Forensic Toxicology – Findings in DRDs

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- Dept of Forensic Medicine and Science, est. 1839
- Pathologists and Toxicologists
- Toxicology
  - Provides postmortem toxicology service to COPFS to investigate any sudden, suspicious, unexplained or unexpected death in most of Scotland
- Covers ~85% of population
- Around 3200 cases per year
What drugs do we find in deaths?

- Alcohol (39%)
- Morphine* (20%)
  * Mixture of prescribed morphine, heroin and metabolite of codeine
- Diazepam (17%)
- Methadone (14%)
- Codeine** (14%)
  ** Mixture of codeine and heroin use
- Paracetamol (12%)
- Mirtazapine (12%)
- Etizolam (11%)
- Gabapentin (9%)
Benzos and Gabapentinoids

Postivity Rate in All Casework

Year (April to March)

13/14 14/15 15/16 16/17

Diazepam  Etizolam*  Pregabalin  Gabapentin

*Not licensed for medicinal use in UK
Increasing

- Benzos and Gabapentinoids
  - Etizolam
  - Pregabalin
  - Gabapentin
- Opioids
  - Morphine
  - Codeine
  - Methadone
  - Buprenorphine
  - Oxycodone
- Antidepressants
  - Mirtazapine
- Stimulants
  - MDMA
  - Cocaine

Decreasing or Stable

- Diazepam
- Paracetamol
- Amitriptyline
- Tramadol
- Dihydrocodeine
- Citalopram
- Fluoxetine
% of Cocaine positive cases with Morphine

- 13/14: 25%
- 14/15: 35%
- 15/16: 40%
- 16/17: 30%
Gabapentin

Interpretation of post-mortem concentrations

- A single oral dose of 400 mg of gabapentin to healthy individuals gave an average concentration of 3.4 mg/L (range, 2.2 - 6.1 mg/L).
- Healthy male volunteers administered between 300 and 4800 mg single doses gave peak plasma concentrations ranging from 2 – 12 mg/L.
- In three separate cases, individuals survived concentrations of 45 mg/L, 85 mg/L and 105 mg/L after supportive care.
- One study, of 13 fatalities, reported post-mortem gabapentin concentrations between 30 and 82 mg/L, and these were considered elevated. All of these cases listed mixed drug toxicity as the cause of death, potentially including gabapentin.

\[ V_d = 0.8 - 1.3 \text{ L/Kg} \rightarrow \text{less likely for post-mortem redistribution} \]

R. C. Baselt, Disposition of Toxic Drugs and Chemicals in Man, Biomedical Publications, Seal Beach, California, 11th edn (2017).
Gabapentin Concentrations in 2016

- 217 Cases
- Range from <2 - 580 mg/L
What about NPS?
History of NPS at FMS

- **Dec 2009**: BZP and GBL Class C
  - Synthetic cannabinoid receptor agonists Class B
- **Late 2009**: Deaths reported due to Mephedrone in England
- **Apr 2010**: Mephedrone and Naphyrone deaths in Scotland
- **2010**: Cathinones (including Mephedrone) Class B
- **July 2010**: Naphyrone Controlled Class B
- **2011**: PMMA deaths in Scotland Phenazepam detected
- **2012**: AMT Class A
- **2013**: PMA Ethylphenidate Camphetamine DOC Methiopropamine Etizolam 25I-NBOMe Flubromazepam Diclazepam BZP
- **2014**: Pyrazolam 4,4 DMAR Methoxphenidene Diphenidine Methylethcathinone 5F-AKB48
- **2015**: Alpha-PVP MDMB-CHMICA DNP Mitragynine Flubromazolam 25C-NBOMe 25B-NBOMe
- **2016**: 4-Fluoroethylphenidate Ethylone 5F-MDMB-PINACA
- **2017**: Despropionylfentanyl 4-Fluoroisobutyrfentanyl
- **2018**: New Benzos Class C Ethylphenidates Class B U47700/AH7921 Class A
Initially found something which looked like methylphenidate
Since July 2013 – 26 positive cases (only 4 named in COD)
Mostly confined to East of country
Usually injecting heroin users
Poly drug use (mainly diazepam, heroin, methadone etc.)

A review of ethylphenidate in deaths in east and west Scotland
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ABSTRACT
Ethylphenidate is a psychostimulant and analogue of methylphenidate. Interestingly it is also produced as a metabolite from the co-ingestion of methylphenidate and alcohol (ethanol). In the UK, between April and June 2015, ethylphenidate and 6 other methylphenidate based novel psychoactive substances (NPS) were subjected to a temporary class drug order under the Misuse of Drugs Act 1971. Ethylphenidate is being abused by both novel and habitual drug users, more prominently in the East of Scotland. What is unknown in the literature is the contribution of ethylphenidate in deaths. A search was conducted for an 18 month period (July 2013 to December 2014) to identify cases where ethylphenidate was detected during post-mortem toxicological analysis. Nineteen cases were identified and these cases were examined with regards to case circumstances, pathology findings, toxicology results and adverse effects. The individuals ranged in age from 20 to 54 (median 37) and the majority were male (n = 14) and from the East of Scotland (n = 16), more specifically Edinburgh and surrounding area. Current or previous heroin abuse was a common theme in these cases (n = 16) and injection was a common route of administration of “legal highs” or “bursts”. The concentration of ethylphenidate in the cases ranged from
# New Benzodiazepines in Fatalities

<table>
<thead>
<tr>
<th>Drug</th>
<th>Date First Case Received</th>
<th>No. Post-Mortem +ve Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenazepam</td>
<td>Dec-10</td>
<td>~260</td>
</tr>
<tr>
<td>Etizolam</td>
<td>Apr-13</td>
<td>~450</td>
</tr>
<tr>
<td>Diclazepam</td>
<td>Dec-13</td>
<td>~80</td>
</tr>
<tr>
<td>Pyrazolam</td>
<td>Jan-14</td>
<td>3</td>
</tr>
<tr>
<td>Flubromazepam</td>
<td>Jul-14</td>
<td>3</td>
</tr>
<tr>
<td>Flubromazolam</td>
<td>Feb-16</td>
<td>1</td>
</tr>
</tbody>
</table>
Detected regularly in PM cases since October 2013
Seemed to be tailing off mid 2015
Recent increase in incidence since late 2015

Presence of Etizolam in Post-mortem Cases from Oct 2013 to Jun 2016

- Number of Etizolam Positives in PM Cases
- % Cases Positive for Etizolam

Month - Year
- Oct 13
- Nov 13
- Dec 13
- Jan 14
- Feb 14
- Mar 14
- Apr 14
- May 14
- Jun 14
- Jul 14
- Aug 14
- Sep 14
- Oct 14
- Nov 14
- Dec 14
- Jan 15
- Feb 15
- Mar 15
- Apr 15
- May 15
- Jun 15
- Jul 15
- Aug 15
- Sep 15
- Oct 15
- Nov 15
- Dec 15
- Jan 16
- Feb 16
- Mar 16
- Apr 16
- May 16
- Jun 16

- Etizolam Positives
- % Etizolam Positive
Diclazepam

Noticed several Lorazepam positives (no hospital stay)
Delorazepam (Italy) detected in unknown screen
 Usually positive with diazepam

Moosmann B et al. Drug Test Anal. 2014;6(7-8):757-63
Trends we see

Cocaine
- Increase in Cocaine and Heroin use
- More injecting

Ecstasy
- Increase in MDMA positives in PM data
- High purity tablets
- Smoking/injecting ecstasy crystals

Heroin
- DRDs increasing
- Poly-drug use increasing
"You're fired, Jack. The lab results just came back, and you tested positive for Coke."

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