Drug & Alcohol

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Size of the Problem in the UK

- 250,000 dependent on benzodiazepines
- 100,000 premature deaths annually from smoking
- 10 millions alcohol-related visits to the NHS a year
- 8,000 deaths annually directly from alcohol (ONS)
- 3,300 “drug-related” deaths in E&W in 2014 (ONS)
  - 1-2% untreated opiate addicts die per year
- 70 deaths “related” to Ecstasy in 2014

New psychoactive substances (NPS)

19 deaths in prison in UK between April 2012 and September 2014 in which NPS were thought to be involved (Synthetic cannabinoids, stimulants and hallucinogens)

Source: prison and probation ombudsman

Deaths directly linked to New Psychoactive Substances (UK)

- 2009 – 1
- 2010 – 42
- 2011 – 51
- 2012 – 68

Source: National Programme on Substance Abuse Deaths

This session aims to ........

Explain
- How to make a diagnosis of drug / alcohol dependence
- Overview of drugs misused
- The signs and symptoms of addiction and withdrawal
- Treatment of addiction and withdrawal
- How to take a drug / alcohol history

“The Usual Suspects”

- Alcohol
- Nicotine
- Cannabis
- Stimulants
  - Amphetamine
  - Cocaine
    - Crack
  - Ecstasy
- Psychedelic
  - LSD
  - Magic mushrooms
- Opioids
  - Heroin
  - Df118
- Solvents
- Amyl nitrate
- Poppers
- Anabolic steroids
- Tranquillisers
  - Benzodiazepines e.g. valium, rohypnol
- NPS
Heroin has many advantages over morphine. It's not hypnotic and there is no danger of acquiring a habit.'
Boston Surgical and Medical Journal 1900

Classification system under the Misuse of Drugs Act 1971 – updated 2015

- The classification of drugs, in Schedule 2 of the MDA 1971, is based on the harm they may cause as defined in sec 1 of the MDA 1971. The maximum penalties for supply and possession of drugs in
- Class A: The most harmful category that includes dimorphine (heroin), cocaine, LSD, magic mushrooms, crystal meth.
  - Supply: Life imprisonment +/- unlimited fine
  - Possession: 7 years imprisonment +/- unlimited fine
- Class B: An intermediate category that includes cannabis, synthetic cannabinoids, ketamine, amphetamines, and barbiturates.
  - Supply: 14 years +/- unlimited fine
  - Possession: 5 years imprisonment +/- unlimited fine
- Class C: Includes anabolic steroids, benzodiazepines, GHB/GBL, Khat
  - Supply: 14 years + unlimited fine
  - Possession: 2 years imprisonment +/- unlimited fine (except anabolic steroids – it is not an offence to possess them)
- Psychoactive Substances Act (2016): for substances not covered by the Misuse of Drugs Act – “Things that cause hallucinations, drowsiness or changes in alertness, perception of time and space, mood or empathy with others” (excludes alcohol, caffeine, nicotine, some medicinal products)
  - Supply: 7 years imprisonment + unlimited fine
  - Possession: 5 years imprisonment + unlimited fine
  - Possession: No penalty unless in prison

Harm caused by drugs

<table>
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<tr>
<th>Substance</th>
<th>Harm to others</th>
<th>Harm to users</th>
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<tr>
<td>Heroin</td>
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<tr>
<td>Crack cocaine</td>
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<td>Amphetamine</td>
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<tr>
<td>Cannabis</td>
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<tr>
<td>GHB</td>
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<tr>
<td>Benzodiazepines</td>
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<td>Ketamine</td>
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<tr>
<td>GHB</td>
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<td>Barbiturates</td>
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<td>Anabolic steroids</td>
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<tr>
<td>Busparone</td>
<td>0</td>
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<tr>
<td>Mushrooms</td>
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Source: "Drug harms in the UK", by David Nutt et al, The Lancet

Which is the most addictive?

Relapse rates

<table>
<thead>
<tr>
<th>Substance</th>
<th>% abstinent</th>
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<tr>
<td>Heroin</td>
<td>90</td>
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<tr>
<td>Smoking</td>
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<tr>
<td>Alcohol</td>
<td>70</td>
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</table>

Time since detox (0-1 year)

Harmful use ICD 10 (F10-19.1)

- A pattern of psychoactive substance misuse which is causing damage to physical or mental health
- Negative social consequences (eg relationship split, job loss, arrest) are not sufficient for a diagnosis or harmful use
- Only in the absence of a diagnosis of dependence syndrome

ICD-10: Criteria for Substance Dependence

Dependence syndrome (F10 to F10)

3 or more present in the last 12 months

1) strong desire or compulsion to take the substance
2) difficulty in controlling use (amount/time/termination)
3) physical withdrawal state
4) tolerance
5) progressive neglect of other interests, increasing time spent obtaining and taking substance
6) persistence with substance despite detrimental effects: social, cognitive, physical
Patterns of Drug Use

Not all use is addiction

Experimental Use (large numbers)
Recreational use (fewer numbers)
Spiralling dependence (small number)
Increasing problems

The Mesocorticolimbic Dopaminergic Pathway

Cocaine
Amphetamine
Alcohol
Opioids
Nicotine
Cannabinoids
MDMA

Dopamine (DA) is increased in the nucleus accumbens by different mechanisms

Why can't addicts just quit?

Because Addiction Changes Brain Circuits

Adapted from Volkow et al., Neuropharmacology, 2004.

Model proposing a network of interacting circuits

Different Methods of Drug Use

Pharmacokinetics

"Cheering the rush"

- Faster onset of drug effect = "better rush"

Chewing tobacco
Coca leaves
LAAM
Methadone
Morphine
Snorted heroin
IV heroin

Smoked drug
Snorted or injected drug
rest of body
Desired outcomes of treatment

Drug use hierarchy
- Abstinence from all drugs
- Abstinence from primary drug
- Occasional use
- Controlled, less problematic use
- Uncontrolled use

Risk hierarchy
- Abstinence
- Using, but not injecting
- Injecting with clean / sterile needles
- Injecting but not sharing
- Injecting & sharing

How do we know if there is a problem?

- Assessment and Diagnosis
  - History & Examination
  - Bloods (e.g. LFT, GGT, MCV)
  - Screening eg CAGE (note: sensitivity increased if CAGE questions are asked at the beginning of the session), AUDIT

- Recognition
  - Acute effects – intoxication
  - Chronic effects

- Underlying or Co-existing Morbidity:
  - Physical / Psychological

OVERVIEW OF COMMONLY MISUSED SUBSTANCES

Alcohol

More chronic: Alcohol effects many parts of the body
At a population level, increasing consumption is related to increased risk of damage.
Individually it is often difficult to predict when and where damage will occur.

My Doctor said "Only 1 glass of alcohol a day". I can live with that.
How many units has Harry consumed?

1 Unit = 8 grams or 10mls of pure alcohol

3 large (250ml) glasses of 12% wine
2 pints of Stella (5.5%)
5 standard shots of tequila (40%)

Current Guidelines
14 units a week
Spread evenly over at least 3 days
With alcohol free days

Old guidelines

Normal state: GABA – Glutamate balance

GABA
The main inhibitory NT in the brain
Calm
Relaxation
Sleepiness

Glutamate
The main excitatory NT in the brain
Arousal
Alterness
Learning
Memory

Alcohol intoxication

Alcohol potentiates GABA-R and inhibits NMDA-Receptors
Effect: anxiolytic, relaxing sedation, slurred speech, ataxia, memory loss

Alcohol - acute Vs chronic

1. No alcohol
GABA - Glutamate balance

2. Acute alcohol intoxication
Alcohol activates the GABA system and inhibits the Glutamate system

3. Chronic alcohol use
Increased number of NMDA receptors & downregulation of the GABA system to achieve balance despite presence of alcohol

4. Alcohol withdrawal
The GABA system is inhibited because there are now fewer GABA receptors AND the GABA effect of alcohol is lost
Conversely, the Glutamate system is in overdrive

Alcohol withdrawal

Sudden lack of GABA
Effect: Tremor, anxiety, sweating, confusion, hallucinations, seizures

Sudden excess of Glutamate
Alcohol Withdrawal

→ activity in NMDA receptor → Ca\(^{2+}\) flux
- Hyper-excitability
- Cell death

↓ GABA-ergic activity

1) Withdrawal symptoms: (start < 12 hrs)
2) Seizures: (Peak 7 - 48 hrs)
3) Delirium Tremens (DT): (Peak 48 - 72 hrs)

Alcohol withdrawal

Time since last drink ↓ Withdrawal (<12hrs)
- tremor
- nausea and vomiting
- anxiety, irritability, depression
- ↑ BP, ↑ pulse, ↑ temp
- insomnia
- transient hallucinations/illusions

48 hours ↓ Seizures (7 - 48 hours)

72 hours ↓ DT - Delirium Tremens (48 – 72 hours)
- Fluctuating consciousness, tremor, hallucinations (auditory: persecutory, visual: small moving animals);
- delusions, insomnia and agitation, autonomic hyperactivity (BP, HR)

DT mortality: 15-40% without treatment – 1-4% with treatment

Pharmacological treatment of alcohol withdrawal – an overview

- Benzodiazepine (reducing regimen)
  Most commonly Chlordiazepoxide (Librium)
  In liver impairment: Oxazepam (no metabolites) or Lorazepam (short half life)
  Acamprosate (NMDA antagonist): neuroprotective
  Pabrinex IV/IM
  Thiamine & Vitamin B Co-strong
- Delirium Tremens:
  Treat in ICU
  Benzodiazepine
  +/- Haloperidol

Acamprosate reduces brain damage during alcohol withdrawal

Hippocampal cultures (CA3) from female rat neonates
Propidium iodide staining of damaged/dying cells

Control Alcohol Withdrawal + Acamprosate (200 mM)

Courtesy of Prendergast & Littleton

Benzodiazepine treatment regimes

- Fixed dose schedule
  Typically Chlordiazepoxide 20 - 40mg qds reducing to 0, over 8 - 10 days.

- Symptom triggered therapy
  Given as needed
  Based on withdrawal rating scale
  Needs careful and regular monitoring
  Can mean less medication used, shorter regime
  (NICE CG 100: guidelines for withdrawal in general hospitals)

A typical chlordiazepoxide [librium] fixed regimen

<table>
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<tr>
<th>Day</th>
<th>Morning</th>
<th>Noon</th>
<th>6pm</th>
<th>Night</th>
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<tbody>
<tr>
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<td>Seven</td>
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<tr>
<td>Eight</td>
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Wernicke's encephalopathy - Korsakoff syndrome

- Wernicke’s encephalopathy
  - confusion
  - ataxia
  - ophthalmoplegia (most commonly lateral rectus)
  - Triad seen in 10% of cases
  - Peripheral neuropathy is an early sign

- Korsakoff syndrome
  - Anterograde (and retrograde) memory loss
  - Confabulation
  - Hallucinations
  - Prophylactic treatment with Vitamins

Vitamin supplementation

- Oral Thiamine 100 mg bd
- Oral Vitamin B Co Strong 1 Tablet bd
- IM/IV Pabinex for 3 days

Vulnerability
- Poor diet
- Vomiting
- Weight Loss

Alcohol Detox Prescribing - Summary

1. Benzodiazepines
   Chlordiazepoxide most commonly used

2. Acamprosate
   Neuroprotection

3. Vitamin supplementation
   Especially Thiamine (Oral/IM/IV)

Common Drugs

Opiates

- All abused opiates act at the mu-receptor
- Develop tolerance to large degree
- Marked withdrawal syndrome
- Heroin, morphine, methadone,
- dihydrocodeine (DF118, DHC)
- codeine (co-codamol, etc),
- dextropropoxyphene (co-
- proxamol)
- buprenorphine (Subutex,
- Temgesic)

Opiates

Intoxication / Overdose
- Pinpoint pupils
- Euphoria,
  "gouched out"
  - eyelids drooping
  - head nodding
  - lip movements (tasting)
- Itching,
- Nausea
- Bradycardia
- Drowsiness
- Respiratory depression
  can be fatal
Opiate Withdrawal

- Non-fatal (unlike alcohol)
- Symptoms: flu-like, "cold turkey"
  - Aching muscles, joints
  - Dilated pupils
  - Shivering, piloerection
  - Sweating
  - Insomnia
  - Aching muscles, joints
  - Rhinorrhea
  - Sneezing
  - Diaphoresis
  - Tachycardia
  - Restlessness
- Most physical symptoms due to release of chronic inhibition of noradrenaline in the locus coeruleus (see next slide) and subsequent up regulation of NA receptors (Noradrenergic storm)
- Treat with Lofexidine (or Clonidine)

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Neurobiological basis of opiate withdrawal: The noradrenergic storm

A. Baseline: Normal production of NA

B. Acute opioid inhibition of converting enzyme: Abnormally low production of NA

C. Chronic opioid inhibition leads to increased converting enzyme activity: Normal NA level

D. Discontinuing opioid leads to increased cyclic AMP due to loss of inhibition: NA excessively high

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Substitute prescribing aims to reduce harm

- HIV / AIDS / Hep C
  - high risk due to sharing of needles and work in sex industry
  - far more dangerous to health than opiates
- Crime
  - earlier feature of opiate abuse and crack use due to higher prices

- Injection risks
  - HIV / AIDS / Hep C
  - infections
  - infarctions & emboli
- Stability
  - more time for other things than drug acquisition
  - overdose risk

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Pros & cons of substitute prescribing

- Cons:
  - Diversion
    - selling methadone
  - increase street availability
  - Costs
    - dispensing costs
    - time spent negotiating script
  - Change in relationship
    - power balance
    - barrier to honesty
  - No reason to stop
    - cheap drug for user
    - stable supply
    - no need to challenge own use
- Pros:
  - Harm reduction
    - HIV
    - injecting
  - Stabilisation
    - away from street
    - not injecting
    - able to work
  - No need to score
    - time for therapy
    - less property crime
  - Maintain in treatment

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Opiate Substitute Prescribing

- Methadone
  - long acting
  - overdose risk
  - ECG at 100ms (QTc prolongation)
- Dihydrocodeine
  - pain killer
  - not typically used as a substitute
  - short acting
  - weaker
- Buprenorphine
  - partial agonist at Mu
  - K antagonist
  - better liked
- Diamorphine
  - well liked
  - short acting
  - higher street value

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Pharmacokinetics of Opiates

[Graph showing the pharmacokinetics of Heroin, Methadone, Buprenorphine 4mg, and Buprenorphine 8mg]
**Stimulants**

- Cocaine, crack, amphetamine and most of its derivatives
- Little physical dependence, but psychological dependence can be marked.
- Short term tolerance develops.
- May induce sensitisation - possible cause of psychosis associated with stimulant use.
- Withdrawal includes hypersonnia following prolonged use.
- Depression (of suicidal severity) may present suddenly after 7-10 days post use/detox. Treat with antidepressants if persists.

**Intoxication – cocaine**

- Dilated pupils
- Tachycardia
- Overconfidence / aggression
- Restlessness
- Pressure of speech
- Paranoia and psychosis

**Others**

MDMA (ecstasy)

- 5-HT releaser
- 5-HT uptake inhibitors and tolerance
- No dependence syndrome

Misc.

- LSD
- Barbiturates
- Mushrooms
- GHB
- NPS

- Cannabis
  - Not generally considered addictive
  - "Amotivational" syndrome reported with heavy use
  - Specific cannabinoid receptors widespread in the brain

- Ketamine
  - A widely used dissociative anaesthetic agent
  - Causes Ketamine bladder syndrome

**Intoxication – others**

- Ecstasy
  - Over-familiar, increased energy
  - Very dilated pupils
  - Increased temperature, tachycardia
  - "Gurning" – the muscle tension in the face that usually ends up with the jaw and tongue rolling and teeth grinding
  - Risk of dehydration and/or over-hydration

- LSD
  - Altered sensory perceptions/hallucinations (can be pleasant or frightening)
  - Dilated pupils
  - Change in body temp/HR/BP
  - Salivation
  - Sweating, chills
  - Sleepiness
  - Tremors
  - Flashbacks possible post-use

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**New Psychoactive Substances - Synthetic cannabinoids (spice)**

- Often labelled as incense or pot pourri and "not for human consumption"
- A generic term that includes different man-made chemicals, usually crudely made in illegal labs, that bind to cannabinoid receptors
- Strong THC effect but no Cannabidiol (CBD) effect
- Dosage and molecular structure can vary greatly between and within "brands"
  - There are over 700 Synthetic Cannabinoids in existence
  - 13 new compounds come to market every year

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**Traditional cannabis**

- Hydroponic engineered cannabis (Skunk)
- 3% THC + cannabidiol
- 5-15% THC Less CBD

**Synthetic cannabinoids**

- Full agonists at CB1 & 2
- 2-100 times more potent than THC
Side – effects of Synthetic Cannabinoids

HIGHLY UNPREDICTABLE

Depend on:
- The specific formulation of the synthetic cannabinoid used
- Quantity ingested
- Mode of ingestion:
  - Liquid form which can be sprayed on paper, dry grass, cigarettes and smoked
  - Brewed (tea)
  - E-liquid form can be vaped

Spice - Pleasant side effects

- Relaxation
- Elevated mood
- Heightened perceptions
- Disinhibition

Spice - Less pleasant

- Increased heart rate
- Increased blood pressure
- Agitation
- Vomiting
- Sweating
- Uncontrollable body movements — cerebellar ataxia, hypotonia
- Lack of emotional attachment
- Psychosis: paranoia, increased anxiety and hallucinations — typically much more severe than after smoking marijuana or skunk
- Red eyes
- Dry mouth
- Loss of appetite (more common than increased appetite)

Psychological treatments

Motivational interviewing
- elicit self-motivational statements from patient
- non-confrontational
targets ambivalence

Cognitive therapy
- as for depression
cue to drug use

Useful for addiction to all substances

Motivation for change

Motivation at each stage:

- Pre-contemplation – raise doubt by awareness of risks/impact of use
- Contemplation – elicit pros & cons of use
- Decision/Action – agree treatment plan specific to individual needs
- Maintenance – identify & use strategies to prevent relapse
- Relapse – renew process of change

DEATH

- Seizures
- Hypokalaemia
- Hyperthermia
- Rhabdomyolysis
- Renal failure
- ECG changes, cardiac arrest
Taking a History 1

- Presenting Complaint
  - what drugs used
- HPC
  - daily routine of use
  - daily amount used
  - route of use
  - where used
  - information to make a diagnosis of dependence
  - funding for use

Taking a History 2

- Medical and Psychiatric History
  - co-morbid psychiatric and physical illness common
  - blood borne viruses for IV users
- Personal History
  - focus on criminality, especially acquisitive crime
- Family History
  - drug and alcohol use
  - other psychiatric illnesses

Taking a History 3

- Social History
  - accommodation
- Mental State Examination
  - appearance and behaviour important
  - look out for signs of intoxication or withdrawal
  - look out for psychotic symptoms
- Physical Exam - eg
  - Stigmata of liver disease in Alcohol Dependence
  - Needle marks