Problems in Post-Mortem Toxicology

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Post-Mortem Toxicology

Objective: to determine....

as accurately as possible
the concentrations of drugs
existing in blood

at the time of death
and then interpret the result
Post-Mortem Toxicology

Problem areas:

- Post-mortem drug redistribution
- Post-mortem drug absorption
- Post-mortem drug degradation
Post-Mortem Drug Redistribution

Diffusion from solid organs

Drugs with high volume of distribution
Concentrate in organs in life
Following death and cellular autolysis
Diffuse from organs (lung, liver, heart)
Raise drug conc. in blood
Post-Mortem Drug Redistribution

Diffusion from solid organs

Drugs with high volume of distribution Concentrate in organs in life Following death and cellular autolysis Diffuse from organs (lung, liver, heart) Raise drug conc. in blood
Post-Mortem Drug Redistribution

Volume of distribution (Vd)

Pharmacokinetic concept

Theoretical not physiological volume

“necessary if the total body drug load were distributed at the same concentration as in plasma”
Post-Mortem Drug Redistribution

Volume of distribution (Vd)

25 yr female, 60 kg, mixed drug overdose, DOA, autopsy at 12 hours post-mortem, 10 blood samples

<table>
<thead>
<tr>
<th>Drug</th>
<th>Vd</th>
<th>Range in blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>0.64</td>
<td>151 - 175 mg%</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>0.75 - 1</td>
<td>55 - 65 mg/L</td>
</tr>
<tr>
<td>Codeine</td>
<td>5</td>
<td>0.33 - 0.89</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>3 - 7</td>
<td>0.34 - 2.07</td>
</tr>
<tr>
<td>Imipramine</td>
<td>11 - 16</td>
<td>2.1 - 16.0</td>
</tr>
<tr>
<td>Desipramine</td>
<td>1.4 - 10.6</td>
<td></td>
</tr>
</tbody>
</table>
Post-Mortem Drug Redistribution

47 yr male, 92 kg, drug overdose, blood taken
2 hr a-m, cardiac arrest 1hr a-m, autopsy at
7.25 hr p-m

<table>
<thead>
<tr>
<th>Drug</th>
<th>a-m</th>
<th>p-m (11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imipramine</td>
<td>2.3</td>
<td>4.1 to 18.1</td>
</tr>
<tr>
<td>Desipramine</td>
<td>0.6</td>
<td>1.0 to 3.6</td>
</tr>
</tbody>
</table>
Post-Mortem Drug Redistribution

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Post-Mortem Drug Redistribution

Post-mortem biochemical changes

electrolytes

- glucose & lactate

- liver enzymes

- cardiac enzymes

- amino acids
Post-Mortem Drug Redistribution

Diffusion from solid organs

Drugs with high volume of distribution
Concentrate in organs in life
Following death and cellular autolysis
**Diffuse** from organs (lung, liver, heart)
Raise drug conc. in blood
Post-Mortem Drug Redistribution

Fick’s law of diffusion

Concentration gradient
Temperature
Time
Post-Mortem Drug Redistribution

Diffusion from solid organs

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Raise drug conc. in blood
Post-Mortem Toxicology

Sampling recommendations:

- early
- peripheral venous
- uncontaminated
- standardized
  (corroborating samples)
Post-Mortem Toxicology

Sampling recommendations:

pre-evisceration, admission, scene
femoral or external iliac vein
exposed, clamped vessel, needle & syringe
written protocol, record variations
( + vitreous, urine, liver, muscle ? )
Post-Mortem Toxicology

Problem areas:

- Post-mortem drug redistribution
- Post-mortem drug absorption
- Post-mortem drug degradation
O true apothecary
Thy drugs are quick

Shakespeare: Romeo and Juliet
Act V, scene 3, line 119
Post-Mortem Toxicology

Post-mortem drug absorption

Gastro-oesophageal residue

Airways contamination by gastric material
# Post-Mortem Toxicology

## Post-mortem drug absorption

<table>
<thead>
<tr>
<th>Location</th>
<th>Ethanol (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>case 1</td>
</tr>
<tr>
<td>Stomach cont.</td>
<td>5500 (300ml)</td>
</tr>
<tr>
<td>Femoral vein</td>
<td>114</td>
</tr>
<tr>
<td>Pericardial fluid</td>
<td>1060</td>
</tr>
<tr>
<td>Aorta</td>
<td>147</td>
</tr>
<tr>
<td>L Heart</td>
<td>238</td>
</tr>
<tr>
<td>R Heart</td>
<td>184</td>
</tr>
</tbody>
</table>
Post-Mortem Toxicology

Problem areas:

- Post-mortem drug redistribution
- Post-mortem drug absorption
- Post-mortem drug degradation
Post-Mortem Toxicology

Bacterial drug degradation

- O to N, but not to C or S
- Thiono-group (C = S, P = S)
- Aminophenols
- S in heterocyclic ring
Post-Mortem Toxicology

Bacterial drug degradation

Benzodiazepines

- chlordiazepoxide
- chlorazepam
- trinitrazepam
- nitrazepam
- flunitrazepam
Post-Mortem Aspects of Alcohol

Post-Mortem Synthesis

Micro-organisms
- bacteria
- yeasts

Carbohydrate substrates
- glycogen/glucose
- lactate
- mannitol
# Post-Mortem Aspects of Alcohol

## P-M Synthesis

<table>
<thead>
<tr>
<th>Case series</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>975 aviation deaths</td>
<td>circumstances</td>
</tr>
<tr>
<td>79 &gt; 40mg%</td>
<td>vitreous humour</td>
</tr>
<tr>
<td>27% p-m, 45% uk</td>
<td>urine</td>
</tr>
<tr>
<td>95% &lt; 150mg%</td>
<td>other volatiles</td>
</tr>
<tr>
<td>max 300mg%</td>
<td>n-butyric acid</td>
</tr>
<tr>
<td></td>
<td>n-propanol</td>
</tr>
</tbody>
</table>
Post-Mortem Aspects of Alcohol

Corroborating vitreous/urine

USS Iowa
- blood 190mg%, urine -ve

Mr Henri Paul
- blood 175mg%, vitreous 170mg%

Moorgate disaster train driver
- blood 20-80mg% (4 samples)
Post-Mortem Toxicology

Interpretation recommendations:

- all case data
- check blood sampling method
- drug Vd, redistribution literature
- drug structure, degradation literature
- databases
Post-Mortem Toxicology

Databases

Propoxyphene: 6 fatalities by OD
(>1 mg/L = ‘toxic’; >2 mg/L = ‘lethal’)

<table>
<thead>
<tr>
<th>fem. v.</th>
<th>4.6</th>
<th>3.2</th>
<th>3.9</th>
<th>3.1</th>
<th>1.4</th>
<th>3.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>pul. v.</td>
<td>25</td>
<td>18</td>
<td>5.5</td>
<td>22.2</td>
<td>14.4</td>
<td>27.7</td>
</tr>
</tbody>
</table>
Post-Mortem Toxicology

Traditional databases:
- Multi-centre, publications
- Blood sample-site variable
- Analytical methods variable
- Single and multiple-drug fatalities
- Clinical therapeutic ranges
- Clinical toxic ranges
Post-Mortem Toxicology

Swedish national database:
- Femoral venous blood, exclusively
- Single-centre, standardised analyses
- Single-drug fatalities
- Multiple-drug fatalities
- Other COD, no drug incapacitation
- Suspected drugged-drivers (‘toxic’)
Post-Mortem Toxicology

Drug dose calculation

by Vd
assumes clinical pharmacokinetics

by tissue load addition
assumes uniform drug levels in tissues
assumes total tissue weights (muscle, fat)
Post-Mortem Toxicology

Drug dose calculation

69 yr, 43 kg, female, severe CAD, ‘suicide’
‘Co-proxamol’ (325mg acet., 32.5mg propox.)
blood: acet. 337 mg/L, propoxyphene 17mg/L
stomach: acet 9.26g, propox. 0.69g (= 20 tabs)
calculated dose: ‘150 tabs’

admission of murder with 30 tabs