## K14 Postmortem Redistribution: Practical Considerations in Death Investigation

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After attending this presentation, the attendee will be able to appreciate issues of postmortem redistribution and how practical accounting for this phenomena is of value in death investigation. Use of heart and peripheral (femoral) blood findings along with background investigation and prompt case disposition facilitates interpretation of cause and manner of death. These postmortem case finding considerations allow practical insights into understanding the impact of drug redistribution in interpretation of cause and manner of death.

Postmortem redistribution (PMR) of drugs in heart blood samples has been an ongoing subject of debate in interpretation of cause and manner of death (COD, MOD). The phenomenon's origins through drug redistribution along significant concentration gradients, release from protein bound sights, movement of drug due to decomposition bacterial activity and traumatic contamination is the subject of a large number of research papers. Drug redistribution occurs to the greatest extent in the initial 24 hours following death, and refrigeration with facilitated case disposition will retard the process. Arguably, the importance of the size and extent that redistribution plays in interpreting postmortem findings in routine medical examiner cases remains a topic of debate.

The Wayne County Medical Examiner's office (WCMEO) has an annual caseload of 2,900-3,300 cases. The large majority of cases arrives at the office within 24 hours of being reported and is placed into refrigerated storage. Toxicology studies on this population have demonstrated an incidence of up to 15% of death either directly or indirectly due the presence of drugs in the general population and up to 54% in the pended case population (Table 1).

**Table 1: WCMEO Drug Related Fatalities 1998-2002**

| YEAR | # DRUG DEATH CASES | # PENDING CASES (%) DRUG DEATH | #TOTAL CASES (%) DRUG DEATH |
|---|---|---|---|
| 1998 | 370 | 692 (53.4) | 2924 (12.6) |
| 1999 | 404 | 831 (48.6) | 3288 (12.2) |
| 2000 | 495 | 916 (54.0) | 3306 (14.9) |
| 2001 | 470 | 990 (47.4) | 3263 (14.4) |
| 2002 | 466 | 1089 (42.8) | 3178 (14.7) |

Practical considerations of case history, time of death, time of arrival at the Medical Examiner's office, comparison to reference data, and a consistent system of collection, storage and analysis protocols, can lead to a reasoned and meaningful assessment of postmortem drug findings. Tabulation of over 5 years of analysis data of comparative heart blood and femoral blood data for 50 drug analytes are presented on Table 2. These data are presented as a function of drug Vd heart blood (B1)/ peripheral blood (B2) average ratio, median ratio, SD, and ratio range for cases of an "n" of 4 or greater. Heart bloods were collected primarily from the left side of the intact heart by needle puncture. Peripheral blood samples, 6.93 mL (+/- 4.24 mL SD) were collected from non-ligated femoral veins 96.2% of the time with the remaining samples collected from a subclavian or a non-specified "peripheral" site.

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**Table 2: Tabulation of Postmortem Redistribution Ratios for Heart and Femoral Blood Concentrations**

| DRUG | Vda L/kg | n | B1/B2b Ratio Average | B1/B2b Ratio Median | SD[c] | B1/B2[b] Ratio Range Low | B1/B2[b] Ratio Range High |
|---|---|---|---|---|---|---|---|
| Acetaminophen | 0.8-1.0 | 16 | 1.083 | 1.037 | 0.345 | 0.693 | 1.987 |
| Alprazolam | 0.9-1.3 | 9 | 0.898 | 0.930 | 0.230 | 0.519 | 1.273 |
| Amitriptyline | 6-10 | 52 | 1.982 | 1.408 | 1.880 | 0.273 | 9.885 |
| Benztropine | NAd | 11 | 2.490 | 1.231 | 2.484 | 0.600 | 7.667 |
| Bupropion | 40 | 7 | 1.033 | 0.652 | 0.956 | 0.375 | 3.099 |
| Carbamazepine | 0.8-1.8 | 4 | 0.969 | 1.003 | 0.144 | 0.782 | 1.088 |
| Chlorpheniramine | 5.9 | 6 | 1.171 | 1.159 | 0.518 | 0.560 | 1.880 |
| Chlorpromazine | 10-35 | 6 | 1.968 | 0.946 | 2.564 | 0.762 | 7.193 |
| Citalopram | 12-16 | 10 | 2.492 | 1.536 | 2.908 | 0.727 | 10.400 |
| Clozapine | 2-7 | 10 | 1.684 | 0.991 | 2.227 | 0.753 | 8.000 |
| Codeine | 3.5 | 21 | 1.385 | 1.243 | 0.852 | 0.064 | 3.750 |
| Cyclobenzaprine | NA | 8 | 1.220 | 1.192 | 0.523 | 0.500 | 2.056 |
| Desipramine | 22-59 | 5 | 2.795 | 1.410 | 2.871 | 0.929 | 7.727 |
| Desmethyldiazepam | NA | 45 | 1.268 | 1.250 | 0.449 | 0.288 | 2.308 |
| Dextromethorphan | 255-316 | 11 | 1.721 | 1.694 | 0.856 | 0.105 | 3.158 |
| Diazepam | 0.7-2.6 | 38 | 1.299 | 1.235 | 0.533 | 0.331 | 3.053 |
| Diltiazem | 3-13 | 9 | 3.271 | 1.515 | 5.302 | 0.879 | 17.333 |
| Diphenhydramine | 3-4 | 48 | 1.956 | 1.536 | 1.487 | 0.356 | 8.200 |
| Doxepin | 9-33 | 22 | 1.604 | 1.258 | 0.939 | 0.612 | 3.300 |
| Doxylamine | 2.7 | 6 | 3.808 | 1.877 | 4.764 | 0.625 | 13.333 |
| EDDP (Meth. Mtb.) | NA | 4 | 0.686 | 0.540 | 0.433 | 0.351 | 1.313 |
| Fluoxetine | 20-42 | 21 | 2.395 | 1.379 | 1.917 | 0.586 | 5.909 |
| Hydrocodone | 3.3-4.7 | 20 | 1.580 | 1.275 | 0.824 | 0.576 | 3.646 |
| Hydroxyzine | 13-31 | 4 | 1.018 | 1.066 | 0.416 | 0.481 | 1.459 |
| Meperidine | 3.7-4.2 | 4 | 2.537 | 1.739 | 1.877 | 1.360 | 5.313 |
| Mesoridazine | 3-6 | 6 | 1.508 | 1.581 | 0.622 | 0.704 | 2.222 |
| Methadone | 4-5 | 53 | 1.684 | 1.290 | 1.113 | 0.327 | 5.185 |
| Mirtazepine | 10-14 | 4 | 1.064 | 1.125 | 0.612 | 0.269 | 1.737 |
| Morphine | 2-5 | 24 | 1.231 | 1.155 | 0.580 | 0.045 | 2.846 |
| Nicotine | 1.0 | 41 | 1.363 | 1.200 | 0.749 | 0.157 | 3.846 |
| Norclozapine | NA | 5 | 1.116 | 1.123 | 0.239 | 0.847 | 1.429 |
| Nordoxepin | NA | 20 | 2.720 | 1.967 | 2.204 | 0.280 | 7.400 |
| Norfluoxetine | NA | 7 | 2.751 | 1.500 | 2.034 | 1.000 | 5.550 |
| Norsertraline | NA | 16 | 2.092 | 1.673 | 1.505 | 0.241 | 5.263 |
| Nortriptyline | 20-57 | 43 | 2.152 | 1.235 | 1.896 | 0.196 | 9.600 |
| Olanzapine | 10-20 | 22 | 1.902 | 1.540 | 1.120 | 0.360 | 5.357 |
| Orphenadrine | 4.3-7.8 | 5 | 2.308 | 1.688 | 1.654 | 1.143 | 5.158 |
| Oxycodone | 1.8-3.7 | 4 | 2.196 | 2.203 | 1.031 | 1.200 | 3.167 |
| Paroxetine | 3-28 | 24 | 2.993 | 1.829 | 2.889 | 0.292 | 10.278 |
| Phentermine | 3-4 | 7 | 1.887 | 1.857 | 1.103 | 0.720 | 3.898 |
| Promethazine | 9-19 | 4 | 1.215 | 0.747 | 1.168 | 0.430 | 2.938 |
| Propoxyphene | 12-36 | 62 | 1.622 | 1.211 | 1.095 | 0.365 | 4.571 |
| Salicylate | 0.15-0.20 | 4 | 1.058 | 0.882 | 0.395 | 0.821 | 1.646 |
| Sertraline | 76 | 16 | 2.452 | 1.407 | 2.433 | 0.415 | 9.167 |
| Thioridazine | 18 | 5 | 1.277 | 1.111 | 0.713 | 0.600 | 2.130 |
| Tramadol | 2.6-2.9 | 9 | 1.358 | 1.431 | 0.465 | 0.556 | 2.107 |
| Trazodone | 0.9-1.5 | 14 | 1.535 | 1.182 | 1.095 | 0.583 | 4.800 |
| Venlaflaxine | 4-12 | 6 | 1.506 | 1.495 | 0.403 | 0.864 | 2.071 |
| Verapamil | 2.5-6.5 | 4 | 1.595 | 1.440 | 0.707 | 1.000 | 2.500 |
| Zolpidem | 0.5-0.7 | 8 | 1.474 | 1.452 | 0.337 | 1.056 | 2.000 |

a Vd = Volume of distribution values taken from Randall C. Baselt, "Disposition of Toxic Drugs and Chemical in Man", 6th Edition Biomedical Publications 2002. b B1 = Heart Blood Sample; B2 = Peripheral (Femoral) Blood Sample. c SD = Standard Deviation. d NA = Not Available.

These data indicate that despite size of Vd, under the conditions of case disposition for WCMEO, some drug analytes tend towards redistribution (e.g. amitriptyline, citalopram, doxylamine, paroxetine) while others do not (e.g., acetaminophen, alprazolam, hydroxyzine, mirtazepine,). When individual case tabulations are considered, in all categories PMR may or may not be a factor in cause and manner of death.

Full tabulations of all cases for each analyte with COD and MOD will be presented.

Conclusions drawn from this survey indicated that in all cases where borderline drug toxicity is an issue in COD and MOD of death, it is essential to account for PMR. These data also suggest that when actual concentrations are excessively high or low, regardless of PMR, the interpretation of drug involvement or lack thereof in COD and MOD does not change.

**Postmortem Redistribution, Postmortem Release, Multi-site Testing**

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