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and Clinical Toxicologists (EAPCCT)  
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## Novel and Emerging Recreational Drugs: A Hong Kong Perspective

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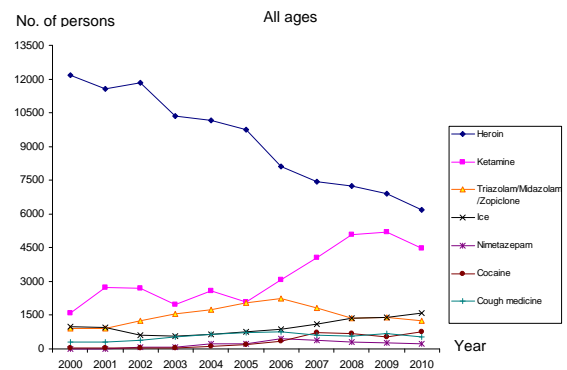
## Outline of presentation

- The trend for drug abuse
- The increasing importance of ketamine as an abuse drug
- The toxic effects of ketamine – upper GIT and lower urinary tract complications
- The problem of drug driving
- The emerging recreational drugs

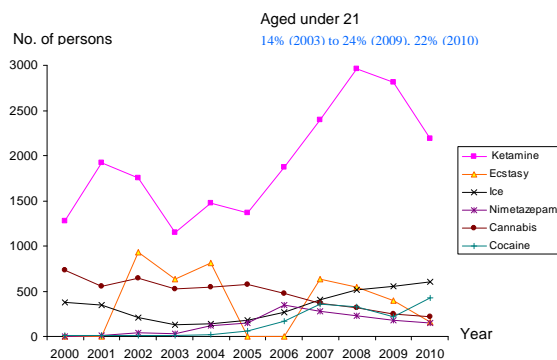
## Central Registry of Drug Abuse (since 1972)

- Provides drug abuse statistics for monitoring changes in drug abuse trends, characteristics of drug abusers to facilitate the planning of anti-drug strategies and drug abuse programmes
- Collates information regularly on drug abuse cases reported by law enforcement departments treatment and welfare agencies, hospitals and clinics and tertiary institutions
- Voluntary, cooperation of reporting agencies
- Compiles/releases latest drug abuse statistics on a quarterly basis, individuals not identified

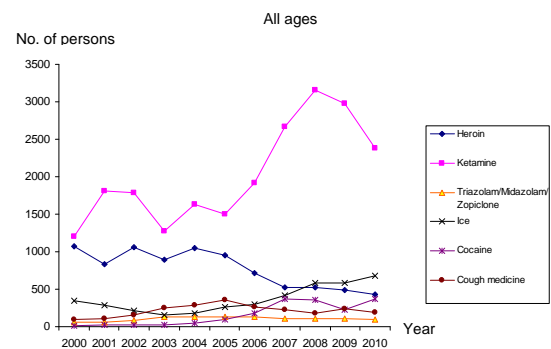
## Reported drug abusers in Hong Kong



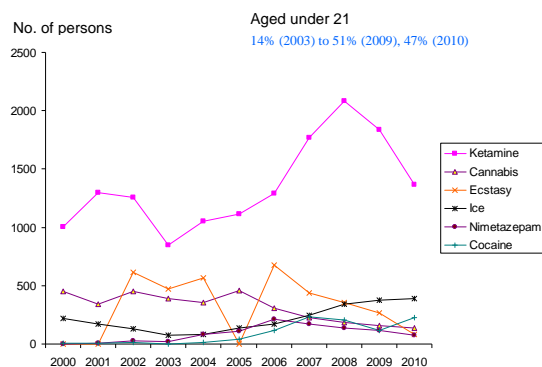
## Reported drug abusers in Hong Kong



## Newly reported drug abusers in Hong Kong



## Newly reported drug abusers in Hong Kong



## Ketamine abuse in Hong Kong

- Since 2001, ketamine = most commonly abused psychotropic substance, followed by triazolam/midazolam/zopiclone, "ice", cough med., cannabis, cocaine, ecstasy
- In 2010, 36% of abusers of all ages and 80% of abusers aged <21 years abused ketamine
- In 2010, 65% of newly reported abusers of all ages and 78% of abusers aged <21 years abused ketamine

### 233 ketamine abusers presented to A&E department

7/2005-6/2008, 13-60 y (median 22 y), 68.2% males

Insufflation 88%, oral 5%, unknown 7%

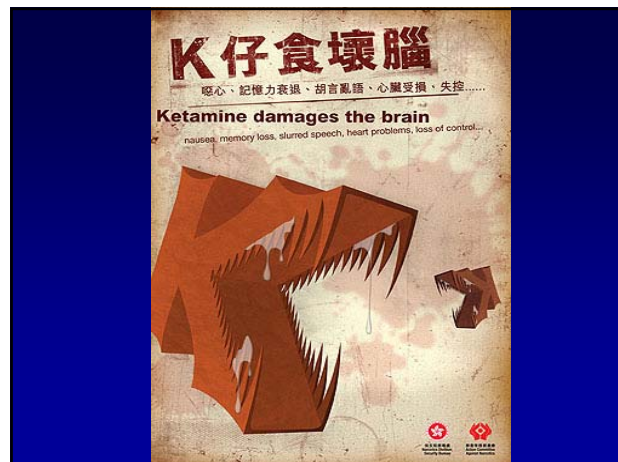
Impaired consciousness 45%, abdominal pain 21%, lower urinary tract symptoms 12%, dizziness 12%

High BP 40%, tachycardia 39%, abdominal tenderness 18%, white powder in nostrils 17%

35 had evaluation of hepatobiliary or urological systems  
→ 2 with dilated CBD, 4 with hydronephrosis

5 with co-ingested agents needed ICU care

Ng SH et al. Hong Kong Med J 2010; 16: 6-11



### A study on the cognitive impairment and other harmful caused by ketamine abuse (Narcotics Division, 2005)

15-30 y, 95 ketamine users ( $\geq 2/\text{month} \times > 6$ ), 26 controls

Dependence syndrome → 79%, after  $12.7 \pm 9.3$  months

More psychiatric disturbance (e.g. psychotic symptoms)

26.3% with lifetime history of psychiatric diagnosis – depressive disorder 12.6%, Rx-induced psychosis 6.3%

Neurological deficit in motor coordination

Difficulty in organising performance tasks

Impaired memory

Accelerated neuroapoptosis (Green SM et al, 2009)

### 37 ketamine abusers with upper GI problems

2001-2008, 2 surgical units, insufflation (mean 4 y)

Past hx of upper GI problems, other drugs, NSAID use, *H. pylori* infection excluded

33 (89.2%) had urological symptoms

28 (75.5%) had upper GI symptoms (epigastric pain 62.2%, epigastric pain/vomiting 10.8%)

14 of the 28 patients with upper GI endoscopy – gastritis 85.7%, gastroduodenitis 7.1%, normal 7.1%

Mean ALT and ALP marginally elevated

H<sub>2</sub>-blockers or PPIs

Abstinence from ketamine use leads to symptom relief

Poon TL et al. J Digest Dis 2010; 11: 106-10

### 3 ketamine abusers with dilated CBDs

2008, 2M, 1F, 21-27 y, used for 1.5-7 y

Recurrent epigastric pain (gastritis, gastric erosions), ↑ ALT (75-333 IU/L), ↑ ALP (122-137 IU/L) but normal bilirubin

US or CT – dilated CBDs (maximum 9-17 mm, normal 3.1mm) and CHDs and normal GB

Radiologically – fusiform dilatation of entire common hepatic and bile ducts, resembling choledochal cyst

After cessation of ketamine misuse, complete resolution of symptoms and radiological abnormalities

Wong SW et al. Hong Kong Med J 2009; 15: 53-6

**Ketamine damaged my bladder - now every bus trip becomes very long.**



**No drugs No self-destruction  
Not Now + Not Ever**

Heroinics Division, Security Bureau  
Action Committee Against Narcotics  
www.ad.gov.hk

### 10 ketamine abusers with bladder dysfunction

2000-2007, 2 hosp, 7M, 2F, 20-30 y, used for 1-4 y

Severe LURT symptoms – dysuria, urgency, frequency (to void Q15 min), urge incontinence, painful hematuria

Functional bladder capacity – 30-100 ml

Urodynamic studies (n=7) → detrusor overactivity, urine leakage when bladder filled to a capacity of 30-50 ml

US – bilateral hydronephrosis (n=7)

Contracted, trabeculated bladder, cystitis glandularis

All had ↑ ALT (27-1141 IU/L), ↑ ALP (107-624 IU/L)

Plasma creatinine 177-400 μmol/L in 5

Chu PSK et al. Hong Kong Med J 2007; 13: 311-3

### 59 ketamine abusers with bladder dysfunction

2000-2007, 2 hosp, 38M, 21F, 18-35 y, used for 0.5-10 y

Severe LURT symptoms, micturition Q15-90 min

Difficulty in maintaining work and daily activities

Unilateral/bilateral hydronephrosis 51%, plasma cr >120 μmol/L 14%, vesicoureteral reflux 13%

Detrusor overactivity or ↓ bladder compliance

Histological features resembling interstitial cystitis

7% radiological features suggestive of papillary necrosis

7 patients (bladder capacity >300 ml, no VUR, normal US), stopping or reducing ketamine use → normal

Chu PSK et al. Br J Urol Int 2008; 102: 1616-22

### Ketamine abusers with severe destruction of LURT

Bilateral hydronephrosis with hydroureters down to the level of vesicoureteric junction

3 out of 8 patients with bilateral hydronephrosis required temporary urinary diversion with PCN because of ↓ RF

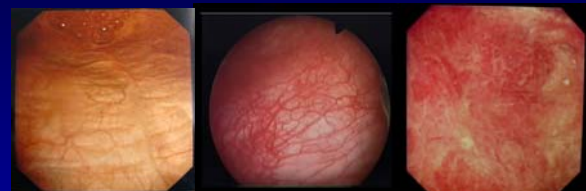
Antegrade pyelography → near-complete or complete obstruction of both ureters below the PUJ

One patient continued ketamine abuse, required surgery, developed ureteric stricture, fibrosis secondary to intense transmural inflammatory response (caused by ketamine)

Chu PSK et al. Hong Kong Med J 2007; 13: 311-3

Chu PSK et al. Br J Urol Int 2008; 102: 1616-22

### **Cystoscopic findings in ketamine abusers**



Normal

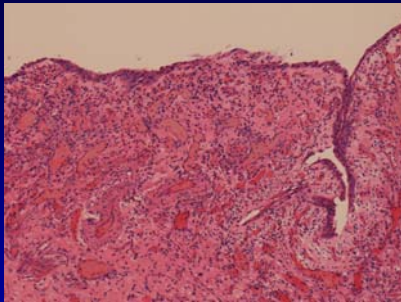
Daily use for 4 y

Daily use for 7 y

Epithelial inflammation and neovascularisation of various degrees, petechial haemorrhages in severe ones

(Dr. Peggy Chu)

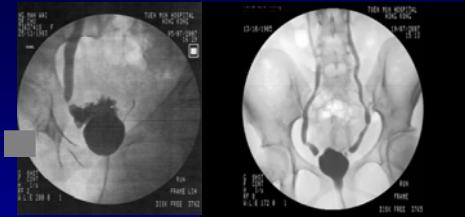
## Bladder biopsy



Cystitis – varying degrees of inflammation, with cellular infiltrates (predominately lymphocytes, also eosinophils)

(Dr. Peggy Chu)

## Cystogram



Unilateral or bilateral vesicoureteral reflux was a secondary event to the severely contracted bladder with high detrusor pressure

(Dr. Peggy Chu)

## Ketamine and destroyed LURT – pathogenesis

Rehabilitation centre survey → 30% had symptoms

Lower URT affected more frequently than upper URT

Long-term ↓ bladder compliance ± VUR → upper URT

The high concentrations of ketamine and its metabolite (glucuronide of hydroxy-norketamine)

- Direct toxic effects → chronic inflammatory responses
- Microvascular changes → ischaemia
- Autoimmune reactions

Toxic cystitis, renal papillary necrosis – prognosis?

Chu PSK et al. Br J Urol Int 2008; 102: 1616-22

## Drug driving

Use of illegal drugs can affect drivers and the driving task

- Slowing down the reaction time
- Dulling the thinking process making it difficult to multi-task ("process information quickly and manage several tasks simultaneously")
- Causing a distorted view of time and distance
- Stimulating the CNS → aggressive/dangerous driving, ↓ attention span, unaware of impaired driving, over-confidence, sudden fatigue

Centre for Accident Research & Road Safety, 2010

## Drug driving in Hong Kong

Higher incidence and changing pattern

- Arrest cases increased from 26 (2006-2009) to 73 (Jan-Nov 2010, ketamine in 63)
- 197 fatal vehicle crashes, 1996-2000 (FSI 2005)
  - 91 SVC → drugs 7%, drug/alcohol 5% (CNS stimulants inc. "ecstasy", cannabis, benzo, K)
  - 106 MVC → drugs 1%
  - SVC + MVC → drugs/alcohol 6%
- 69 fatal vehicle crashes, 1/2005-10/2007
  - Drugs (all)/alcohol 8.7% (Tsui KL, 2011)

## Prevalence of drug use among drivers

Non-fatal car casualties presented to a trauma Centre, HK

- Jan-Dec 2007, non-fatal MV driver casualties
- 395 agreed to bedside urine drug screening
- 18-63 y (median 28), 91% males, 38% private cars, 20% motor cycles
- 38 (10%) tested positive for ≥1 drug (ketamine 17, morphine 12, benzodiazepines 9, cannabis 6, "ice" 6, cocaine 5 ....)
- Age <25y and 00:00-07:59 associated with +ve

Wong OF et al. Hong Kong Med J 2010; 16: 246-51

## Legislative proposals to combat drug driving

To amend the Road Traffic Ordinance

- To make it an offence to drive with any amount of the commonly abused illegal drugs – heroin, ketamine, "ice", cannabis, cocaine, "ecstasy" – without the need to test for influence and impairment
- To empower Police to require persons suspected to be under the influence of drugs to take the preliminary drug tests; failure in rapid oral fluid test and/or impairment → blood and/or other body fluid specimens for laboratory analysis

## Emerging drugs of abuse in Hong Kong

- Derivatives of piperazines (police seizures since 5/2009 and case reports)
- Cathinone derivatives – mephedrone  
Cathinone (alkaloid extracted from the leaves of the khat plant *Catha edulis*); synthetic derivatives of cathinone in the recreational drug market
- Synthetic cannabinoids (police seizure 6/2010)
- The Dangerous Drugs Ordinance (Amendment of First Schedule) Order 2011 to impose legislative control to deter trafficking and abuse

## Piperazines: a new class of drug of abuse has landed in Hong Kong

Hong Kong Med J Vol 16 No 1 • February 2010 •

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- M/28 presented to hospital with tachycardia and chest discomfort
- Cocaine, ketamine and 1-(3-Trifluoromethylphenyl)-piperazine (TFMPP) detected in urine
- Serotonin receptor agonist, mild hallucinogenic effect  
1st reported 1996 → vomiting, headache, palpitations, anxiety, insomnia, confusion, irritability and tremors

## Hong Kong Poison Information Centre cases

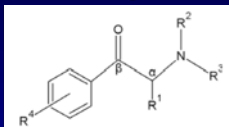
(Dr. S.H. Ng)

	Place	Drug	Clinical features	Remarks
F/24	Disco	Likely Ecstasy	Intense discomfort, anxiety, nausea. HR 100 bpm, drowsy, dilated pupils	Known ketamine abuse TFMPP and phentermine in urine
M/34	Private club	Ecstasy	Flushing, dry mouth, restlessness, hotness, palpitations BP 152/110 mmHg, HR 120 bpm. Dilated pupils	Known cocaine abuse TFMPP, ketamine, MA, amphetamine, cocaine, nimetazepam in urine
M/34	Private club	Ecstasy	Hotness, dry mouth, palpitations, generalised discomfort, agitation. BP 158/97 mmHg, dilated pupils	TFMPP, ketamine, cocaine in urine

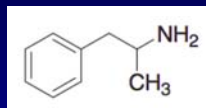
Patients aware of the different experience

## Mephedrone is an amphetamine "by another name", drug adviser tells MPs

BMJ News, 2010



Cathinone backbone



Amphetamine

Acute sympathomimetic toxidrome (e.g. hypertension, tachycardia and agitation) (Wood DM et al, 2010)

Mephedrone related deaths (Maskell PD et al, 2011)

Seizure of 0.47 g of mephedrone in Hong Kong, 6/2010

## Novel and Emerging Recreational Drugs in Hong Kong

- There was a rising trend for young drug abusers and ketamine was the most commonly involved.
- Ketamine abusers had with upper GI symptoms which improved after abstinence from use.
- Ketamine abusers presented with a syndrome of cystitis and contracted bladder, with secondary renal damage in severe cases; the duration and frequency of use correlated with the severity of symptoms & degree of damage to urinary tract.
- The prevalence of drugged drivers among non-fatal driver casualties was on the increase and ketamine was most commonly involved.