Monitoring Therapeutic Levels
National Prescribing Service Data

The ‘average’ General Practitioner writes 130 ‘Opioid’ analgesic scripts a year
60+ Panadiene Forte
30+ Tramadol

Less than 3 scripts/month are S8
Rationale for Blood Monitoring

Blood monitoring is used to assess if

Medication is being taken appropriately
Medication is being taken at all
Medication is in ‘therapeutic’ range
Medication is ‘dependent’ range
Ms M.B.

34 year old single mother with 2 children
Sustained an injury at work
Smokes 20/day
Rarely drinks alcohol
No significant hobbies or activities
Presenting History

1999 - back injury/repetitive strain
Workers Compensation claim settled but dissatisfied with the outcome
Treated 2-3 times a year with spinal cortisone injections since injury
Secondary depression,
Opioid dependence
# Morphine Monitoring

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Blood Morphine</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/03/04</td>
<td>n/a</td>
<td>9ng/ml</td>
<td>Kapanol 100mg bd</td>
</tr>
<tr>
<td>21/05/04</td>
<td>09.35</td>
<td>610ng/ml</td>
<td>Kapanol 200mg bd</td>
</tr>
<tr>
<td>21/05/04</td>
<td>13.40</td>
<td>320ng/ml</td>
<td>Kapanol 200mg bd</td>
</tr>
</tbody>
</table>

Results in bold are supervised doses.
Outcome

Admitted injecting medication
Relatives known Opioid abusers
Persistent prescription-shopper
Refused transfer to Opioid Substitution
Treatment ceased
Mr J.N.

50 year old married with 2 daughters
Disability pensioner
Smokes 6 rollies a day - less post infarct
Non-drinker - ceased after pancreatitis 2000
Presenting History

1994: Back pain, disc bulge present conservative therapy.

**Pain clinic investigations**
positive response to Opioid therapy.

**Pancreatitis 2000 from excess alcohol**

**Hep C +ve**
from a blood transfusion before 1990 or childhood tattoo in Europe.

**Cirrhosis**
recurrent upper quadrant pain requiring injections of morphine
Presenting History

Suicidal from Pain
  Prior overdose of Benzodiazepines.

Oesophagitis

Sleep apnoea
  diagnosed 2001, CPAP effective.

Hypertension & Myocardial Infarct
  Stent 2001

Numerous fractures
  Motor Vehicle Accidents - no compensation involved.
# Initial Morphine Monitoring

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Blood Morphine</th>
<th>Medication daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>06 June</td>
<td>17.00</td>
<td>Nil</td>
<td>Ms Mono 360mg</td>
</tr>
<tr>
<td>07 June</td>
<td>08.30</td>
<td>24ng/ml</td>
<td>Ms Mono 360mg</td>
</tr>
<tr>
<td>07 June</td>
<td>12.00</td>
<td>172ng/ml</td>
<td>Ms Mono 360mg</td>
</tr>
<tr>
<td>10 July</td>
<td>11.15</td>
<td>9ng/ml</td>
<td>Ms Mono 360mg</td>
</tr>
<tr>
<td>01 August</td>
<td></td>
<td>528ng/ml</td>
<td>Ms Mono 480mg</td>
</tr>
<tr>
<td>07 August</td>
<td>pre</td>
<td>36ng/ml</td>
<td>Ms Mono 480mg</td>
</tr>
<tr>
<td>07 August</td>
<td>post</td>
<td>49ng/ml</td>
<td>Ms Mono 480mg</td>
</tr>
</tbody>
</table>
Background

Collecting full script monthly
He was often in pain
He used extra medication most months
Breakthrough pain was common

Transferred to daily collection
# Daily Morphine Collection

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Blood Morphine</th>
<th>Medication Daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>19 Feb</td>
<td>08.45</td>
<td>82ng/ml</td>
<td>Kapanol 300mg</td>
</tr>
<tr>
<td>19 Feb</td>
<td>post</td>
<td>96ng/ml</td>
<td>Kapanol 300mg</td>
</tr>
<tr>
<td>06 April</td>
<td>07.55</td>
<td>78ng/ml</td>
<td>Kapanol 400mg</td>
</tr>
<tr>
<td>06 April</td>
<td>12.30</td>
<td>115ng/ml</td>
<td>Kapanol 400mg</td>
</tr>
</tbody>
</table>
Follow up

Changed to Ms Mono to allow once daily dosing with no loss of pain control
Mr J.N. was unhappy collecting daily
He ‘always takes his medication correctly’
He felt like a ‘drug addict’
Successfully pressured to resume weekly collection
<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Blood Morphine</th>
<th>Medication</th>
<th>Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>04 May</td>
<td></td>
<td>&lt; 10ng/ml</td>
<td>Ms Mono</td>
<td>420mg</td>
</tr>
<tr>
<td>24 May</td>
<td></td>
<td>170ng/ml</td>
<td>Ms Mono</td>
<td>420mg</td>
</tr>
<tr>
<td>09 June</td>
<td>08.40</td>
<td>77ng/ml</td>
<td>Ms Mono</td>
<td>420mg</td>
</tr>
<tr>
<td>09 June</td>
<td>18.15</td>
<td>222ng/ml</td>
<td>Ms Mono</td>
<td>420mg</td>
</tr>
</tbody>
</table>

Supervised doses.
Daily collection resumed

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<th>Date</th>
<th>Time</th>
<th>Blood Morphine</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>14/06/05</td>
<td>13.30</td>
<td>63ng/ml</td>
<td>Ms Mono 420mg</td>
</tr>
<tr>
<td>14/06/05</td>
<td>20.30</td>
<td>112ng/ml</td>
<td>Ms Mono 420mg</td>
</tr>
<tr>
<td>29/12/05</td>
<td>20.00</td>
<td>114ng/ml</td>
<td>Ms Mono 420mg</td>
</tr>
<tr>
<td>30/12/05</td>
<td>08.00</td>
<td>114ng/ml</td>
<td>Ms Mono 420mg</td>
</tr>
</tbody>
</table>
Discussion

Mr JN denies ever varying the consumption of his medication

His wife says he collects his script takes most of the medication, then goes into withdrawal

He then attends the emergency department for relief of his ‘pain’
Outcome

Transferred to Durogesic 150mcg/hour
Pain resolved
Fentanyl levels – therapeutic & stable
Returned to GP for on-going prescribing
Resumed chaotic management
Started on Methadone Maintenance
Mr C.S.

47 year old single male with one adult son
Disability pensioner
Non-smoker
Non-drinker
No hobbies or activities
Presenting history - Mr C.S.

Withdrawal fits from Tramal or Benzodiazepine
Fractured lumbar spine in MVA
  T12, L1, L4, L5 80% loss of anterior height T12
Chronic pain
Depression
Pain Clinic assessment 1994
Treated with various opioids including methadone.
No significant relief
<table>
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<tr>
<th>Date: Time</th>
<th>Blood Morphine</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>17/10/04</td>
<td>10.30</td>
<td>6ng/ml</td>
</tr>
<tr>
<td>19/10/04</td>
<td>16.30</td>
<td>8ng/ml</td>
</tr>
<tr>
<td>20/10/04</td>
<td>01.30</td>
<td>3ng/ml</td>
</tr>
<tr>
<td>20/10/04</td>
<td>11.20</td>
<td>25ng/ml</td>
</tr>
</tbody>
</table>

Bold Supervised
Issues

In constant pain
Not obtaining therapeutic levels
A reasonable doses of Morphine
Methadone had also offered no relief
Blood methadone levels were not taken
Outcome

Transferred to Buprenorphine S/L 2mg die
Greatly improved pain relief
Transferred to Norspan 20mg patches
Dose increased to 2*20mg Norspan weekly
Or
About 1mg S/L Buprenorphine daily
Pain controlled
Therapeutic Blood Monitoring
Is it Worth The Effort?

Therapeutic monitoring is an additional tool
It provides information for interpretation
It raises questions
  If the medication is NOT there, why not?
  Why is it varying so much?
Levels vary over time and the reasons may be obvious (or not)
What benefit will be achieved with an increase/decrease in dose?
Recent additions to Blood Monitoring

Fentanyl, Hydromorphone levels are readily available
Ranges are being developed
Morphine and Methadone have consistent therapeutic ranges
Blood levels are most useful with stable delivery systems
Morphine/Methadone/Fentanyl are available in sustained release preparations
Problems

Blood monitoring is not suitable for short acting agents
  – Anamorph, Oxycodone etc
## Features of Addiction

<table>
<thead>
<tr>
<th>More Predictive Features</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple episodes of prescription loss</td>
<td>Selling prescription drugs</td>
</tr>
<tr>
<td>Repeatedly seeking prescriptions from other physicians or emergency departments without informing the prescriber or after warnings to desist</td>
<td>Prescription forgery</td>
</tr>
<tr>
<td>Evidence of deterioration in function, at work, in the family, or socially that appear to be drug related</td>
<td>Stealing or borrowing drugs from others</td>
</tr>
<tr>
<td>Repeated resistance to therapy changes despite clear evidence of adverse physical or psychological effects from the drug</td>
<td>Injecting oral formulations</td>
</tr>
<tr>
<td></td>
<td>Obtaining prescription drugs from non medical sources</td>
</tr>
<tr>
<td></td>
<td>Concurrent abuse of alcohol or illicit drugs</td>
</tr>
<tr>
<td></td>
<td>Multiple non-sanctioned dose escalations</td>
</tr>
<tr>
<td>Less Predictive Features</td>
<td></td>
</tr>
<tr>
<td>-------------------------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td>Aggressive complaining about the need for more drugs</td>
<td>Openly acquiring similar drugs from other medical sources</td>
</tr>
<tr>
<td>Drug hoarding during periods of reduced symptoms</td>
<td>Unsanctioned dose escalation</td>
</tr>
<tr>
<td>Requesting specific drugs</td>
<td>Unapproved use of the drug to treat other symptoms</td>
</tr>
</tbody>
</table>