Detecting and monitoring new psychoactive substances in wastewater

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# New Psychoactive Substances in Wastewater

<table>
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<th>Institution</th>
<th>Country</th>
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<tbody>
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The driver for change

new compounds are used as drugs because they fall outside legislation

the law catches up

The consequence is that vulnerable young people are exposed to a succession of compounds that have never been tested for safety
Designer drugs

Increasing number of new “designer drugs” reported through Early Warning System
New Psychoactive Substances in Wastewater

Substances reported to EMCDDA (1997 – 2010)

- Phenethylamines
- Tryptamines
- Piperazines
- Cannabinoid receptor agonists
- Cathinones
- Others
The new UK process

- monitor the appearance of new compound
- report to ACMD, EMCDDA (EWS)
- constitute a sufficient problem to warrant Temporary Class Drug Order (TCDO) or import ban (OGIL) ?
- TCDO (for 1 year)
  - perform rigorous risk assessment by observation of drug users
  - assess pharmacology
    * literature review
    * mechanistic studies (in vitro, in animals)
- Amend Misuse of Drugs Act or remove from TCDO
- Enforce legislation
New drugs of abuse

But how much is used?

- Self report
- Questionnaires / website monitoring
- Hospital admissions
- Deaths
- Border agency / Police activity
- Wastewater analysis?
How we find new compounds

Club “amnesty” bins
- sealed “postbox” near club entrance
- permission to search is condition of entry to club
- drugs deposited voluntarily or as a result of search
- contraband discovered on premises

Music festivals
- Glastonbury
- Creamfields

Drugs purchased from websites
- “Herbal highs” and “Research chemicals”
- analysed to identify new active constituents
- systematic repeat purchases to monitor effects of legislation

Police
- non forensic submissions

Border Agency
- Seizure of miss-declared imports
New Psychoactive Substances in Wastewater

Minimum data required for new compound

- Certified reference sample
- Analytical data
  - GC/MS
  - Resolution of isomers
- Pharmacological data
  - Activity
  - Dose
  - Duration of action
  - Toxicity
  - Health & Safety advice for handling bulk drug

Cost about €5,000 per compound
Additional data required for wastewater analysis

- Human excretion & metabolism
  - Synthesis of metabolites

- Bacterial metabolism
  - GC/MS
  - Resolution of isomers

- Stability in wastewater
How do we assess risk posed by new compounds?
Which compounds should we control?

About 40 new substances reported to EWS in 2010

- Assess harm
  - Deaths
  - A&E surveillance
  - Analysis of biological samples

- Assess usage
  - Questionnaires
  - Urine analysis
  - Wastewater analysis?
# Risk assessments under the EWS (1999 - 2010)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Year</th>
<th>EU Control?</th>
<th>Group</th>
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<tbody>
<tr>
<td>MBDB</td>
<td>1999</td>
<td>No</td>
<td>Phenethylamine</td>
</tr>
<tr>
<td>4-MTA</td>
<td>1999</td>
<td>Yes</td>
<td>Phenethylamine</td>
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<tr>
<td>GHB</td>
<td>2002</td>
<td>No *</td>
<td>Other</td>
</tr>
<tr>
<td>Ketamine</td>
<td>2002</td>
<td>No</td>
<td>Other</td>
</tr>
<tr>
<td>PMMA</td>
<td>2003</td>
<td>Yes</td>
<td>Phenethylamine</td>
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<tr>
<td>TMA-2</td>
<td>2004</td>
<td>Yes</td>
<td>Phenethylamine</td>
</tr>
<tr>
<td>2C-I</td>
<td>2004</td>
<td>Yes</td>
<td>Phenethylamine</td>
</tr>
<tr>
<td>2C-T-2</td>
<td>2004</td>
<td>Yes</td>
<td>Phenethylamine</td>
</tr>
<tr>
<td>2C-T-7</td>
<td>2004</td>
<td>Yes</td>
<td>Phenethylamine</td>
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<tr>
<td>BZP</td>
<td>2007</td>
<td>Yes</td>
<td>Piperazine</td>
</tr>
<tr>
<td>Mephedrone</td>
<td>2010</td>
<td>Pending</td>
<td>Cathinone</td>
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* GHB subsequently scheduled by UN
New Psychoactive Substances in Wastewater

Usage data from wastewater monitoring

- Whole population estimates
  - Town / City level

- Institutions
  - Hospitals
  - Prisons
  - Factories
  - Universities
  - Gymnasia
  - Military establishments

- Entertainment venues
  - Dance venues / Clubs
  - Music festivals
How do we choose which compounds to monitor in wastewater?
New Psychoactive Substances in Wastewater

Piperazines

- BZP (1-benzylpiperazine)
- DBZP (dibenzylpiperazine)
- TFMPP (m-trifluoromethylphenylpiperazine)
- MBZP (1-Methyl-4-benzylpiperazine)
- mCPP (m-chlorophenylpiperazine)
- pMPP (p-methoxyphenylpiperazine)
- pFPP (p-fluorophenylpiperazine)
New Psychoactive Substances in Wastewater

**Mephedrone, MeOW, Mcat, 4-MMC, bubbles**

4-methylmethcathinone, mephedrone
Controlled Class B

120 grams

3.8 grams
**Mephedrone metabolism**

- **Hydroxymephedrone**
  - 4-methyl ephedrine

- **Mephedrone**
  - 4-methylmethcathinone

- **Desmethylinephedrone**
  - 4-methyl cathinone

- **Hydroxymephedrone**
  - 4-methyl ephedrine

Ketamine

Chronic ketamine use and urinary tract pathology

An emerging problem?

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.

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.

B S Dhillon (benjieyg@doctors.net.uk), foundation year 2 doctor, M C Nuttall, specialist registrar, N Coull, specialist registrar, T S O’Brien, consultant, department of urology, Guy’s Hospital, London SE1 9RT

Patient’s consent: Obtained.
"Spice" synthetic cannabinoid receptor agonists

23 Compounds reported through EWS

The Emergence & Analysis of Synthetic Cannabinoids
Drug Testing and Analysis, Simon Hudson, HFL Sport Science Ltd
John Ramsey, TICTAC Communications Ltd
New Psychoactive Substances in Wastewater

“Cannabinoid” white powders

- Contains cannabinoid receptor agonists
- Mostly aminoalkylindoles
- Seizures of bulk white powder
  - Guernsey JWH - 018
  - Estonia JWH - 200
  - Websites AM – 694
  - Germany CRA-13
  - Latvia AM-2201
- Some controlled (Class B) from 23rd December 2009

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New Psychoactive Substances in Wastewater

**Pipradrol analogues**

- **Pipradrol**
  - Controlled drug Class C
  - CNS stimulant

- **D2PM (diphenyl-2-pyrrolidinyl-methanol)**
  - Not a controlled drug
  - CNS stimulant ??

- **2-DPMP (desoxypipradrol)**
  - Not a controlled drug
  - Not a controlled drug

- **Desoxy D2PM (S)-(−)-2-(diphenylmethyl)pyrrolidine**
  - Not a controlled drug
  - CNS stimulant ??
New Psychoactive Substances in Wastewater

**GHB, precursors & pro-drugs**

GHB controlled Class C

GBL controlled but only when intended for human consumption

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Recent findings

Amphetamine like compound

Ketamine like compounds

Methamphetamine

Methedrine, Methiopropamine
N-methyl-1-(thiophen-2-yl)propan-2-amine

Ketamine

Methoxetamine

4-Methoxyphencyclidine
Suitability for wastewater monitoring

- Probability of large population using compound
- High dose
- Amenable metabolism

- Stability in wastewater
- Sensitive analytical technique
## Candidates for wastewater monitoring?

<table>
<thead>
<tr>
<th>Category</th>
<th>Substance</th>
<th>Mark</th>
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<tbody>
<tr>
<td><strong>Depressants</strong></td>
<td>Ketamine</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>GHB / GBL</td>
<td>✗</td>
</tr>
<tr>
<td></td>
<td>Cannabinoid receptor agonists</td>
<td>?</td>
</tr>
<tr>
<td><strong>Stimulants</strong></td>
<td>Mephedrone</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>BZP</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>TFMPP</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>mCPP</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>D2PM</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td>Desoxypipradrol</td>
<td>?</td>
</tr>
<tr>
<td><strong>Hallucinogens</strong></td>
<td>LSD</td>
<td>✗</td>
</tr>
<tr>
<td></td>
<td>Tryptamines</td>
<td>✗</td>
</tr>
<tr>
<td><strong>Anabolics</strong></td>
<td>Anabolic steroids</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td>Human growth hormone</td>
<td>✗</td>
</tr>
</tbody>
</table>
Glastonbury festival

- tickets are £175
- 134,000 weekend tickets, 37,500 passes (for crew, performers, stewards, traders etc,) and 6,000 Sunday tickets
- the site is enormous - more than a mile and a half across, with a perimeter of about eight and a half miles
- as the organisers say “British law applies, but the rules of society are a bit different, a little bit freer”
All the sewage gets tipped into a huge container now and we feed it out slowly into local sewage works over the next few weeks, so the haulage of sewage has been cut down by about 80 per cent.
Conclusions

- Wastewater analysis may help us decide which new compounds constitute sufficient risk to warrant formal risk assessment.

- Need rapid response as new compounds appear.

- Wastewater analysis may enable us to assess consumption in institutions.