尿系损害

# Asia

## Taiwan

### Ulcerative Cystitis Associated with Ketamine

Authors: Jui-Hsiu Tsai<sup>a</sup>; Kun-Bow Tsai<sup>b</sup>; Mei-Yu Jang<sup>c</sup>

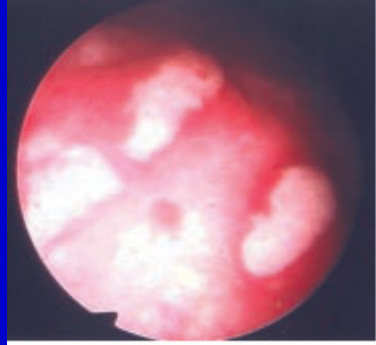
Affiliations: <sup>a</sup> Department of Psychiatry, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Medical University, Taiwan

<sup>b</sup> Department of Pathology, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Medical University, Taiwan

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# Asia

## Taiwan



*Am J Addict* 2008; 17(5):453

# Canada

## Ketamine-Associated Ulcerative Cystitis: A New Clinical Entity

Rohan Shahani, Cathy Streutker, Brendan Dickson, and Robert J. Stewart

<b>OBJECTIVES</b>	Ketamine hydrochloride is an <i>N</i> -methyl-D-aspartic acid receptor antagonist used as an anesthetic agent in human and veterinary procedures. Increasingly, it is being used as a recreational drug. Recreational ketamine users have anecdotally reported increased lower urinary tract symptoms while using the substance.
<b>METHODS</b>	We describe a series of 9 patients, all of whom were daily ketamine users, who presented with severe dysuria, frequency, urgency, and gross hematuria. Investigations, including urine culture, microscopy, and cytology, in addition to computed tomography, cystoscopy, and bladder biopsies, were performed to identify a relationship between recreational ketamine use and these symptoms.
<b>RESULTS</b>	The urine cultures were sterile in all cases. Computed tomography revealed marked thickening of the bladder wall, a small capacity, and perivesicular stranding, consistent with severe inflammation. At cystoscopy, all patients had severe ulcerative cystitis. Biopsies in 4 patients revealed epithelial denudation and inflammation with a mild eosinophilic infiltrate. Cessation of ketamine use, with the addition of pentosan polysulfate, appeared to provide some symptomatic relief.
<b>CONCLUSIONS</b>	This case series has described a new clinical entity of severe ulcerative cystitis as a result of chronic ketamine use. As illicit ketamine becomes more easily available, ulcerative cystitis and potential long-term bladder sequelae related to its use may be a more prevalent problem confronting urologists. <i>UROLOGY</i> 69: 810–812, 2007. © 2007 Elsevier Inc.

*Urology* 2007; 69(5): 810-2



## Europe

- UK : 1<sup>st</sup> reported case from Guy's Hospital



A 27 year old man with a history of ketamine use presented with acute right loin pain and a history of lower urinary tract symptoms. Discontinuing ketamine relieved symptoms temporarily. Intravenous urography showed distension suggesting bilateral obstruction, not present six months before, and a small contracted bladder. Previous bladder biopsies showed ulcerative cystitis with neutrophilic and eosinophilic infiltration. On further questioning, the patient said that several friends who used ketamine had similar symptoms. These findings suggest ketamine associated cystitis. The clinical course in this newly described condition is unknown, but over six months our patient's urinary function deteriorated.

*BMJ* 2008; 336: 898

## Europe

- UK: echoed by urologists from Bristol

### **AN EMERGING PROBLEM**

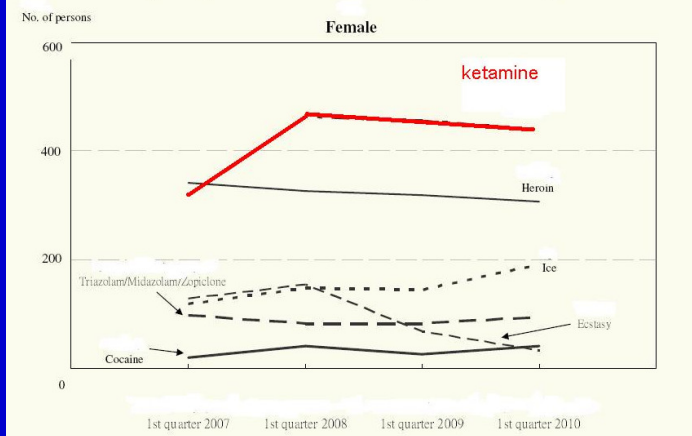
#### **Urinary tract disease associated with chronic ketamine use**

Regarding the case study by Dhillon et al,<sup>1</sup> we have seen an alarming increase in people presenting to urological services in South West England with bladder symptoms associated with chronic ketamine use.

*BMJ* 2008; 336: 973

# New Problems with ketamine abuse

Reported drug abusers by sex by common type of drugs abused (1st quarter 2007 to 1st quarter 2010)



# PUF score

Patient's Name: \_\_\_\_\_ Today's date: \_\_\_\_\_

**PELVIC PAIN and URGENCY/FREQUENCY PATIENT SYMPTOM SCALE**

Please circle the answer that best describes how you feel for each question.

	0	1	2	3	4	SYMPTOM SCORE	BOTHER SCORE
1. How many times do you go to the bathroom during the day?	3-6	7-10	11-14	15-19	20+		
2. a. How many times do you go to the bathroom at night?	0	1	2	3	4+		
b. If you get up at night to go to the bathroom, does it bother you?	Never	Occasionally	Usually	Always			
3. a. Do you now or have you ever had pain or symptoms during or after sexual intercourse?	Never	Occasionally	Usually	Always			
b. Has pain or urgency ever made you avoid sexual intercourse?	Never	Occasionally	Usually	Always			
4. Do you have pain associated with your bladder or in your pelvis (vagina, labia, lower abdomen, urethra, perineum, testes, or scrotum)?	Never	Occasionally	Usually	Always			
5. a. If you have pain, is it usually:		Mild	Moderate	Severe			
b. Does your pain bother you?	Never	Occasionally	Usually	Always			
6. Do you still have urgency after going to the bathroom?	Never	Occasionally	Usually	Always			
7. a. If you have urgency, is it usually:		Mild	Moderate	Severe			
b. Does your urgency bother you?	Never	Occasionally	Usually	Always			
8. Are you sexually active? Yes No							

SYMPTOM SCORE = (1, 2a, 3a, 4, 5a, 6, 7a)

BOTHER SCORE = (2b, 3b, 5b, 7b)

TOTAL SCORE (Symptom Score + Bother Score) = \_\_\_\_\_

**盆腔痛楚及尿急/尿频病人症状尺度**

	0=	1=	2=	3=	4=	症状分數	困擾分數
1. 你在日間上廁所多少次?	3-6	7-10	11-14	15-19	20+		
2. a. 你在夜間上廁所多少次?	0	1	2	3	4+		
b. 如果你在夜間起廁所，這情況有礙你生活嗎?	從不	間中	經常	經常			
3. a. 你現在或以曾有否在進行房事時或之後感到痛楚/不適?	從不	間中	經常	經常			
b. 你會否因感到痛楚/不適而避免房事?	從不	間中	經常	經常			
4. 你有沒有膀胱或盆腔痛楚（如：睪丸、睪丸、睪丸、睪丸、睪丸）的痛楚？	從不	間中	經常	經常			
5. a. 如果你有痛楚，程度是：		輕微	中度	嚴重			
b. 這些痛楚有礙你生活嗎?	從不	間中	經常	經常			
6. 你排尿時有尿急的感覺嗎?	從不	間中	經常	經常			
7. a. 如果你有尿急，程度是：		輕微	中度	嚴重			
b. 尿急的頻度有礙你生活嗎?	從不	間中	經常	經常			
8. 你有否進行房事?	有/沒有						

困擾分數 (1, 2a, 3a, 4, 5a, 6, 7a) = \_\_\_\_\_

症狀分數 (2b, 3b, 5b, 7b) = \_\_\_\_\_

總分 (困擾分數 + 症狀分數) = \_\_\_\_\_

## Neurogenic Bladder arising from ketamine abuse



## ketamine cystitis

social problem  $\longleftrightarrow$  medical problem

Thank You