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<tr>
<th>Speaker Name</th>
<th>Statement</th>
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<tr>
<td>Gary Whitlock</td>
<td>I have received speaker fees from Gilead, Viiv &amp; Cepheid</td>
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<tr>
<td>Date</td>
<td>27th June 2016</td>
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</table>
Issues in practice, pharmacology, medical priorities & interactions

Dr Gary Whitlock

56 Dean Street
Chelsea & Westminster Hospital
QUESTION

Do you ask about recreational drug use in PLWH?

If so, how do you bring it up?
Obstacles

● Not a problem in your population

● You forget to ask
  – Proformas; ?prompts

● Panic!
  – Your own knowledge
    • Drugs; effects; potential problems
  – Authenticity
    • Terminology
    • Local use – which ones are out there
Patients and recreational drug use

- Patients seeking help
  - Addiction, harmful behaviours
  - A&E/drug services/HA intervention

- Unperceived problematic use
  - Recognise/education

- Unproblematic use
  - Education
Education

● Negative effects
  – Anxiety/toxicity on organs; social consequences

● Increase risk of STIs
  – HCV, HIV

● Poor adherence of ART
  – Emergence of resistance

● Drug-drug interactions
Education

• What to do in an emergency
  – What to look for
  – Who to call

• Referral pathways for support
GHB/GBL

- Gamma-hydroxybutyrate + its precursor (GBL)
  - CNS depressants

- GHB naturally in brain
  - Metabolite and precursor of GABA

- Ubiquitous
  - Chemical solvent
  - Cleaning agent
  - Superglue remover(!)

GHB/GBL

Neuromodulates the GABA system, acting on dopamine release

Effects: induces euphoria and relaxation
enhances libido → facilitating sexual intercourse

Physically addictive

GHB/GBL

- Consumed as a colourless liquid
- Short half-life (~30 mins)
  - Multiple doses
- NARROW THERAPEUTIC INDEX
- Metabolised by plasma enzymes
  - Excreted mainly breath as CO2

High doses e.g. 3 mL can be life threatening
(normal doses 0.5 – 1.5 mL)

GHB/GBL

ADVERSE EFFECTS

- Respiratory depression
- Tonic-clonic seizures
- CNS depression and coma
- Death

- **Withdrawal syndrome:** auditory and visual hallucinations, tremors, tachycardia and hypertension - can last for several days, potentially life-threatening

Crystal Methamphetamine

Potent psychostimulant (phenethylamine and amphetamine classes), acts through release of noradrenaline, dopamine and serotonin

EFFECTS:
- Increases energy
- Induces confidence
- Enhances libido
- Allows for long-lasting sexual intercourses

Kish, CMAJ 2008,178:1679-1682
Crystal Methamphetamine

- Costly: £100 per gram - usually unadulterated & in crystalline form
- Consumed in different ways (snorted, injected, smoked in a pipe)

Pharmacokinetic/dynamic data:

- Long half-life (up to 12 hours)
- High bioavailability
- Lipophilic, easily passes the BBB and reaches high concentrations in the CNS

Metabolised by enzyme CYP2D6 (CYP450 family)

Lin Drug Metab Dispos 1997, 25:1059-1064
Crystal Methamphetamine

ADVERSE EFFECTS

- Anxiety
- Psychosis with persecutory delusions
- Hallucinations & paranoia
- “Comedown” post use: sleeplessness followed by increased somnolence, low mood, malaise

Chronic use:
- neurocognitive impairment
- pulmonary hypertension
- dilated cardiomyopathy

Mephedrone

“Amphetamine-like” substance: it promotes the release of monoamine neurotransmitters and inhibits their reuptake
Mephedrone

- Semi-synthetic substance
  - Belongs to class of CATHINONE derivatives
    - Synthetic cathinones (mephedrone, methcathinone and methylone) used to be sold as “plant food” or “salt baths” – (legal highs)

- Available as a white/yellowish powder, soluble in water

- Snorted (common), ingested (bombed), inserted in rectum, injected

- Generally it’s highly adulterated and quite cheap (£10 to £15 per gram)
Mephedrone

Pharmacokinetic/dynamic data:

• Short half-life (0.5-1.5 h):
  following oral ingestion/nasal insufflation the effects last up to 2 – 3 hours
  following intravenous injection, about 15 – 30 minutes

• Tolerance mechanism

• Multiple doses to maintain the desired effects (1-4 g of mephedrone per session)

Mephedrone metabolism occurs mainly through enzyme CYP2D6, with minor contribution of other enzymes
Mephedrone

ADVERSE EFFECTS

- Tremors
- Anxiety
- Hallucinations
- Tachycardia
- High blood pressure
- Respiratory and urinary difficulties
- Nasal irritation and bleeds

Schifano et al. Psychopharmacology. 2011;214(3):593-602
TABLE 1. Party drugs’ pharmacological characteristics.

<table>
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<tr>
<th>Drug name (alternative/ street names)</th>
<th>Route of administration</th>
<th>Bioavailability when orally administered</th>
<th>Metabolism</th>
<th>Half-life</th>
<th>Interaction potential</th>
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<tr>
<td>Crystal methamphetamine (Crystal, Tina, Meth)</td>
<td>Oral ingestion, smoke, insufflation, rectal insertion, IV</td>
<td>67–80%</td>
<td>CYP2D6; Other non-CYP pathways (minor)</td>
<td>~12 h</td>
<td>Moderate (COBI/RTV inhibition of CYP2D6)</td>
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<td>MDMA (Ecstasy, X, Mandy)</td>
<td>Oral ingestion insufflation (capsules/ tablets/powder)</td>
<td>40–60%</td>
<td>CYP2D6; CYP1A2, CYP2B6 and CYP3A4 (minor)</td>
<td>~7 h</td>
<td>Moderate (COBI /RTV inhibition of CYP2D6)</td>
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<td>Mephedrone (Miaow Miaow, plant food, bath salts)</td>
<td>Oral ingestion, insufflation (most common), rectal insertion (dissolved or as gel forms), IV</td>
<td>10%</td>
<td>NAPDH-dependent enzymes (minor) Plasma/liver cholinesterases</td>
<td>30min–1.5 h</td>
<td>Moderate (COBI /RTV inhibition of CYP2D6)</td>
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<td>Cocaine (Charlie, C, Coke)</td>
<td>Oral ingestion Insufflation (most common), smoke, IV</td>
<td>30–60%</td>
<td>CYP3A4; Plasma/liver cholinesterases</td>
<td>0.5–2 h</td>
<td>Low to moderate</td>
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<td>Ketamine (K, vitamin K, special K)</td>
<td>Oral ingestion, insufflation, IV or IM</td>
<td>20–45%</td>
<td>CYPB6 and CYP2C9 (minor)</td>
<td>1.8–2.8 h</td>
<td>High (COBI /RTV inhibition of CYP3A4)</td>
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<td>GHB/GBL/1,4 GD (G, Gina, liquid E)</td>
<td>Oral ingestion (liquid), (rarely IV)</td>
<td>GHB: 59–65%</td>
<td>GHB: GHB-DH and SSA-DH</td>
<td>GHB: 20–60 min</td>
<td>(GLB and 1,4 BD are rapidly converted to GHB) Unknown</td>
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<td>GBL: 85%</td>
<td>GBL: Lactonase 1,4 BD: alcohol DH and aldehyde DH</td>
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<td>Benzodiazepines (alprazolam, diazepam)</td>
<td>Oral ingestion (tablets) rectal (gel forms) or rectal tablets IV</td>
<td>Diazepam: 100%</td>
<td>Diazepam: CYP3A4; Alprazolam: CYP3A4; CYP2C19 (minor)</td>
<td>Alprazolam: 12–15 h</td>
<td>High (COBI /RTV inhibition of CYP3A4)</td>
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<td>EDAs (sildenafil, tadalafl, vardenafil)</td>
<td>Oral ingestion (tablets)</td>
<td>Alprazolam: 90%</td>
<td>Alprazolam: CYP3A4</td>
<td>Diazepam: 43–56 h</td>
<td>High (COBI /RTV inhibition of CYP3A4)</td>
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<td>Tadalafil: 80%</td>
<td>Sildenafil: 4 h</td>
<td>Tadalafil: 17.5 h</td>
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<td>Vardenafil: 15%</td>
<td>Vardenafil: 4.5 h</td>
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1,4 BD, 1,4 butanediol; COBI, cobicistat; DH, dehydrogenase; EDA, erectile dysfunction agents; GBL, gamma-butyrolactone; GHB-DH, gamma-hydroxybutyrate dehydrogenase; IM, intramuscular; IV, intravenous; RTV, ritonavir; SSA-DH, succinic semialdehyde dehydrogenase.

Increasing use of ‘party drugs’ in people living with HIV on antiretrovirals: a concern for patient safety

Margherita Bracchi\textsuperscript{a}, David Stuart\textsuperscript{b}, Richard Castles\textsuperscript{c}, Saye Khoo\textsuperscript{d}, David Back\textsuperscript{d} and Marta Boffito\textsuperscript{a,b,e}
Bracchi et al 2015

- AIDSMAP (Aug 2015) – R Pebody

- Boosters: ritonavir & cobicistat
  - Metabolised by CYP2D6 & CYP3A4

- Case reports:
  - Death: crystal meth & ritonavir; MDMA & ritonavir
Ritonavir & cobicistat interactions

● HIGH
  – Ketamine
  – ED drugs (Viagra, Cialis, Levitra)
  – Benzodiazepines (Valium, Xanax)

● MODERATE
  – Crystal meth
  – MDMA
  – Mephedrone
NNRTI interactions

- Efavirenz, Nevirapine, Etravirine
  - Can induce drug metabolism
  - *LOWER* levels of recreational drug
    - ?less harmful
    - BUT users may combine drugs/increase doses/IV?
    - Consequences?
### Antiretrovirals and Recreational Drugs

Charts produced October 2014. Full information available at [www.hiv-druginteractions.org](http://www.hiv-druginteractions.org) and [www.hiv-druginteractions-lite.org](http://www.hiv-druginteractions-lite.org)

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Guidelines on when to call an ambulance to take recreational drug users to A&E

Call an ambulance if **ANY** of the following are present:

1. AVPU assessment graded as either P or U
   - A=Alert
   - V=Responds to voice i.e. talking to
   - P= Responds to painful stimuli only
     (e.g. pressure across a finger nail)
   - U=Unconscious

2. Chest pain similar to a 'heart attack' (i.e. like a pressure on the chest, like a band around the chest).

3. Any history of seizures (i.e. a convulsion similar to an epileptic fit) during this episode

4. More than 2 'poisoned clubbers' per 'club medic'

5. Temperature >38°C not settling after 15 minutes of rest
   OR a temperature >40°C at any time

6. Heart rate >140 beats per minute not settling within 15 minutes

7. Blood pressure Systolic <90 or >180, Diastolic >110 on 2 readings 5 minutes apart

8. Confusion, significant agitation (e.g. pacing around the room) or significant aggression not settling within 15 minutes

9. Any concerns on behalf of the medical personnel involved

10. IF IN DOUBT CALL AN AMBULANCE
Management: crystal meth psychosis

- Presents with apparent drug-induced psychosis:
  - Reassure that they are safe
  - Assess if patient is a risk to:
    - Themselves
    - Others
  - Refer to A&E if appropriate
    - Liaison psychiatry
Management: G detox

- If patients are using G:
  - If using daily for 4 consecutive days or more
  - Do *not* stop without medical advice
  - Immediately to A&E if no more supply
    - Call ahead to A&E to alert staff about G withdrawal symptoms
Thanks

- Staff at CODE clinic
- David Stuart
- Marta Boffito