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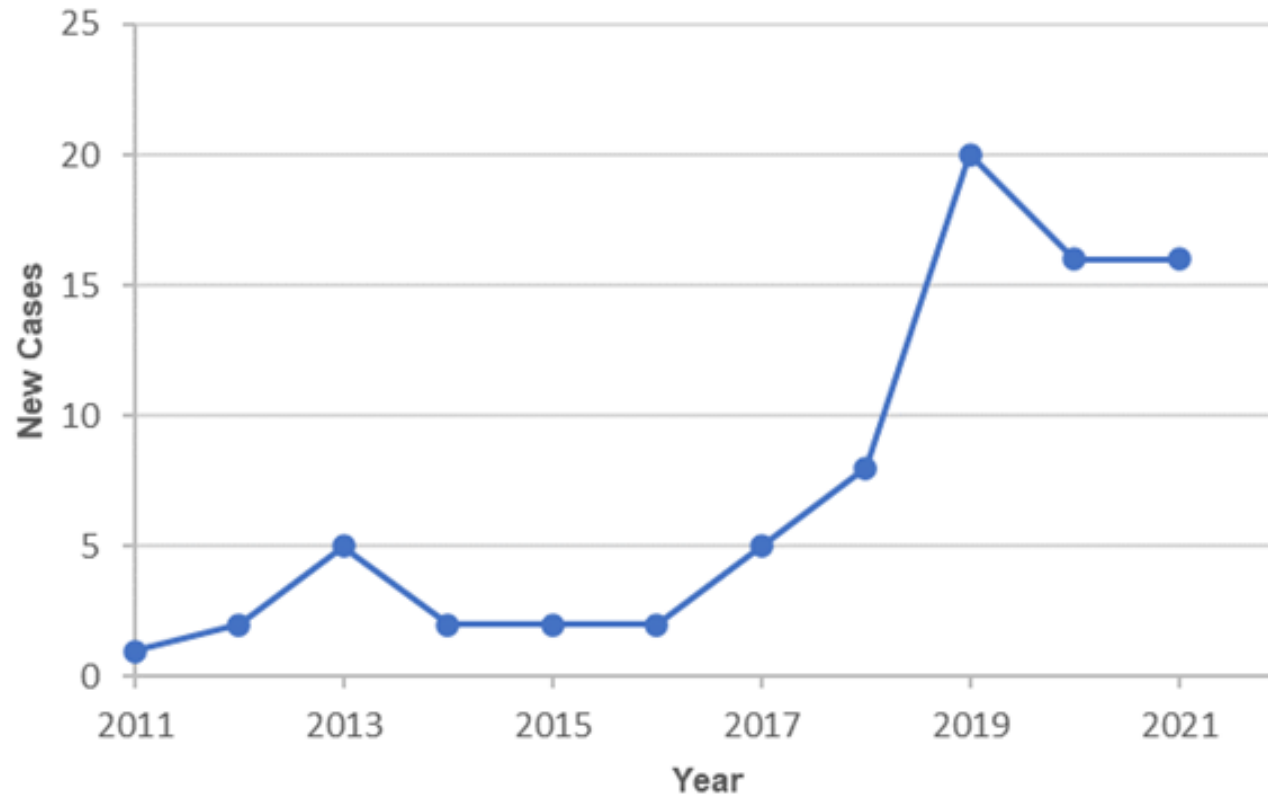


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# Ketamine Uropathy – Update and Discussion

Alison Downey  
Consultant Urologist  
MidYorks NHS Trust

# Background



**Figure 1:** Incidence of new diagnoses of ketamine uropathy per year (2011-2021).



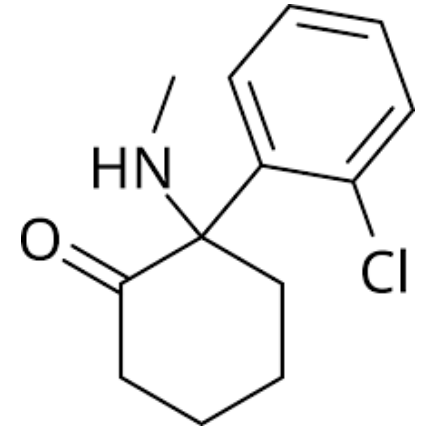
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# Ketamine

- Non-competitive NMDA acid receptor complex antagonist
- Licensed for use in the induction and maintenance of anaesthetic, refractory status epilepticus, acute and chronic pain and an antidepressant
- Metabolised in the liver by cytochrome P450 to active metabolite nor-ketamine
- Un-metabolised ketamine and norketamine are water soluble and excreted in the urine
- Maximum medical dose is 600mg/day orally
- Onset 3-5 mins, lasts 1hr
- S/E: Hypertension, apnoea, airway obstruction, arrhythmia, respiratory depression



# Illicit Use

- 1990's became a popular “rave” culture drug
- Relatively cheap - £20/g vs £50/g for cocaine, £45/g heroin
- Age of first use in the population is around 16
- 3% of 16-24 year olds are using ketamine
- Physiological dependence develops in 78.9% of users after 1 year
- Relatively low risk of antisocial behaviour



> [Urology](#). 2007 May;69(5):810-2. doi: 10.1016/j.urology.2007.01.038.

# Ketamine-associated ulcerative cystitis: a new clinical entity

[Rohan Shahani](#)<sup>1</sup>, [Cathy Streutker](#), [Brendan Dickson](#), [Robert J Stewart](#)

**BJUI** The destruction of the lower urinary tract by ketamine abuse: a new syndrome?  
BJU INTERNATIONAL

Peggy Sau-Kwan Chu, Wai-Kit Ma\*, Simon Chun-Wing Wong, Ringo Wing-Hong Chu, Cheung-Hing Cheng, Shun Wong<sup>†</sup>, Johnny Man-li Tse<sup>†</sup>, Fei-Lung Lau<sup>§</sup>, Ming-Kwong Yiu\* and Chi-Wai Man

How ketamine has become the drug of choice at middle-class dinner parties as well as cocaine among people earning over £52,000 a year



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## Ketamine to become Class B drug, say ministers

© 12 February 2014



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## Ketamine user: It's not taken long to ruin my bladder

© 10 December 2013

# Clinical Syndrome

## **Bladder**

- Severe Storage LUTs
- Urge Incontinence
- Small capacity bladder
- Painful Bladder
- Visible Haematuria

## **Upper Tract**

- Vesico-ureteric reflux
- Ureteric Strictures
- Papillary Necrosis
- Renal Infarction
- Chronic Renal Failure

# Mechanism of Damage

(A) Direct toxic damage to the urothelium by ketamine and metabolites

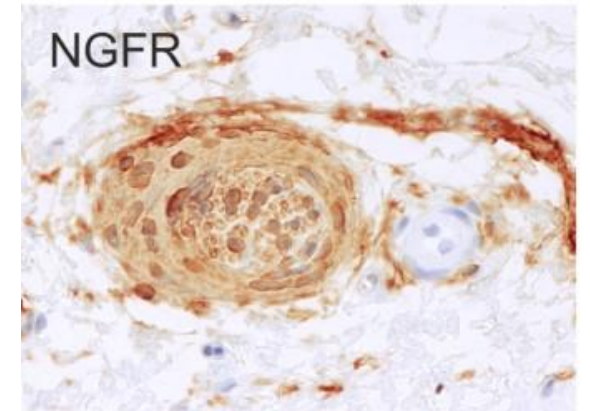
(B) Bladder barrier dysfunction: epithelial dysfunction with urinary leakage

(C) Neurogenic inflammation

(D) Eosinophilic infiltration - IgE mediated inflammation

(E) NOS-COX mediated inflammation

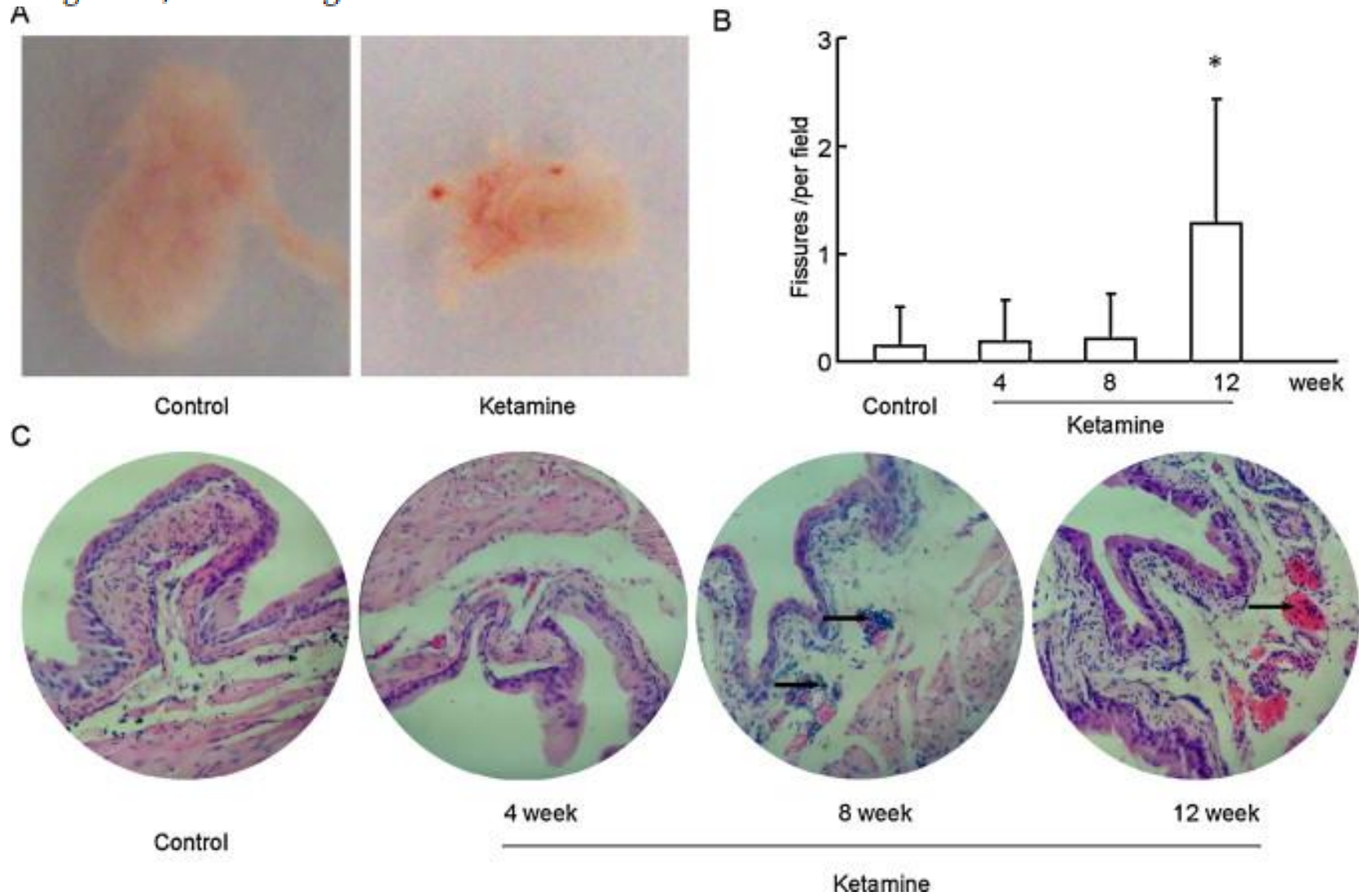
(F) Microvascular injury – NMDA receptors on endothelial cells

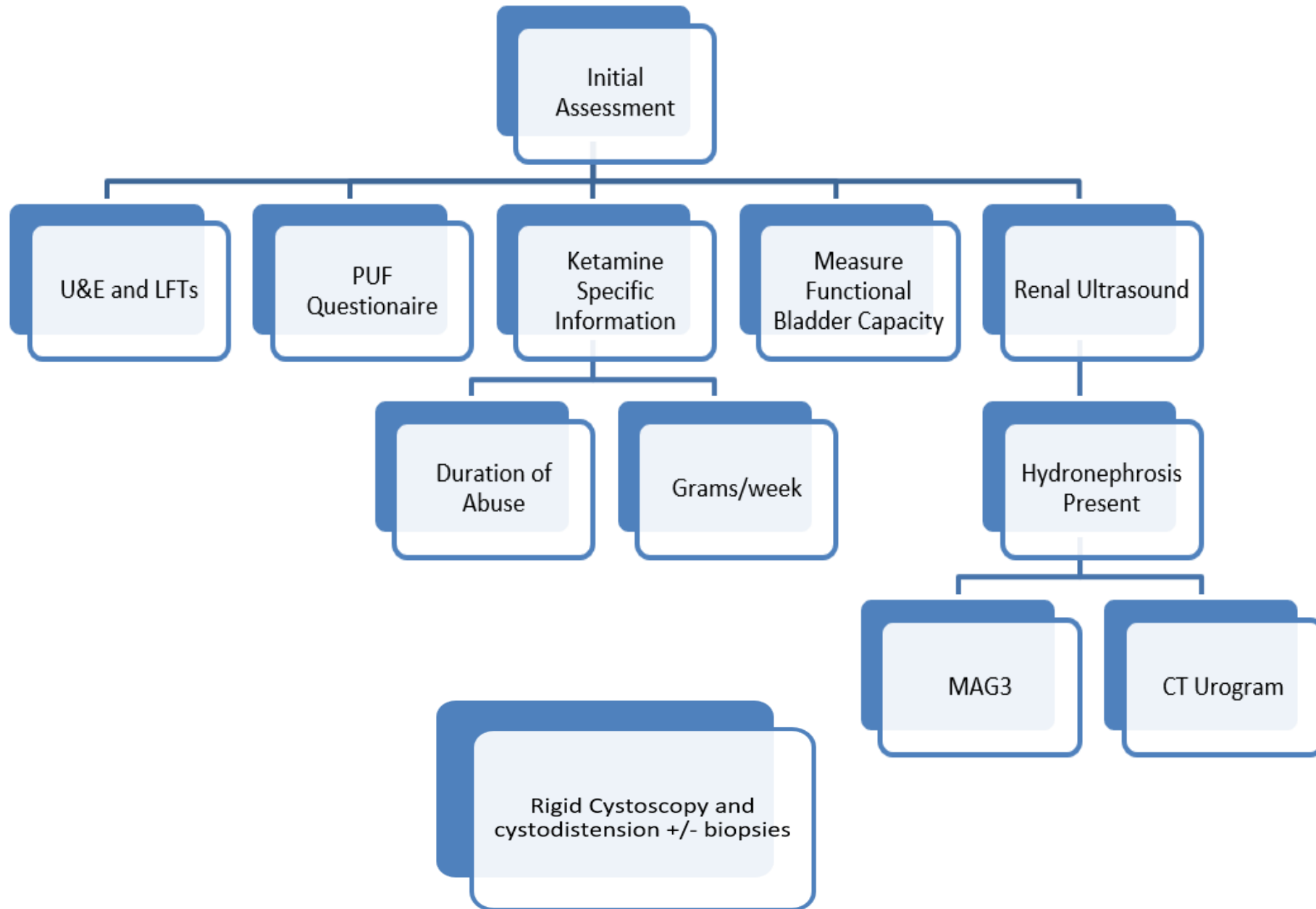




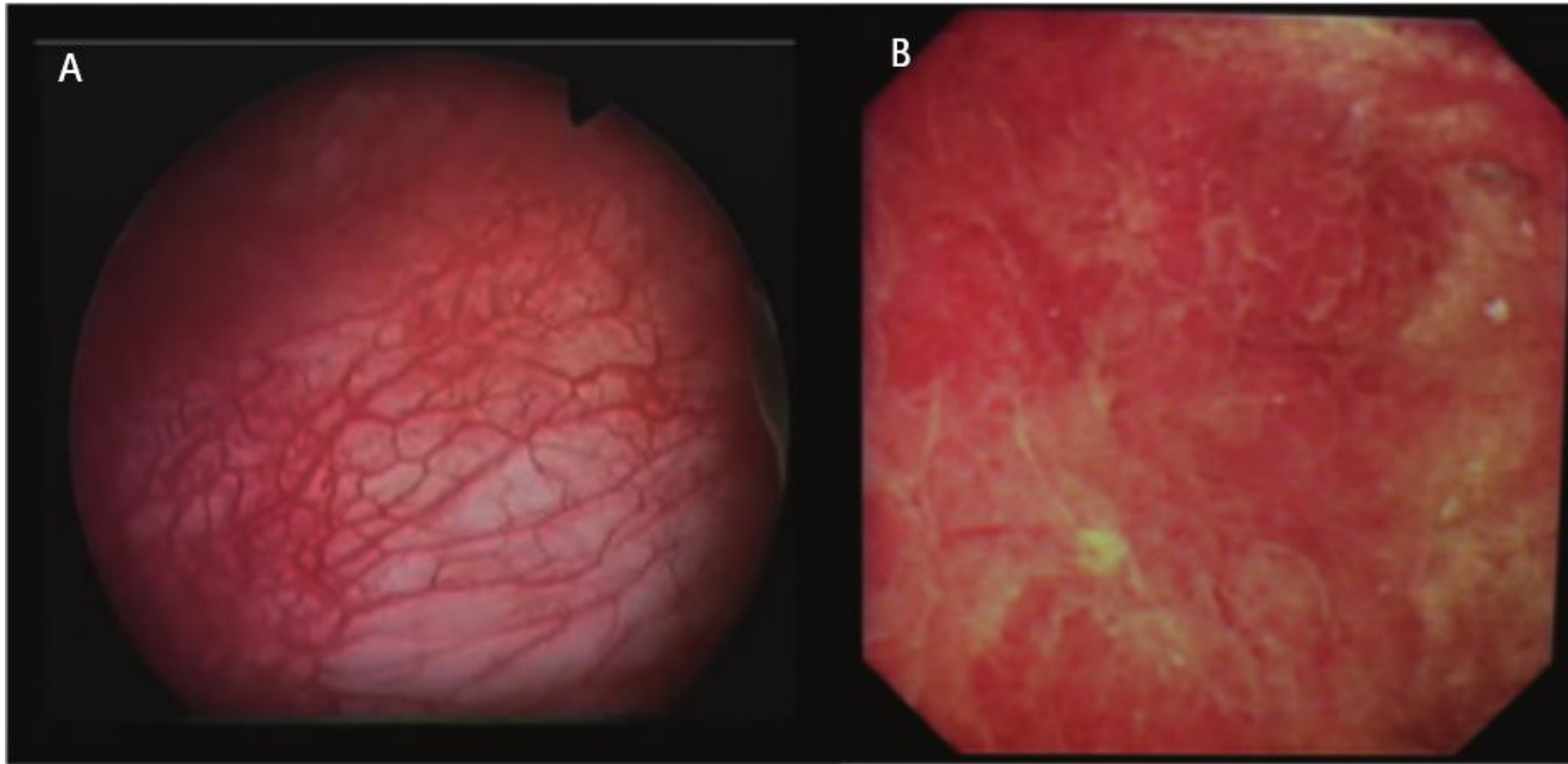
# Mast cells infiltration and decreased E-cadherin expression in ketamine-induced cystitis

Mengqiang Li<sup>a</sup>, Kang Yang<sup>b</sup>, Xiujian Wang<sup>b</sup>, Xiaodong Xu<sup>c</sup>,  
Ling Zhu<sup>b</sup>, Huili Wang<sup>b,+</sup>

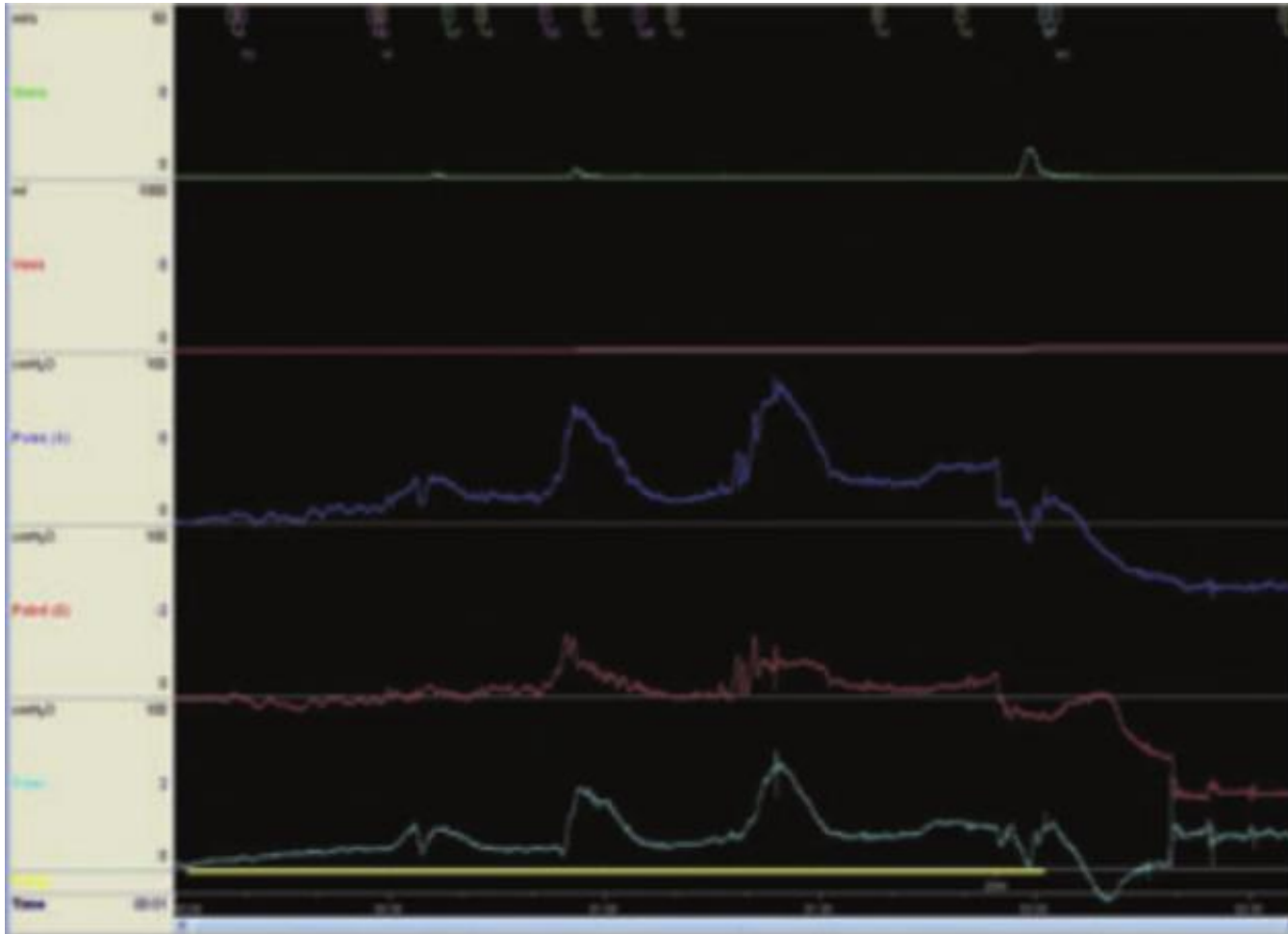


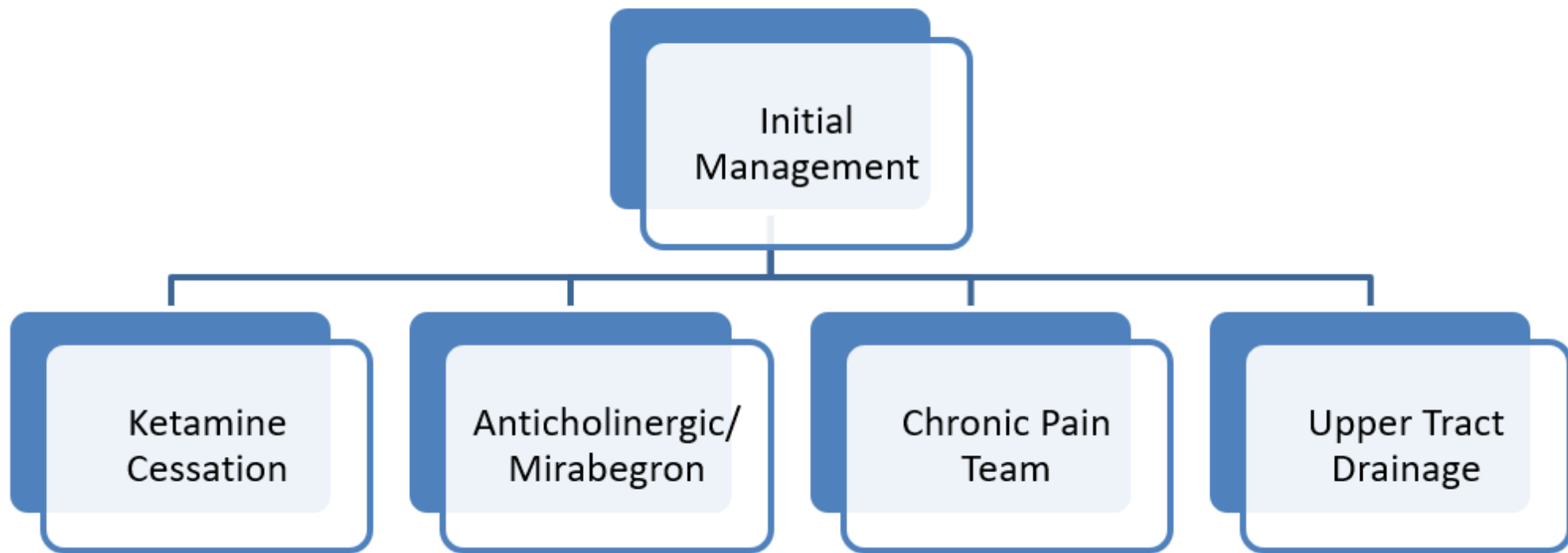


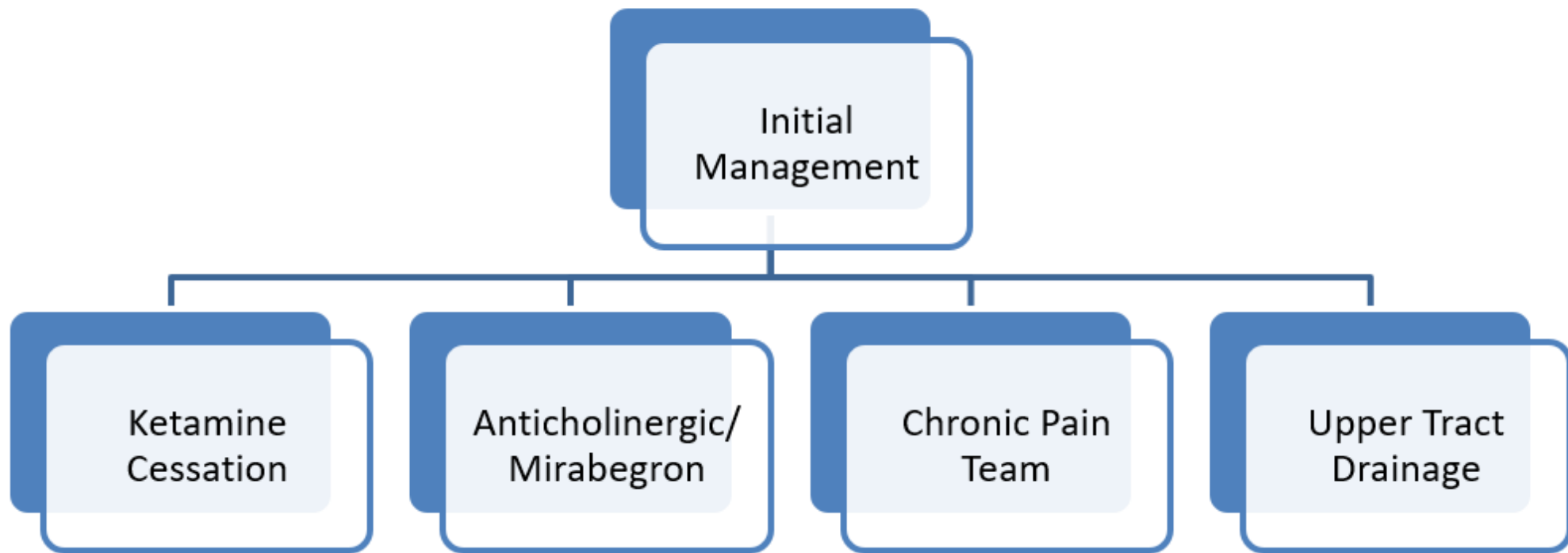
# Cystoscopic Appearance

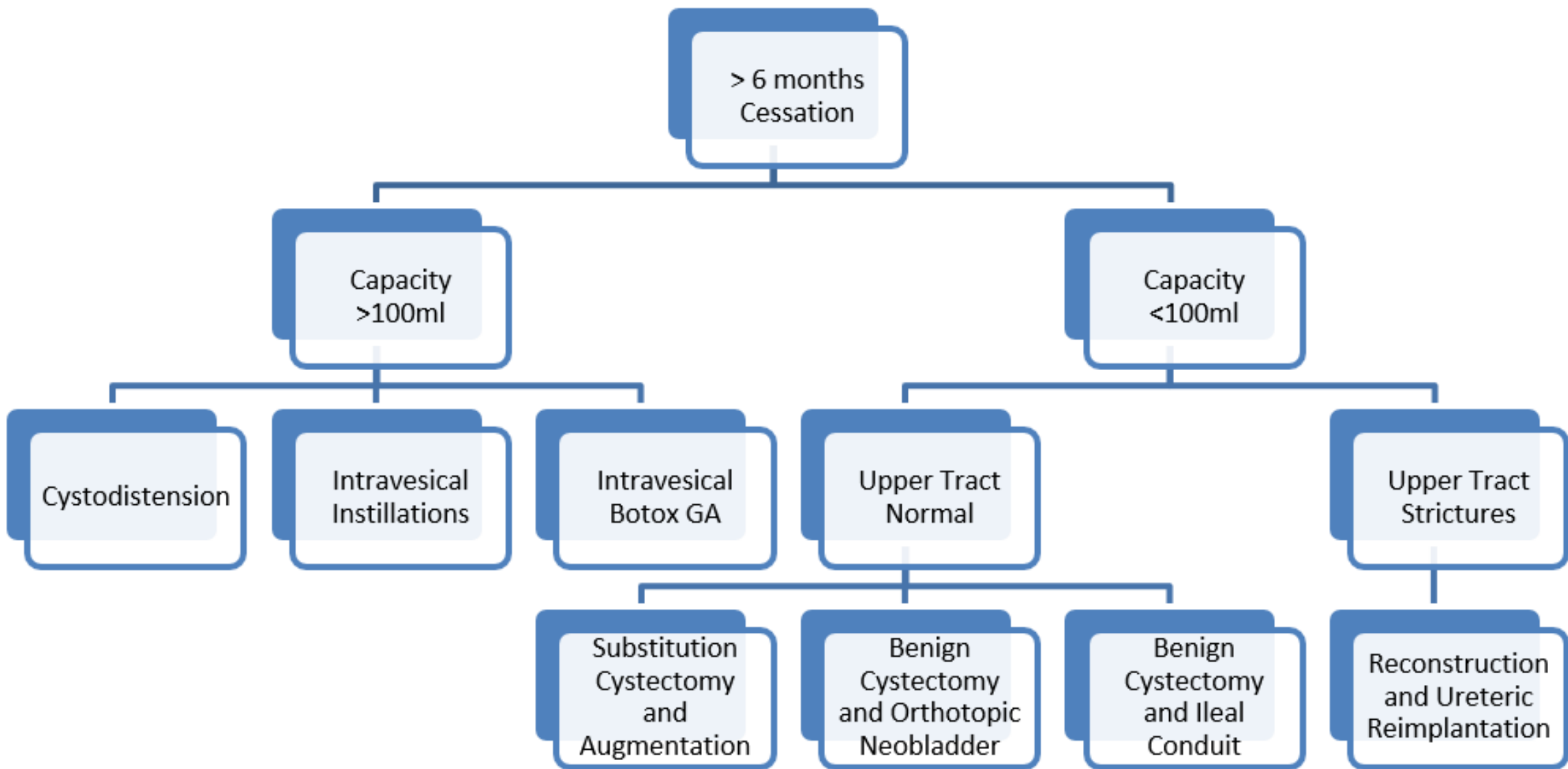


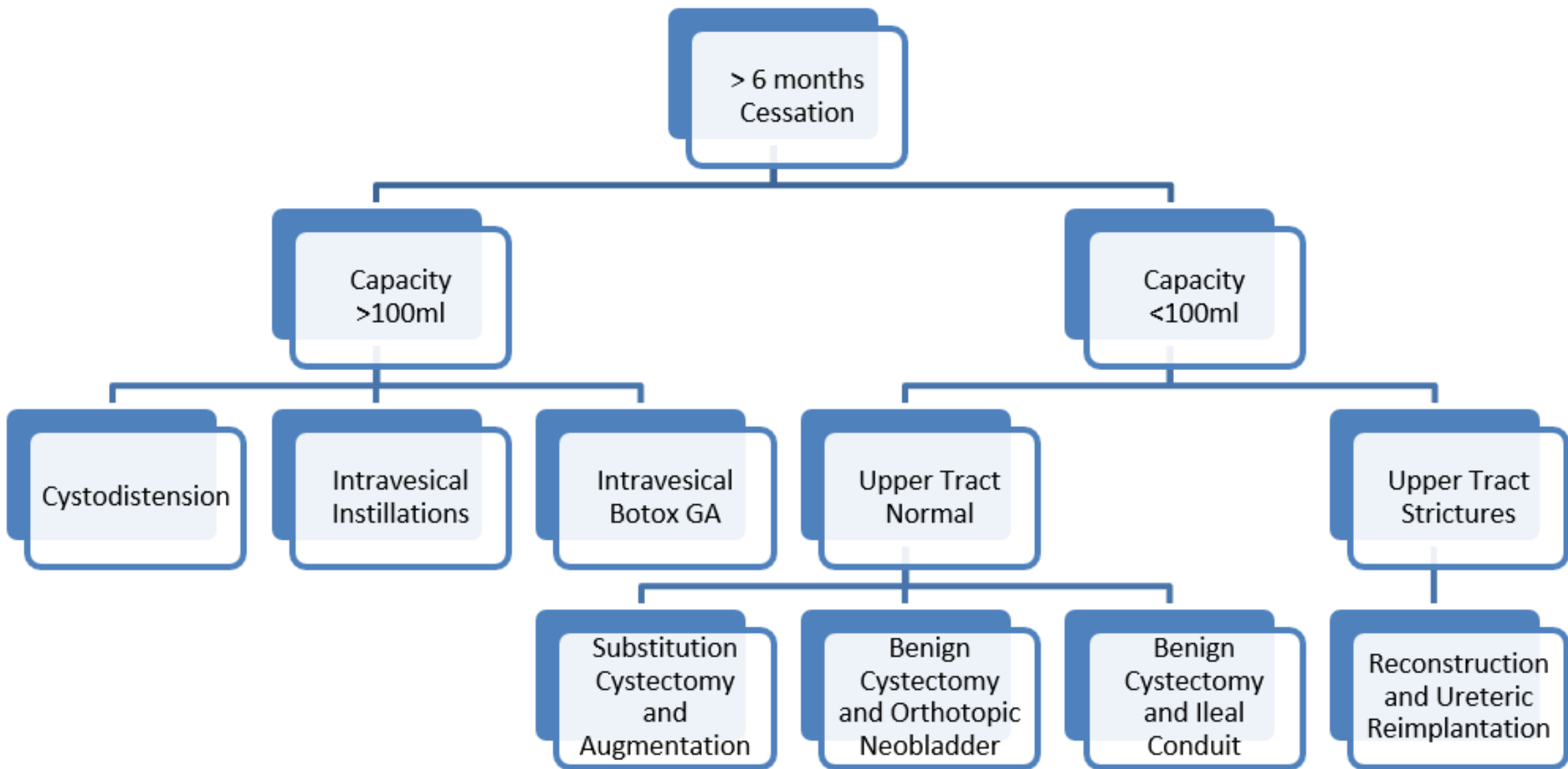
# Video Urodynamics













# Reconstructive Surgery

Absolute pre-requisite to cease ketamine use

Careful patient and procedure selection

Psychology Input

Stoma Team input

Need to manage patient expectations

# The effects of recreational ketamine cystitis on urinary tract reconstruction – a surgical challenge

Néha Sihra , Jeremy Ockrim and Dan Wood

*Department of Urology, University College London Hospital, London, UK*

- 10 year retrospective review of ketamine uropathy patients
- 14 patients underwent major surgical reconstruction
- Higher rate of post-operative complications than expected

Indication	Primary procedure	Complication	Management	Further complications	Long-term outcome
Small capacity, painful fibrotic bladder	Cystectomy, orthotopic right colonic neobladder and Mitrofanoff	Left ureteric stricture	Ureteric re-implantation	Nil	Pain free, normal renal function
Bladder pain	Ileal conduit	Uretero-ileal anastomotic leak and collection	Bilateral nephrostomies followed by antegrade stents	Nil	Pain free, normal renal function; awaiting long-term plan
Severe LUTS with fibrotic bladder	Cystectomy and neobladder	Postoperative high-pressure DO	Intermittent self-catheterisation	Nil	Asymptomatic, normal renal function
Bladder pain with fibrotic bladder	Cystectomy and ileal neobladder and Mitrofanoff	Adhesional small bowel obstruction with avulsed ureters from neobladder	Laparotomy, small bowel resection, adhesiolysis and ureteric re-implantation	Ascitic drainage, debridement of necrotic wound, ureteric leak requiring nephrostomies and stents, left-sided obstruction requiring re-implantation	Recurrent UTIs but pain free and normal renal function
Bilateral ureteric strictures, high-pressure small capacity bladder, chronic renal failure	Augmentation cystoplasty and Mitrofanoff plus insertion of bilateral ureteric stents	Further renal impairment	Left kidney transplant		Poor renal function requiring ureteric stents and dialysis
Small capacity bladder with painful voiding	Cystectomy and orthotopic ileocolonic neobladder and Mitrofanoff	Nil			Died – IP mortality unrelated to surgery, cause unknown
Bilateral ureteric strictures, small capacity fibrosed bladder with pain and severe LUTS	Cystectomy and orthotopic colonic neobladder, right ureteric ileal chute and left ureteric re-implantation	Candida urosepsis			Recurrent UTIs and persistent hydronephrosis – lost to follow-up
Small capacity bladder with severe LUTS	Augmentation cystoplasty	Nil			Asymptomatic, normal renal function
Small capacity fibrosed bladder with pain and severe LUTS	Cystectomy and neobladder	Right ureteric obstruction	Nephrostomy, followed by ureteric stent	Left ureteric obstruction	Awaiting bilateral ureteric re-implantation
Small capacity fibrosed bladder with pain and severe LUTS	Cystectomy and Indiana ileocolonic orthotopic neobladder and Mitrofanoff	Urinary leak and sepsis, acute ileo-colonic leak and faecal fistula	Laparotomy, peritoneal washout, drainage of subphrenic collection and end colostomy	Pneumonia and upper limb DVT. Elective reversal of colostomy and repair of incisional hernia with post-operative wound infection	Pain free, normal renal function
Small capacity bladder with pain	Augmentation cystoplasty and Mitrofanoff	Nil			Pain free, normal renal function
Bilateral ureteric strictures, small capacity bladder with pain	Augmentation cystoplasty, ureteric re-implantation into ileal chute	Further renal impairment			Awaiting nephrology input
Small capacity bladder with pain	Augmentation ileocystoplasty and Mitrofanoff	Nil			Pain free, normal renal function
Bilateral ureteric strictures, small capacity bladder with pain	Caecocystoplasty, bilateral ileal ureteric chute, Mitrofanoff	Postoperative intra-abdominal collection managed conservatively. Bilateral ureteric strictures at level of anastomosis	Bilateral nephrostomies		Awaiting revision of anastomosis

What about the upper tract?



# The Risk of Upper Urinary Tract Involvement in Patients With Ketamine-Associated Uropathy

Chi-Hang Yee<sup>1</sup>, Jeremy Yuen-Chun Teoh<sup>1</sup>, Pui-Tak Lai<sup>1</sup>, Vivian Yee-Fong Leung<sup>2</sup>, Winnie Chiu-Wing Chu<sup>3</sup>, Wai-man Lee<sup>1</sup>, Yuk-Him Tam<sup>4</sup>, Chi-Fai Ng<sup>1</sup>

Variable	Entire Cohort (n = 572)	Without hydronephrosis (n = 476)	With hydronephrosis (n = 96)	P-value
Age (yr)	25.3 ± 3.8	25.0 ± 3.8	26.3 ± 3.7	0.002
Sex				0.280
Female	323 (56.5)	264 (55.5)	59 (61.5)	
Male	249 (43.5)	212 (44.5)	37 (38.5)	
Achieved abstinence	207 (36.2)	175 (36.8)	32 (33.3)	0.523
Duration of abuse (mo)	86.8 ± 37.7	84.6 ± 37.7	97.6 ± 35.7	0.002
Amount consumed per week (g)	20.4 ± 18.1	20.7 ± 18.1	18.6 ± 18.1	0.306
PUF total score	21.0 ± 7.6	20.6 ± 7.7	22.9 ± 6.8	0.006
Functional bladder capacity (mL)	139.9 ± 125.5	147.3 ± 130.8	103.1 ± 86.5	0.002
Serum creatinine > 100 µmol/L	25 (4.4)	15 (3.2)	10 (10.4)	0.001
Deranged serum liver enzymes	258 (45.1)	200 (42.0)	58 (60.4)	< 0.001

# Autotransplantation for the management of ketamine ureteritis

Raison NTJ, et al. *BMJ Case Rep* 2015. doi:10.1136/bcr-2014-207652

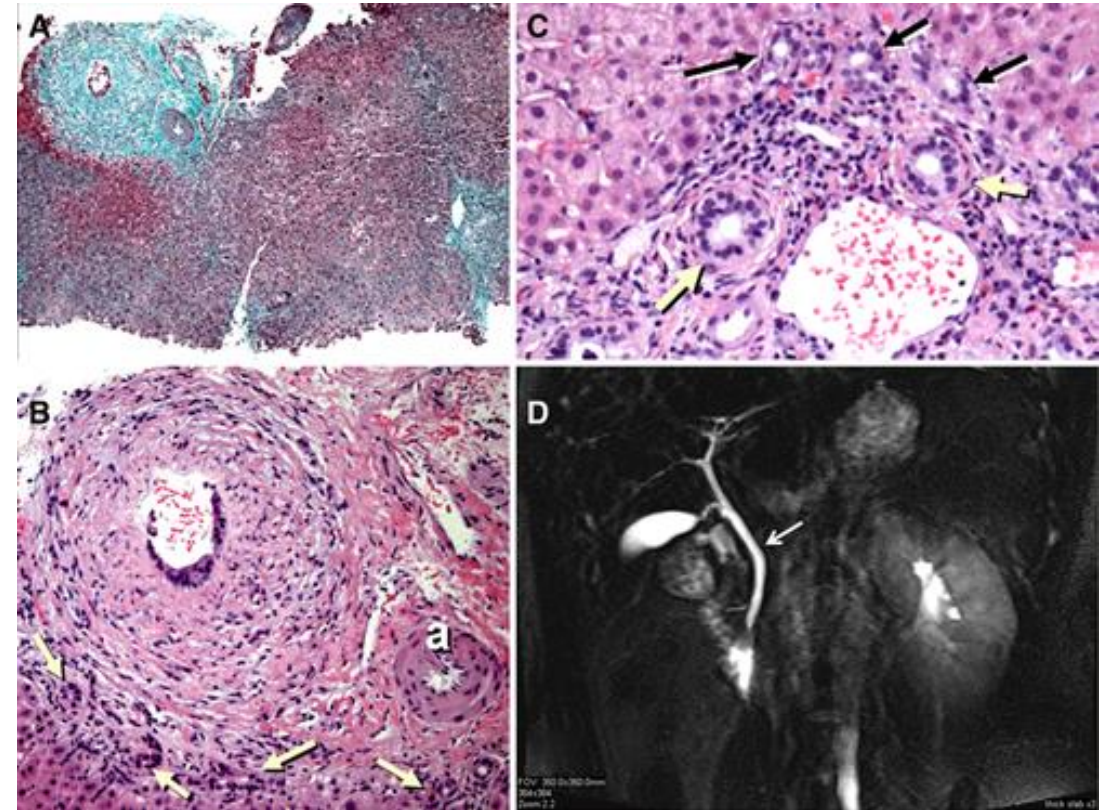
- 33yr old male
- Initial imaging – no hydronephrosis
- Underwent subtotal cystectomy and studer pouch
- 3 months post-op developed hydronephrosis and reduced eGFR
- Initial attempt at refashioning left ureteric anastomosis failed – ongoing ketamine use
- Ultimately required bilateral autotransplantation in staged procedures with significant complications
- Now eGFR 20 and developed nephrogenic diabetes insipidus





# Other Effects

- Sexual Dysfunction
- GI Dysfunction
- Hepatobiliary Dysfunction
- Cognitive Impairment
- ??Potential Malignancy



# Local Issues

- Significantly higher prevalence in Barnsley area compared regionally and nationally
- Young age of first use and perception that ketamine is safe
- Access to rehab – particularly young women
- Provision of pain management services
- Educational drive





# How can primary care help?

- Initial management – commencing anticholinergic/mirabegron and early pain management
- Signposting to drug cessation groups
- USS renal tracts and U&E/GGT (early identification of upper tract issues)
- Reinforce advice from urology!