Overview

• Initial clinical assessment
  – Toxidromes
  – Critical care

• Specific strategies to minimise toxicity
  – Oral charcoal
  – Lipid administration
Background & scale

• Major public health issue
  – 1-2% of ED attendances (half million per year)
  – 140,000 NHS admissions per year
  – Presentations increasing

• 2000 deaths annually
  – Less than a third are in hospital
Clinical Toxicology & NPIS

www.toxbase.org

- Around 600,000 enquiries per year (UK)
- Around 1500 cases referred to NPIS consultant

https://www.gov.uk/government/organisations/public-health-england
Patterns of poisoning

- Intentional (85%)
- ‘Accidental’ or unintentional
  - Childhood exposures (<3 years)
  - Elderly patients
  - Analgesia in dental pain
  - Illicit drug use
- Occupational & environmental
Clinical history

- Self-reported drug & dose
- Supporting information – Drug packaging – Bystander accounts
- Limited laboratory support

Waring WS et al. QJM 2008;101:121-5.
Clinical assessment

• Patient may be unresponsive, uncooperative
• Undeclared poisoning
  – Severe, unexplained features
• Covert poisoning
  – Natural toxins, drugs, radioactive material

Toxidromes
Toxidrome recognition (1)

- Features common to groups of drugs with similar pharmacological properties
- Laboratory confirmation if needed
- Empirical treatment e.g. antidote

A helpful pointer rather than definitive diagnosis
Toxidrome recognition (2)

- Eyes open spontaneously, orientated speech, obeys commands → A
  - Give verbal stimulus (shout loudly) or gentle shake → V
    - Any verbal, motor, or eye response to verbal stimulus → P
      - Apply painful stimulus (e.g., nailbed pressure)
      - Any verbal, motor, or eye response to painful stimulus → U
        - No response
  - Apply painful stimulus (e.g., nailbed pressure)
  - No response

Graph: GCS score
GCS & mortality in overdose

Lapostelle F. Rev SAMU 2005
GCS & mortality in overdose

<table>
<thead>
<tr>
<th>Degree of CNS-depression</th>
<th>Number of patients</th>
<th>Mean age (years)</th>
<th>Mean S-ethanol on admission</th>
<th>Hospital mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCS score 3–6</td>
<td>444 (58%)</td>
<td>41.6</td>
<td>58.6 mmol/L (n = 265) (270 \text{ mg/dL})</td>
<td>4.3% (n = 19)</td>
</tr>
<tr>
<td>GCS score 7–10</td>
<td>327 (42%)</td>
<td>42.2</td>
<td>52.8 mmol/L (n = 196) (243 \text{ mg/dL})</td>
<td>0.3% (n = 1)</td>
</tr>
</tbody>
</table>

GCS = Glasgow coma scale.

Consideration of critical care

- AVPU or need intubation
- Seizures
- Hypoxaemia
- Atrioventricular block or QRS ≥ 120 ms
- Hypotension

Clinical scenario 1

- 30 yr old woman found at home surrounded by wine bottles and lots of tablet strips. Last seen well 8 hrs before.

- Unknown quantities of:
  - alcohol
  - sodium valproate
  - olanzapine
  - amitriptyline
  - citalopram
  - co-codamol
Clinical scenario 1

<table>
<thead>
<tr>
<th>Conscious level</th>
<th>AVPU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Maintaining airway</td>
</tr>
<tr>
<td>HR, BP, temp</td>
<td>HR 109</td>
</tr>
<tr>
<td></td>
<td>BP 110/60</td>
</tr>
<tr>
<td></td>
<td>T = 37.1</td>
</tr>
<tr>
<td>Respiratory</td>
<td>100% on 6L</td>
</tr>
<tr>
<td></td>
<td>RR = 14, shallow</td>
</tr>
<tr>
<td>Pupils, reflexes</td>
<td>1 mm unresponsive</td>
</tr>
<tr>
<td></td>
<td>Plantars absent</td>
</tr>
<tr>
<td>Mucous membranes</td>
<td>Normal</td>
</tr>
</tbody>
</table>
Clinical scenario 1

- **Opioid toxidrome**
  - Reduced conscious level
  - Shallow respirations
  - Small pupils

- **Significance?**
  - Consider naloxone, maintaining airway
  - Close clinical observation
Clinical scenario 1

- **Naloxone** administration
  - Competitive opiate antagonist
  - Antidote dose versus drug dose
- Issues about dose
  - Titrate to clinical response
  - High doses e.g. tramadol
- Duration of effect
Clinical scenario 1

IV naloxone

No pupil response

Pupils: dilate

Other diagnosis:
mirtazapine
olanzapine
brainstem stroke

Inadequate response:
Hypnotic/sedative toxidrome

Good response:
observe


Fig. 1. Serum olanzapine concentrations in two patients who presented to hospital after massive olanzapine ingestion that had prolonged features of severe toxicity (the therapeutic reference range is 20 to 50 μg/l).
Clinical scenario 2

• 30 yr old woman found at home surrounded by wine bottles and lots of tablet strips. Last seen well 8 hrs before.

• Unknown quantities of:
  - alcohol
  - sodium valproate
  - olanzapine
  - amitriptyline
  - citalopram
  - co-codamol
Clinical scenario 2

<table>
<thead>
<tr>
<th>Conscious level</th>
<th>AVPU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Maintaining airway</td>
</tr>
<tr>
<td>HR, BP, temp</td>
<td>HR 139</td>
</tr>
<tr>
<td></td>
<td>BP 110/60</td>
</tr>
<tr>
<td></td>
<td>T=36.9</td>
</tr>
<tr>
<td>Respiratory</td>
<td>98% on RA</td>
</tr>
<tr>
<td></td>
<td>RR=18</td>
</tr>
<tr>
<td>Pupils, reflexes</td>
<td>9 mm L=R</td>
</tr>
<tr>
<td></td>
<td>Diminished, plantars absent</td>
</tr>
<tr>
<td>Mucous membranes</td>
<td>Dry</td>
</tr>
</tbody>
</table>
Clinical scenario 2

- **Anticholinergic toxidrome**
  - Tachycardia
  - Dilated pupils
  - Dry mucous membranes

- **AND**
  - Reduced conscious level
  - Diminished reflexes
Clinical scenario 2

- Wide range of drugs
  - Antihistamines
  - TCAs
  - Antipsychotics
- No specific antidote
- May indicate poisoning severity
Clinical scenario 2

ECG, shown at 25 mm/s, from a 19-year-old woman who presented to hospital after dosulepin self-poisoning. The upper panel, taken when the patient arrived at the hospital, shows a heart rate of 144 bpm, absent P-waves, QRS duration of 223 ms, and QT interval of 539 ms. The lower panel, taken after the patient was administered intravenous sodium bicarbonate, shows a heart rate of 86 bpm, PR interval of 171 ms, QRS duration of 75 ms, and QT interval of 344 ms.

Clinical scenario 2

- Anticholinergic effects
  - May indicate severity of poisoning
  - May predict toxicity due to other mechanisms
- May influence management
  - Airway observation after antihistamine
  - ECG monitoring ?bicarbonate
Clinical scenario 3

• 30 yr old woman found at home surrounded by wine bottles and lots of tablet strips. Last seen well 8 hrs before.

• Unknown quantities of:
  alcohol
  sodium valproate
  olanzapine
  amitriptyline
  citalopram
  co-codamol
# Clinical scenario 3

<table>
<thead>
<tr>
<th>Conscious level</th>
<th>AVPU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Agitated</td>
</tr>
<tr>
<td>HR, BP, temp</td>
<td>HR 139</td>
</tr>
<tr>
<td></td>
<td>BP 110/60</td>
</tr>
<tr>
<td></td>
<td>T=38.2</td>
</tr>
<tr>
<td>Respiratory</td>
<td>97% on RA</td>
</tr>
<tr>
<td></td>
<td>RR=16</td>
</tr>
<tr>
<td>Pupils, reflexes</td>
<td>9 mm L=R</td>
</tr>
<tr>
<td></td>
<td>Brisk, 4-5 beats clonus</td>
</tr>
<tr>
<td>Mucous membranes</td>
<td>Normal</td>
</tr>
</tbody>
</table>
Clinical scenario 3

- **Serotonergic toxidrome**
  - Agitation
  - Tachycardia
  - Dilated pupils
  - Myoclonus ↔ rhabdomyolysis
  - Hyperthermia

- Seizures, renal failure, metabolic disturbance

**Beware:** Sepsis may mimic!
Clinical scenario 3

- Drugs that enhance serotonin
  - SSRIs, SNRIs, MAOIs, TCAs, tramadol, triptans, St John's Wort, recreational agents

- $5HT_{2A}$ antagonists
  - Cyproheptadine
  - Chlorpromazine
Clinical scenario 3

- Citalopram
  - Seizures in 8%
  - Dose-dependent arrhythmia, TdP

Serotonergic effects may indicate large dose

ECG telemetry

Electrolyte monitoring


Fig. 1 Thorough QT study as examined by FDA and MHRA concerning citalopram 20 mg daily and 60 mg daily \((n=119)\) [1–3]. Data presented as mean and 90% confidence intervals; \(QTcF\) QT corrected by Fridericia’s formula.
### Selected toxidromes

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid</td>
<td>fentanyl, oxycodone</td>
</tr>
<tr>
<td>Sedative-hypnotic</td>
<td>diazepam, zopiclone</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>antihistamines, antipsychotics</td>
</tr>
<tr>
<td>Serotonergic</td>
<td>SSRI, tramadol</td>
</tr>
<tr>
<td>Sympathomimetic</td>
<td>cocaine, methoxetamine</td>
</tr>
<tr>
<td>Cholinergic</td>
<td>nerve agents, organophosphates</td>
</tr>
<tr>
<td>Cyanide</td>
<td>industrial chemicals</td>
</tr>
<tr>
<td>Lung irritant (upper)</td>
<td>ammonia, chlorine</td>
</tr>
</tbody>
</table>
Charcoal: minimise drug absorption

- Oral activated charcoal
- Binds non-specifically
  - 10% of charcoal weight
  - Dose 50 g in an adult
Figure 1  Median paracetamol concentrations (mg l⁻¹) over time (min) for all subjects. Study day A (○) = control, e.g. paracetamol ingestion without intervention. Study day B (●) = activated charcoal administered 1 h after paracetamol ingestion. Study day C (■) = gastric lavage followed by activated charcoal 1 h post ingestion. Study day D (□) = activated charcoal administered 2 h post ingestion.
Charcoal & clinical outcomes

- Paracetamol
  - ↓ need for acetylcysteine
- Citalopram
  - ↓ occurrence of QT prolongation
Issues concerning charcoal

• Timing: within 1 h

• Airway - risk of aspiration

• Avoid if intestinal obstruction
Figure 1. The so-called ‘lipid sink’ mechanism is supported by data that show a lower concentrations of bupivacaine are recoverable from cardiac tissue after administration of intravenous lipid emulsion, suggesting that intravenous lipid emulsion has allowed movement of drug between the tissue and circulating compartment.
Lipid as antidote

• AHA & ERC guidelines
  – 1.5 mL/kg 20% emulsion
  – Repeat every 5 mins (up to 3)
  – Infusion 15 mL/kg/hour for ½-1 hour

• Positive response 50% non-anaesthetic ODs
  – NZ Lipid registry
Summary

• Initial approach
  – Toxidromes may help

• Antidotes
  – Naloxone (*adequate dose*)
  – Bicarbonate (*TCA*)
  – Charcoal (*early*)
  – Lipid (*life-threatening cardiotoxicity*)
Thank you for your attention!