DoD's Experience with Prescription Meds

LTC Timothy Lyons, US Army
Deputy Director, Forensic Toxicology
Office of the Armed Forces Medical Examiner
Armed Forces Institute of Pathology

The views expressed in this presentation are those of the author and do not reflect the official policy of the Department of the Army, the Department of Defense, or the U.S. Government

This presentation was modified from its original format for 508 compliancy.

Historical Perspective

- Limited Experience
- Pulse testing
  - Codeine/morphine: October 1987
  - Oxycodone: DATE STARTED October 2005
- Prevalence testing
  - Methadone: October – December 2005
  - Benzodiazepines: May – June 2003
    January – May 2007
- Special testing/post-mortem/investigative

Codeine/Morphine

- Pulse testing
  - Goal- is 15-20% of total screened
  - Screening cutoff- 2,000 ng/mL (morphine used as calibrator)
  - 2 tiered screening
    - 2nd Screen Roche On Line Abuscreen kit
    - Initial Screen Roche On Line Abuscreen kit
- GC/MS confirm cutoff
    - 4,000 ng/mL Morphine
    - 2,000 ng/mL Codeine

Codeine/Morphine

- First 8 months of FY08
  - 2.65 Million samples received
  - 510,644 samples (19%) screened for codeine/morphine
    - 0.04% of samples confirmed positive for morphine
    - 0.11% of samples confirmed positive for codeine
    - 65% Confirmation rate (positive screens confirmed by GC/MS)

Oxycodone/Oxymorphone

- Pulse testing
  - Goal is 15-20% of samples received
  - Screening cutoff- 100 ng/mL (oxycodone used as calibrator)
- 2 tiered screening
  - Initial Screen Microgenics DRI kit
  - 2nd Screen Microgenics DRI kit
- GC/MS confirm cutoff
  - 100 ng/mL oxycodone
  - 100 ng/mL oxymorphone

Oxycodone/Oxymorphone

- First 8 months of FY08
  - 2.65 Million samples received
  - 516,195 samples (19%) screened for oxycodone and oxymorphone
    - 0.34% of samples confirmed oxycodone positive
    - 0.50% of samples confirmed oxymorphone positive
    - 85-90% confirmation rate
    - **90%** positives are legitimate use (cleared by MRO)

Hydroxycodone/Hydromorphone

- No commercial immunoassay kit available
- Anecdotal data, availability, and prescription use support a requirement for a kit
- No prevalence data at this time
- Aggressively lobby vendors for a kit??

6-AM

- 2003, Microgenics provided 6-AM immunoassay
- Cross reactivity to morphine at concentrations above 10,000 ng/mL
- 2004, 100% screening- continued pulse testing for Opiates (codeine / morphine**)**
- 50% Confirmation Rate
  - False positives?
    - High morphines <10,000 ng/mL
  - Conduct study
- Can the 6-AM immunoassay provide an

Fiscal Year DoD Military Personnel Heroin Positives Through June 2008

Fiscal Year	Samples Tested	Notes
1998	4,000,000	Prior to 2005, limited pulse testing for opiates 6-AM analysis conducted only if morphine concentration was >4000 ng/mL
1999	4,000,000	
2000	19,000,000	
2001	12,000,000	
2002	18,000,000	
2003	24,000,000	
2004	24,000,000	
2005	63,000,000	100% 6-AM testing initiated in FY 2005
2006	68,000,000	
2007	84,000,000	
2008	89,000,000	Projected 118,000,000 based on 9 months

Sources of Codeine/Morphine

- Heroin
  - Codeine/Morphine/ 6-AM
  - Codeine/Morphine (ratio low <0.1)
  - Morphine (high concentration)
- Poppy Seed
  - Codeine/Morphine (ratio low)
  - Morphine (low <4,000 ng/mL)
- Codeine
  - Codeine / Morphine (ratio high >2.0)
  - Codeine or Morphine Alone
- Morphine
  - Morphine / Hydromorphone (minor metabolite)
  - Morphine only

Prevalence Study Results

- 6 Month study summary for the 4 participating laboratories

Results	Number
Number of samples tested	1,734,722
Actual member samples 6-AM confirmed positive	59
6-AM AFIP QC positive	146
6-AM confirmed positives received	235
Study opiate screened positives	26
Study morphine opiate confirmed positives	24
Study codeine opiate confirmed positives	1
Study morphine confirmed positives at less than 4000 ng/mL	1

Conclusions

- Morphine causes presumptive positive on 6-AM screen?
- Opiates account for 25 of 26 presumptive positive specimens from 6-AM screen
Morphine causes presumptive positive on 6-AM screen?
- Opiates account for 25 of 26 presumptive positive specimens from 6-AM screen

Proposal

- On 6-AM positive initial screen, rescreen with 6-AM and opiates kits

Procedures

- 6-AM rescreen positive = only 6-AM confirmation
- 6-AM and opiates rescreen positive = both 6-AM and Codeine/Morphine confirmation
- 6-AM negative rescreen and opiate positive rescreen = second opiates screen and if positive confirm only for Codeine/Morphine
- Use current confirmation cutoffs 10 ng/mL for 6-AM, 2,000 ng/mL codeine, and 4,000 ng/mL for morphine
  - Meets DoD requirement for two positive immunoassayscreens and GC/MS confirmation analysis

Methadone

- Prevalence study-
  - Microgenics DRI® reagent
  - Assay specific and minimal cross reactivity with other drugs
- 27,994 samples screened
- Prevalence rate is 0.01% (4 out of 27,994)
  - methadone prescriptions for 2 specimens
- 75% Confirmation rate

Benzodiazepines

- Prevalence study
- Analyzed 12,090 in theater specimens
- 77 specimens screened positive
- 66 specimens confirm positive
  - Drug detected at ≥25 ng/mL
  - 85.7% confirmation rate

Prevalence Results

- Overall positive rate of 0.55% at ≥25 ng/mL
  - Positive rate of 0.49% at a 100 ng/mL cutoff
- Positive specimens consisted of:
  - Oxazepam* (48)
  - Temazepam (41)
  - Alprazolam (6)
  - 7-Aminoclonazepam (2)
  - Nordiazepam (27)
  - Lorazepam (13)
  - α-Hydroxyalprazolam (6)

Prevalence Results

Positive results indicate use of:

- Valium
- Xanax
- Restoril
- Ativan
- Klonopin
- Serax

Prevalence Results

- 10,111 specimens screened with all four assays
- 71 specimens screened positive
- 61 specimens confirm positive
- Presumptive positives that confirmed positive
  - DRI®: 67.2%
  - CEDIA®: 59.0%
  - CEDIA® w/glucuronidase: 98.4%
  - ROCHE: 32.8%

Screening Differences

- CEDIA w/glucuronidase most efficient due to ability to cleave conjugated metabolites
  - Lorazepam: 75% conjugated
  - Oxazepam: 61% conjugated
  - Temazepam: 73% conjugated

Summary

- Overall positive rate higher than 0.25% required for mandatory testing
  - Prescription information-not available for study
  - Pharmacy database now more readily available
- Positive rate consistent with previous prevalence studies

Summary

If DoD decided to initiate testing, analyzing only 5 of the 13 benzodiazepines would still result in a positive confirmation in 63 of the 66 specimens

- Oxazepam
- Temazepam
- Nordiazepam
- Lorazepam
- α-Hydroxyalprazolam

Pain Management

- Pain management drugs
  - High prevalence in DoD
  - Not expected to diminish
    - Short-term care
    - Long-term care
  - High abuse potential
  - No commercially available screening kits

DoD Future Approach

- Considering 6-AM/opiates screening proposal
- Methadone screening
  - Unlikely- too low positive rate
  - Future prevalence studies
- Benzodiazepines
  - Under consideration
  - High prevalence and high prescription use results in low feasibility for production labs

Future, continued

- Hydroxycodone/Hydromorphone
  - Current practice
    - use opiates kit/GC/MS
    - Less than optimal
  - Future Practice
    - Obtain kit
    - Conduct prevalence study
    - Implement testing???