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POST MORTEM ELEVATION OF COCAINE LEVELS IN VITREOUS HUMOR

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Because Vitreous humor (VH) is an isolated medium recent studies have theorized that VH cocaine may not be subject to post mortem degradation and that VH/Blood cocaine ratios may relate time of administration to time of death.

Blood, VH and tissue cocaine levels were analyzed in 67 cocaine related deaths. In 23 cases right and left VH were drawn separately, 0-19 hours apart. Cocaine was quantitated by extraction into heptane:isoamyl alchol (98.5:1.5), back extraction into 0.05M H_2SO_4 and re-extraction into heptane-isoamyl. Concentrated samples were analyzed on a 15m DB-1 megabore column with NPD. Information about time and route of cocaine administration and duration of time between death and autopsy was obtained from police and medical examiner reports.

Cocaine appeared to equilibrate slowly into and out of VH. 9 cases had VH cocaine levels from 0.03-2.3 ug/ml with no detectible cocaine in Blood and known drug administration times up to 20+ hours prior to death. Cocaine VH levels increased post mortem by as much as 330% when VH levels were taken 19 hours apart. Distribution of cocaine into VH and post mortem elevation of cocaine appeared to be a saturable phenomena. Data will be presented to show that VH/Blood cocaine levels are dependent upon time of administration relative to time of death, quantity of cocaine administered previous cocaine use and duration of time between death and autopsy.

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METHAMPHETAMINE IN ANTE-MORTEM BLOOD BY RADIOIMMUNOASSAY AND GC/MS.

Susan A. Rasmussen*, Ray Cole, San Diego Sheriff's Crime Lab, San Diego, CA, Vina Spiehler, PhD., DPC Corp, Los Angeles, CA

Methamphetamine abuse is increasing and methamphetamine is second only to alcohol as a positive finding in cases submitted to the San Diego Sheriff's Crime Lab. In general whole blood specimens are submitted more often than urine. A modified version of a commercially available radioimmunoassay, Coat-A-Count(CAC) Methamphetamine, was investigated as a screen for methamphetamine in whole blood. The assay was modified by using 100 ul of sample, making up standards in whole beef blood, extending the incubation time to 2 hours or overnight and using a cutoff reference of 50 ng/ml methamphetamine in water. The detection limit for the CAC Methamphetamine kit was 20 ng/ml methamphetamine in whole blood. The CAC Methamphetamine results were compared to Abuscreen Amphetamine High Specificity results and to GC/MS quantitation of amphetamine and methamphetamine for 157 positive and 48 negative blood specimens. With the CAC Methamphetamine assay there were 2 false negatives detected, both less than the 50 ng/ml cutoff level. There were 12 (6%) false positives with the CAC Methamphetamine assay and 29 (14%) false positives with the Abuscreen Amphetamine assay. 95% of the positive samples contained only methamphetamine, with an average concentration of 308 ng/ml, and a range of 25 - 2030 ng/ml.

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TANDEM (MS/MS) MASS SPECTROMETRY UTILIZING ELECTRON IMPACT IONIZATION AND MULTIPLE REACTION MONITORING FOR THE RAPID, SENSITIVE, AND SPECIFIC IDENTIFICATION AND QUANTITATION OF MORPHINE IN WHOLE BLOOD WITH 5 METER CAPILLARY COLUMN CHROMATOGRAPHY

W.H. Phillips, Jr., N. Wade*, K. Ota, R. Kitagawa, D. Warden, S. Zehnder, T. Appel, and G. Davis, Department of Justice, Toxicology Unit, Sacramento, California, 95820

The power of tandem (MS/MS) mass spectrometry virtually eliminates background interferences and increases sensitivity, thus allowing for a minimum of sample cleanup. A single step liquid-liquid extraction procedure with pentafluoropropionic anhydride derivitization of the resultant extract and 5 meter column chromatography provides a 3 minute analysis of free morphine in blood samples. The specificity of the method is further enhanced by multiple reaction monitoring which is essentially selective ion recording of two quadrupoles. The first quadrupole is set to transmit only the molecular ion, 577, which then undergoes collision induced dissociation with argon. The last quadrupole is set to transmit only the daughter ion, 414. In the next scan, the daughter ion, 414, is then analyzed for its granddaughter ion, 266. Deuterated morphine was included as an internal standard and analyzed similarly. Linear and reproducible calibration curves have been obtained for morphine at concentrations from 1.0 to 500 ng/ml achieving correlation coefficients of greater than 0.994. A signal to noise ratio of approximately 7:1 was observed for the 1.0 ng/ml samples.

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AN EVALUATION OF THE ABBOTT TDx BENZODIAZEPINE SERUM ASSAY.

Ricky P. Bateh*, PhD: Consolidated Laboratory Services/St. Vincent's Medical Center; Jacksonville, Fl 32204.

This study evaluated the TDx Benzodiazepine Serum Assay. The precision of the assay was assessed by analyzing 3 controls in replicates of 5 on 10 different days over a two week period. The within-run %CV ranged from 1.8 to 2.6% and the between-run %CV ranged from 1.2 to 3.4%. The calibration curve was stable over a 30-day test period. The accuracy of the assay was assessed by cross-analyzing all calibrators and controls of both the TDx method and the HPLC procedure.

One hundred random, 75 "tox negative", and 84 "positive" serum specimens were screened for benzodiazepines by 3 comparative methods (EMIT, TDx, HPLC). The TDx method and the HPLC procedure were in best agreement. The TDx method showed comparable sensitivity to HPLC for several benzodiazepines at low concentrations.

The clinical data show that the TDx BENZODIAZEPINE SERUM ASSAY is useful in detecting several benzodiazepines and/or metabolites with good precision, accuracy, and sensitivity.

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DETERMINATIONS OF ENCAINIDE, ODE (O-DESMETHYL ENCAINIDE), MODE (3-METHOXY-O-DESMETHYL ENCAINIDE) AND NDE (N-DESMETHYL ENCAINIDE) IN THREE FATAL CASES. G.M. Bercowy, M.F. Rieders* T.J. Speaker, and F. Rieders. National Medical Services, Inc. and Temple University School of Pharmacy.

Encainide, a class IC anti-arrhythmic agent is active as parent drug, more potent as metabolites ODE and MODE, and equi-potent as NDE. Reported therapeutic ranges are Encainide: 24 to 35 nanograms/mL, ODE: 80-120 nanograms/mL, and MODE: 80-120 nanograms/mL. Rapid conversion of encainide ($t_{\frac{1}{2}}$~1.5 hours) occurs producing approximately equal amounts of ODE and MODE. Pharmacokinetic studies identified a "slow metabolism" group (~7% of population) resulting in NDE formation. In three death cases attributable to deliberate encainide overdose, encainide concentrations were 12, 20 and 30 micrograms/mL blood, ODE concentrations were 1.8, 2.0 and 0.7 micrograms/mL blood, and MODE concentrations were all less than 1 microgram/mL blood. NDE was present at 0.8 micrograms/mL blood in one case. Encainide and metabolites were isolated using a solid phase extraction technique and quantitated by reverse phase high performance liquid chromatography. Further confirmation by gas chromatography/mass spectrometry was performed in one case.

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MUNCHAUSEN'S SYNDROME BY PROXY: IPECAC POISONING IN A CHILD, A. Poklis, L. Edinboro and J. Saady, Department of Pathology, Virginia Commonwealth University, Medical College of Virginia, Richmond, VA. 23298-0597

A 4 year old girl suffered a 5 month illness of recurrent episodes of vomiting and bloody diarrhea. During 7 hospitalizations and intensive diagnostic testing, fever, emesis and hematochezia were well documented, and colonoscopy showed diffuse mucosal edema and erythema of the large bowel. Mucosal biopsies showed significant but non-specific inflammation. Serum and urine drug screens detected only administered medications. During her 7th hospitalization an initial examination of the stomach and duodenum conducted during an upper G.I. series showed retained fluid although she received nothing by mouth throughout the night. The liquid was withdrawn by nasogastric tube and initial analysis by TLC and U.V. indicated emetine was present. Resolution of the child's symptoms followed separation from the mother.

In such instances ipecac poisoning is a problem to diagnose. Ipecac alkaloids are not detected in serum or urine by usual toxicology screening methods; HPLC with fluorescence or UV/photodiode array detectors are required. Even if detected, the presence of ipecac alkaloids is assumed due to therapeutic administration. A survey of the 25 largest acute care childrens' hospitals revealed that only eight of them include ipecac in their reports.

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RAPID ANALYSIS OF SYMPATHOMIMETIC AMINES COUPLED WITH CONFIDENCE IN THEIR FULL SCAN MASS SPECTRAL IDENTIFICATION., Mark D. Uhrich*, Finnigan MAT, River Oaks Parkway, San Jose, CA 95314, John Buck, Finnigan MAT, 1355 Remington Road, Suite M. Schaumburg, IL. 60173

The detection and identification of sympathomimetic amines in biofluids and tissue is challenging. Many of the amines have high vapor pressures, and are easily lost during post-extraction solvent reduction before derivatization and/or GC analysis.

Additionally, many of the amines generate non-specific electron impact ionization mass spectra which makes their identification ambiguous. We have developed an analytical solution to the problem of extracting and confidently identifying the sympathomimetic amines. We use a single step, 0.5 mL heptane, liquid extraction which requires no solvent reduction or analyte derivatization. This extraction procedure eliminates the risk of analyte and time loss during solvent reduction and derivatization, respectively.

Integral to proper identification of the amines is the generation of a full mass spectrum acquired under methane chemical ionization conditions. The use of a Finnigan MAT ITS40 permits the generation of highly specific CI mass spectra for the amines at senstivities equivalent to 100 pg of analyte injected into the GC/MS. Detection limits for this method are 25 ng/mL, with linear quantitation up to 2000 ng/mL.

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ROLE OF BIODISPOSITION IN TOXICITY AFTER COCAINE FREE BASE INHALATION. J. P. Boni*, W. H. Barr§ and B. R. Martin*, Depts. of Pharmacology* and Pharmacy and Pharmaceutics§, Medical College of Virginia, Richmond, VA 23298.

Mechanisms of acute toxicity following cocaine free base smoking are poorly understood. To investigate the role that duration of exposure has on biodisposition, male S.D. rats (170-210 gm) were prepared with an abdominal aorta cannula. Seventy-two hours after surgery, animals were exposed to ^{3}H-cocaine free base vapor (10 μCi/50 mg) generated by a nose-only manifold system. By sampling from the cannula, plasma cocaine and benzoylecgonine (BE) time courses were generated using GC-MS (range: 0.1-1000 μg/l). Doses of 1.05 ± 0.15 and 1.24 ± 0.07 mg/kg were delivered for 1.5 and 5.0 min exposure periods respectively as determined by liquid scintillation. The cocaine and BE mean biological half-lives were 1.54 ± 0.31 hrs and 1.66 ± 0.13 hrs after the 1.5 min exposure and 1.90 ± 0.19 hrs and 1.21 ± 0.11 hrs after the 5.0 min exposure respectively. Cocaine levels measured immediately after the 5.0 min exposure experiments were 1.50 ± 0.21 mg/kg in brain, 0.51 ± 0.14 mg/kg in heart and 2.02 ± 0.59 mg/kg for lung (n=8 animals) and are consistent with simulated values for individual animals obtained using a physiological flow model (PFM) for cocaine disposition after inhalation. Loo-Riegelman deconvolution analysis of the plasma time courses revealed that inhalation leads to rapid drug delivery to critical organs, especially brain, and that prolonged absorption from deposition sites maintains these high levels long after exposure is terminated.
(Supported by NIDA grant DA-02396).

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FATALITIES DUE TO 3-METHYLFENTANYL, Wagdy W. Wahba, Ph.D.* and Charles L. Winek, Ph.D., Allegheny County Department of Laboratories, Pittsburgh, PA 15219

The potent derivative of fentanyl, 3-methylfentanyl (China White), appeared in the Pittsburgh area around June 1988. With the availability of the drug, many overdoses and some fatalities occurred. Out of 59 fatal cases investigated, samples from 19 cases showed the presence of fentanyl analogs. The highest reported fatalities (75%) occurred between June and November of 1988 with only two cases identified earlier the same year. So far, the 1989 figures show a decline in the number of fatalities (2 cases) due to 3-methylfentanyl abuse. Biological samples were tested for the presence of fentanyl analogs utilizing a radioimmunoassay (RIA) method. Data will be presented as to number of fatalities, limit of detection of fentanyl analogs by RIA and cross sensitivity of the method to other opioids.

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ACCIDENTAL CARBON MONOXIDE POISONING IN POLICE CUSTODY
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Medical Examiner Dept., Miami, Fla.

A man arrested for D.U.I. died while being transported to jail. Toxicological analyses revealed: blood ethanol 0.33%, vitreous ethanol 0.37%, cocaine and benzoylecgonine detected in urine but not blood, and blood carbon monoxide (CO) 27.7% saturation. The deceased had been given pure oxygen during CPR for 45 minutes, so the blood CO had probably been much higher than the measured value. Death was attributed to CO poisoning.

The victim had been hog-tied and left on the ground behind the police car with its motor running for 1/2 hour. He was unconscious when placed in the car for transport and was not breathing upon arrival at the jail.

In an experimental reenactment, CO was measured both inside and outside the police car using a Drager Multi Gas Detector. The concentration in the vehicle was negligible, but it exceeded 800 ppm at ground level at a distance of 7 feet behind the car where the victim had been placed. The vehicle's emission control devices had been disconnected causing it to emit an excessive amount of CO.

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DRUG RECOGNITION METHODS
Marcelline Burns, Ph.D.
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Los Angeles

The Drug Recognition program, which was initiated and developed within the Los Angeles Police Department, trains officers to systematically examine drivers who are suspected of being under the influence of an impairing substance(s). Given the problematic relationship of blood levels of drugs and the associated impairment, the Drug Recognition Expert's (DRE) testimony and the introduction of evidence from a drug evaluation can assume a critical role in court proceedings. The scientific validity of the methods is subject to challenge.

To examine issues of validity, this paper will cover the following:

- the history of the development of the DRE program from inception to the present.
- the rationale, approach, and philosophy of DRE methods.
- a review of two scientific studies of the DRE methods: a laboratory study at Johns Hopkins University and a Los Angeles field study.
- a critique of the DRE methods in comparison to assessment methods in other disciplines.
- the importance of eye signs, including gaze nystagmus, pupil reactivity, rebound dilation.
- key program concepts: standardization, systematization, integration, drug "fingerprints".
- a discussion of the issue of measuring driving skills at roadside vs. the recognition of impairment and/or the presence of impairing substances.

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TRAINING LAW ENFORCEMENT IN DRUG EVALUATION AND CLASSIFICATION TECHNIQUES
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The NHTSA Drug Evaluation and Classification (DEC) Program is comprised, in part, of training law enforcement personnel in a 12-step psychophysical evaluation procedure to identify signs and symptoms of seven identifiable categories of drugs. The evaluation is a post-arrest procedure designed to determine if illness or injury is a cause for an individual's impaired driving ability and, if not, to identify the drug category responsible for the impairment. The Drug Recognition Expert's (DRE) findings, together with a blood/urine sample, is provided to the laboratory. The DRE's opinion is valuable to the laboratory in narrowing the analysis to a category of drugs to test for, thereby lowering the cost and increasing the odds that the test will produce a positive result.

In light of the unavailability of reliable correlations between levels of drugs in the body and degree of impairment, the DEC program is vital in providing the link between the driving impairment and the substance(s) ingested, necessary to allow for the successful prosecution of drug-impaired drivers.

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THE ROLE OF THE TOXICOLOGIST IN THE DUID PROGRAM by Vickie W. Watts*, Mesa Police Department Crime Laboratory, 130 North Robson, Mesa, Arizona 85201-6697

The forensic toxicology lab involved in a DUID program must consider not only the well known illicit psychotropic drugs, but also a wide range of prescription drugs which have the potential to cause driving impairment. Improved detection of the drugged driver by the use of DRT's (drug recognition technicians) provides information to the laboratory on possible drug categories present. Many of these drugs, however, will not be detected using immunoassay. Therefore, a broader analytical approach is required.

For a DUID program, factors that differ from typical ME cases are: single specimen limitation, rapid turnaround time requirement, chain of evidence procedures, and potential courtroom testimony for each case. The choice of specimen involved in the DUID arrest is determined by the law enforcement agencies' capability for collection, handling, and preservation. Often times, the specimen type may not be optimal for the drug category requested. Since a DUID analysis potentially will require expert testimony in court, all screening results are confirmed by separate GC-MS procedures. The goal of our laboratory is to provide a comprehensive drug screen using not more than 8 mL of hemolyzed whole blood with a minimum number of special extractions. Adequate drug LOD/LOQ's for a DUID analysis will also be addressed.

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SOLID PHASE EXTRACT FOR THE IDENTIFICATION AND QUANTITATION OF FATTY ACID ETHYL ESTERS. Jan Johnson*, Kevin A. Brown, Xie Chang-i, Renee C. Lin, Ph.D., Michael A. Evans, Ph.D. Department of Pharmacology and Toxicology and Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana 46202.

Fatty acid ethyl esters have recently been described as products of non-oxidative ethanol metabolism. The formation of these ethyl esters has been suggested as a possible mediator of ethanol induced organ damage and may represent a marker for chronic ethanol ingestion. Ethyl esters of oleic, linoleic and arachidonic acid were isolated from human tissues utilizing acetone as an extraction solvent followed by silica gel solid phase extraction using a solvent system of hexane and chloroform. Quantitation and identification of oleic, linoleic and arachidonic ethyl esters was achieved utilizing gas chromatography/mass spectrometry and linoleic acid propyl ester as an internal standard. Quantitation of these ethyl esters in human tissues may provide a reliable assessment of chronic alcohol use.

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EVALUATION OF THE ABBOTT TDx^{R} FOR DRUGS OF ABUSE TESTING IN A FIELD ENVIRONMENT, Donna M. Bush,* Cathy C. Stevenson, Deanna L. Cibull and Jeffrey A. Gere. US Army Forensic Toxicology Drug Testing Laboratory (FIDTL), Fort Meade, Maryland 20755-5235.

The US Army tests urine specimens for drugs of abuse at the installation shortly after collection (field screening). Specimens which are positive must then be forwarded to the forensic lab (FIDTL) for RIA and GC/MS confirmation. We evaluated the Abbott TDx^{R} (FPIA) analyzer to determine if the TDx^{R} is suitable as a field testing methodology. For this study, a total of 4,000 specimens were collected and tested at the field test sites (Ft Benning and Ft Bragg). They were all forwarded to the FIDTL where they were tested by RIA and GC/MS; if positive they were re-tested by TDx^{R}.

Our results showed that out of 65 specimens confirmed positive by GC/MS, TDx^{R} testing at the field site found 64 positive, while 49 were positive by EMIT^{R} at the field site, 57 were positive by RIA and 58 were positive by re-TDx^{R} at the forensic lab. Of the specimens which were positive by field TDx^{R} but negative when re-tested by TDx^{R}, all were close to the cutoff. These discrepancies may be due to degradation of metabolite(s) during shipping (average time between field TDx^{R} and TDx^{R} at the FIDTL was 11.3 days).

The qualitative results for the THC testing by TDx^{R} agreed well with those for THC testing (RIA), indicating good agreement between the Department of Army cutoff of 100 ng/ml (RIA) and the proposed cutoff of 50 ng/ml (TDx^{R}). For cocaine metabolite(s) the TDx^{R} quantitative results agreed very closely with the GC/MS results. This indicates a need to lower the TDx^{R} cutoff to 150 ng/ml.

In conclusion, the TDx^{R} analyzer was found to be very specific and accurate for THC and cocaine metabolite(s). It would be an acceptable methodology for use by the US Army for field screening.

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DO BREATH TESTS OVERESTIMATE BLOOD ALCOHOL CONCENTRATIONS? YES, NO, MAYBE. N.G.S. Rao, Ph.D.*, A.K. Chaturvedi, Ph.D. Office of the State Toxicologist, North Dakota State University, Fargo, ND 58105

In the United States, blood alcohol determinations are more frequently made by analyzing samples of breath rather than blood. Breath specimens are often preferred over blood, since the analysis is simple, convenient, cost effective to the agency and less traumatic to the individual. Most breath alcohol testing instruments, if not all, operate on the basis that the partition ratio of alcohol in blood vs. breath (deep lung air) is 2100:1. The validity of this ratio has been questioned extensively during the past 5 years and statistically shown to overestimate the blood alcohol concentrations.

This study examines blood and breath samples collected within one hour of each other from over 675 apprehended drivers and indicates that though the difference between blood and breath tests varied widely, from -0.04% to +0.07%, over estimation occured in only 4% of the cases. In 10% of the cases, the tests were identical. The single largest group was 25% in which the breath tests were lower than the blood tests by 0.02%. In 7% of cases, the breath analysis underestimated the blood alcohol concentration by $\geq$ 0.05%.

All the blood tests were conducted at one location while the breath tests were conducted by law enforcement officers at several sites using the Intoxilyzer 5000.

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QUALITY ASSURANCE AND QUALITY CONTROL IN A NIDA FORENSIC URINE DRUG TESTING LABORATORY,

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The Quality Assurance(QA) program undertaken by our lab, is a comprehensive, administrative program that includes the establishment and continual review of all Quality Control(QC) and operational procedures to assure the integrity of the labs overall performance and therefore establish the reliability of the test results. The QC program for the technical portion of the lab includes the use of open and blind controls, from both internal and external sources, with limits established for acceptability. Controls used for screening by EMIT® include: a threshold, negative, 2 positive(20% and 50% above the cutoff),and a negative blind control 30% below the cutoff designed to prevent false positives. For GC/MS analyses, controls include: a threshold, negative, and positive blind. The lab also participates in 2 external proficiency programs.

The CV data for the GC/MS assays is as follows: 9-carboxy-THC 7%, BE 3%, PCP 5%, Codeine 5%, Morphine 7%, Amphetamine 12%, Methamphetamine 7%.

The lab also has a QC program for sample processing and chain of custody, to assure that the proper measures are taken to insure sample integrity. It is a blind internal program arranged such that clients purposely submit unacceptable samples, such as, mislabelling, lack of chain of custody or adulteration.

Also, as part of the QA program, the lab director and certifying scientists conduct a monthly independent self inspection of the lab encompassing all working procedures.

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USE OF VITREOUS HUMOR TO FACILITATE POSTMORTEM ALCOHOL INTERPRETATION

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Many studies have been published comparing blood (B) ethanol (EtOH) and vitreous humor (VH) EtOH concentrations. We conducted a similar study of routinely collected specimens to determine: (1) whether the reported average VH/B ratios are consistent; (2) the percentage of cases with VH/B ratios outside of the expected range; and (3) the magnitude of B EtOH which can be associated with negative VH EtOH (<0.01%). Data were grouped as follows: B EtOH >0.01 and VH EtOH <0.01%; B EtOH <0.10%; and B EtOH $\geq$0.10%. Forty-one specimens were associated with VH EtOH <0.01%; 34 had B EtOH $\leq$0.03% while a B EtOH as high as 0.12% was measured. For B EtOH <0.10%, 67% had VH EtOH within 0.02% of B EtOH (N=101). For B EtOH $\geq$0.10%, the VH/B EtOH ratio ranged from 0.10 to 1.91; the mean ratio was 1.17 and the median ratio was 1.18 (N=205). 64% had a ratio between 1.00 and 1.39. In summary, vitreous humor can be used to help understand the significance of postmortem blood alcohol concentrations.

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A FENTANYL FATALITY INVOLVING MIDAZOLAM

Barry Levine, Ph.D.*, Julia C. Goodin, M.D., and Yale H. Caplan, Ph.D.

A case is presented of a 35-year old Black African male anesthesiology resident, found dead in his apartment. At the scene a syringe, butterfly intravenous line and a bottle of Versed® (Midazolam) were recovered. A comprehensive screen for common drugs of abuse and therapeutic agents failed to detect any drugs in blood and urine. The blood ethanol concentration was 0.06 g/dL. A GC/MS SIM assay for midazolam was developed. A sub-therapeutic midazolam blood concentration of 7.5 ng/mL was detected and concentrations (ng/mL or ng/g) in bile, urine, and liver were 3.3, 7.5, and 96, respectively. The syringe fluid was then analyzed and found to contain only fentanyl, midazolam was absent. The blood fentanyl concentration was 4.9 ng/mL which is consistent with those reported in fentanyl fatalities. Fentanyl concentrations (ng/mL or ng/g) in bile, urine, and liver were 8.8, 5.0, 5.9, respectively. The cause of death was ruled to be fentanyl intoxication and the manner of death undetermined.

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URINE OPIATE DETERMINATIONS FOLLOWING THE INGESTION OF POPPY SEED CAKE

Nancy Solano[1]; *Neil Fortner[2], and C.E. Pippenger[1]; The Cleveland Clinic Foundation[1] and Southgate Medical Laboratories[2], Cleveland, OH.

The occurence of positive opiate screens by immunoassay and GC/MS confirmation of morphine in urine following the ingestion of poppy seeds is well documented. As follow-up to a nurse who was terminated for opiate abuse after eating poppy seed cake, we studied the morphine excretion patterns over 24 to 70 hrs following poppy seed cake ingestion in 11 normal volunteers. Urine was collected at each void. Opiates were quantitated by the EMIT semi-log calibration technique and/or GC/MS. All subjects were negative prior to cake ingestion. Time to positive opiate screen ranged from 0.5-3.3 hrs ($\bar{x}$=2.4) in 11/11. Peak urinary opiate concentrations ranged from 650-1380 ng/ml ($\bar{x}$=1184) and occurred 1.5-7.0 hrs ($\bar{x}$=4.9) postcake. At 24 hrs 9/11 remained positive, at 32 hrs 5/11 and at 48 hrs 2/11. Time to last positive specimen ranged from 4.0-52.5 hrs ($\bar{x}$=36.9). Three subjects whose urine had become negative again exhibited positive screens within 24 hours following the first negative specimen. We conclude there is marked individual variation in urinary opiate excretion patterns following poppy seed cake ingestion. Extreme caution in the interpretation of preemployment opiate screens is essential. New analytical techniques to distinguish true drug abusers from casual poppy seed ingestors are needed.

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USING SOLID PHASE EXTRACTION TO CONFIRM DRUGS OF ABUSE Ritchard C. Parry* and George D. Wachob Supelco, Inc, Supelco Park, Bellefonte, PA 16823

The use of solid phase extraction (SPE) to isolate drugs of abuse and their metabolites, from biological sample matrices, offers several advantages over other popular sample pretreatment techniques, such as liquid-liquid extraction and thin-layer chromatography. SPE provides three degrees of extraction selectivity. Selective extraction allows the analyst to exclude some matrix interferences by using different types of bonded phases, as well as different conditioning solvents with these phases. Selective washing allows the analyst to remove additional matrix interferences from the bonded phase with a series of wash solutions. Finally, selective elution allows the analyst to elute the compounds of interest from the bonded phase, while leaving additional matrix interferences retained on the phase. The greater extraction selectivity provided by SPE results in much cleaner sample extracts, thereby simplifying the analysis and quantitation of the compounds of interest, as well as increasing analytical column life.

The basic principles of SPE methods development will be presented, as well as several examples of SPE procedures. These examples involve the extraction of several common drugs of abuse and/or their metabolites, including 11-nor-tetrahydrocannabinol-9-carboxylic acid, from a variety of biological sample matrices.

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ANALYSIS OF WHOLE BLOOD FOR BENZODIAZEPINES BY RADIOIMMUNOASSAY.
David M. Andrenyak* and Dennis J. Crouch.
Center for Human Toxicology, University of Utah. Salt Lake City, Utah 84108.

The widespread use of benzodiazepines present the need for rapid and sensitive screening methods for these compounds. Although several immunoassays have been developed to screen urine samples, there is a paucity of techniques that can screen benzodiazepines in whole blood. This study describes the application of the Abuscreen Radioimmunoassay (RIA) (Roche Diagnostics) to the analysis of blood samples. Direct analysis of blank blood by the benzodiazepine RIA showed that the blood matrix interfered with the RIA. To reduce the interferences in the blood, the blood samples were buffered with saturated borate buffer (pH 8.5) and extracted with ethyl acetate. The extracts were evaporated to dryness, reconstituted with blank urine, and then analyzed by RIA. The extraction removed the interferences. RIA analysis of the extracted blood samples spiked with the following benzodiazepines concentrations resulted in the following % Bound values: 10 ng/ml alprazolam-67%; 10 ng/ml diazepam-61%; 10 ng/ml triazolam-91%; 100 ng/ml desalkylflurazepam-48%; 1 µg/ml chlordiazepoxide -41%. With the exception of triazolam, the extractive RIA detected therapeutic or subtherapeutic concentrations of the benzodiazepines that were tested. This method will be helpful for screening benzodiazepines in cases where blood is the only specimen available.

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THE INCIDENCE OF ALCOHOL AND DRUGS AMONG MVA TRAUMA ADMISSIONS TO A REGIONAL TRAUMA UNIT.

B.M. Kapur*, E. Vingilis, C.B. Liban, B. McLellan, and W.-J Sheu ; (Addiction Research Foundation, 33 Russell St, Toronto and Sunnybrook Medical Centre, Toronto, Canada.)

Alcohol has shown to be a major factor in MVA fatalities. Good comparative data on non-fatal injuries is not available. In Toronto the Addiction Research Foundation and Sunnybrook Medical Centre Trauma Unit have embarked on a 3 year study to investigate the role of alcohol and drugs in MVA and Non-MVA trauma victims. This paper presents some of the preliminary findings on the incidence of alcohol and other drugs in these trauma victims.

Population characteristics: Over a period of about 16 months 396 patients were screened. 218 were MVA accidents, 178 were non MVA accidents.

Method: Blood and urine samples of all patients admitted to the trauma unit were analyzed for various drugs including alcohol, cocaine, cannabinoids and benzodiazepines using both immunoassay and thin layer chromatography.

Results: 124 (56%) and 98 (55%) of the MVA and N-MVA had one or more drugs in their body fluids. Mean BAC of the MVA-drivers was 149 mg/100ml. In the MVA-Driver category (n=140) 37%, 16% and 7% respectively, had 1,2 or more drugs in them.

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COMPARISON OF TWO COAT-A-COUNT KITS FOR THE DETERMINATION OF MORPHINE IN POST MORTEM BLOOD. Vina Spiehler, Ph.D. and Joseph R. Monforte, Ph.D.*, Wayne County Medical Examiner's Office, 400 E. Lafayette Street, Detroit, MI 48226.

A comparison of immunoassay kits manufactured by Diagnostic Products Corporation for the detection of morphine was performed.

The procedure involves a 1:11 dilution of blood with pH 7.4 buffer, addition of 1.0 ml of tracer, incubation at room temperature for one hour, aspiration of the liquid, and counting each tube for one minute. The quantitative result is obtained from a logit-log plot constructed from four standards.

A total of 31 post mortem blood specimens were analyzed, together with 9 commercial controls. All specimens were analyzed in duplicate, and the average per cent binding calculated to determine the concentration from the calibration plot.

Qualitatively, both kits were in agreement that 16 blood specimens were negative(less than 25 ng/ml). Of the remaining 15 specimens, 13 were positive by both assays, and 2 specimens were positive only with the original kit. In both instances, the blood specimens contained 40 ng/ml, or less, of morphine

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SIMULTANEOUS DETERMINATION OF ALPRAZOLAM AND TRIAZOLAM IN WHOLE BLOOD BY GC/NPD

H. Horton-McCurdy, Ph.D., Division of Forensic Sciences, P.O. Box 370808, Decatur, GA

A method is presented for the simultaneous determination of alprazolam and triazolam in whole blood using the pentyl derivative of nordiazepam as the internal standard. The procedure is to extract blood (5 mL) with n-butyl chloride (10 mL) at pH 9.0. The organic layer is removed after centrifugation and evaporated to dryness. Clean-up is accomplished by dissolving the residue in acetonitrile and washing with hexane. The hexane layer is then aspirated to waste and the acetonitrile layer evaporated to dryness. The residue is then dissolved in 40 mcL of ethanol and 1 mcL analyzed by GC/NPD. Confirmation is by GC/MS. The established linear range is from 25 to 500 ng per mL with a limit of detection of approximately 10 ng/mL. Analysis of alprazolam in DUI cases has ranged from 30-150 ng/mL.

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MANDATORY POST-ACCIDENT TESTING FOR THE FEDERAL RAILROAD ADMINISTRATION. D.E. Moody*, D.J. Crouch, D.M. Andrenyak, and D.E. Rollins. Center for Human Toxicology, Univ. of Utah, SLC, UT 84108

Under Federal regulation, certain railroad employees involved in qualifying accidents and incidents (events) are subject to testing for alcohol and drugs. From 4/1/87 to 3/31/89, blood, urine, and occasional tissue specimens from 1,398 employees have been tested at this facility, providing a basis for comparison between yearly results. There were 175 and 176 events, for which specimens were received from 736 and 662 employees during years 1 and 2, respectively. In total, 49 and 36 employees, (40 and 28 events) tested positive during the first and second years, respectively. Fatal events consistently had more positives (40%, yr. 1: 23%, yr. 2) than non-fatal events (19%, yr. 1: 15%, yr. 2). Cannabinoids were the most commonly encountered single drug finding (61%, yr. 1; 47%, yr. 2), with cocaine (10%, yr. 1; 19%, yr. 2), and ethanol (10%, yr. 1; 8%, yr. 2) also prominent. Increased cocaine detection in year 2 was accompanied by increased cannabinoid-cocaine combination (4.1%, yr. 1; 8.3%, yr. 2). Of the more thoroughly investigated positive events in 1987, approximately one-third of the events with positives (8% of all events) had alcohol or drug findings determined to involve an employee associated with the cause of the accident/incident, with a greater proportion in fatal than non-fatal events.

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FATAL THIAMYLAL INTOXICATION

T. L. Stockham, Ph.D., M.P. McGee, B.S., and M. Stajic, Ph.D.

Thiamylal (Surital, Biotal) is an ultra short acting barbiturate used for the intra-venous induction of anesthesia in both humans and animals. A fatal thiamylal intoxication is reported.
A 21-year-old male was found dead with an IV line from a Biotal bottle attached to his left arm. The decedant had been working for a veterinarian. The autopsy findings were unremarkable with the exception of lung congestion. Toxicologic analysis revealed high concentrations of thiamylal as follows: blood 129mg/L; brain 116mg/kg; liver 366mg/kg. Thiamylal was not detected in urine, bile and gastric contents. Death was attributed to an acute thiamylal intoxication, with the manner being classified as suicide.
Thiamylal analysis was performed by high pressure liquid chromatography and gas chromatography/mass spectrometry. Analytical caveats will be discussed.

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THE DESIGNER DRUG 3-METHYLFENTANYL: IDENTIFICATION AND QUANTITATION. Francis M. Esposito, Ph.D.* and Charles L. Winek, Ph.D., Allegheny County, Department of Laboratories, Pittsburgh, PA 15219.

The "designer drug" 3-methylfentanyl (3-MF) is a synthetic analog of the narcotic analgesic fentanyl. It is an attractive drug to synthesize due to its ease of obtaining starting materials, profitability, and similarities in effects to heroin. Its high potency makes analyses of street samples and biological specimens difficult.

Paraphernalia and plastic bag corners submitted for GC/MS analyses showed the presence of cis and trans isomers of 3-MF. The isomers were differentiated by retention times and the smaller abundance ratios of ions at m/z 160 and 203 to the base ion of 259 for the more stable trans isomer.

Quantitation was accomplished using a GC/MS with a HP5 column (25m x 0.20mm) and ketamine as an internal standard. Two cut street samples revealed higher percentages of the more potent cis isomer (0.26% & 0.37%) than the trans (0.15% & 0.16%). With an average purity of 0.47% (4.7µg/mg), about 100µg of 3-MF would be present in a typical 20mg packet, as compared to 2000µg of heroin with an average street value of 10%. Since the potency of 3-MF is about 1000 times heroin, the 3-MF samples should have been diluted another 50 fold to contain about 0.1µg/mg. The difficulty of cutting and inexperience with 3-MF contributed to the rash of overdoses in our area.

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SCREENING OF BLOOD AND URINE FOR DRUGS OF ABUSE UTILIZING THE DIAGNOSTIC PRODUCTS CORPORATION'S COAT-A-COUNT® RADIOIMMUNOASSAY KITS.

N.A. Wade*, T.A. Appel, Department of Justice, Toxicology Unit, Sacramento, California, 95820

In the past year our caseload has increased over seventy percent, while our supplies budget has remained essentially the same, thus prompting us to seek ways to reduce our cost-per-case by reducing the cost of radioimmunoassay (RIA) reagents. Because blood constitutes eighty percent of our case submissions, enzyme immunoassay was disregarded even though it has been shown to be inexpensive and able to be utilized for the detection of drugs of abuse in blood. It was patently apparent that the lengthy extraction methods published did not conform to our high volume, rapid turnaround-time driving under the influence (DUI) laboratory. Fluorescense polarization was likewise not considered due to our in-house evaluation of its cost-per-case prohibitive value. Our evaluation of these RIA kits was based on their ability to detect amphetamine, methamphetamine, morphine, cocaine and cocaine metabolites, phencyclidine, benzodiazepines, and 9-carboxy-delta-9-THC metabolite. The DPC Coat-a-Count® RIA kits have been successfully utilized on all of our case submissions in the past year with GC/MS confirmation rates of approximately 90% at the 10 ng/ml cutoff level. In a cross-reactivity study for the methamphetamine kit, almost no common drug was found to cross-react with any significance, except MDMA.

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DETERMINATION OF URINARY GLUCURONIC ACID METABOLITES AS A NONINVASIVE ASSESSMENT OF XENOBIOTIC INDUCTION OF HEPATIC BIOTRANSFORMATION IN HUMANS, J. Saady, R. Blanke and A. Poklis, Department of Pathology, Virginia Commonwealth University, Medical College of Virginia, Richmond, VA. 23298-0597

Numerous xenobiotics are known to induce Phase I hepatic biotransformation (HB). Present methods to detect induction of HB have several disadvantages. "Antipyrine half-life" and the "caffeine breath test" require test drug administration and controlled pharmacokinetic studies. Measurement of urinary metabolites from HB substrates such as 6-β-hydroxycortisol or γ-glutamyltranspeptidase are often unreliable as their excretion is also effected by normal variations in physiologic status or incident pathology. However, induction of Phase I HB has been successfully monitored by urinary excretion of D-glucuronic acid (GLU) metabolites in test animals. We monitored GLU metabolites: GLU, glucaric acid, gulonic acid and xylitol in human males and females receiving chronic phenobarbital (PB) therapy. PB is a known inducer of Phase I HB.

A significant increase in the urinary excretion of all GLU metabolites in the PB induced patients compared to controls was observed ($p<.001$). Further, differences by sex (controls male to female) were noted for some metabolites. Monitoring of GLU metabolites may prove useful as an indirect assessment of HB enzyme activity in humans.

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TWO CARISOPRODOL RELATED DEATHS

Ronald C. Backer,Ph.D.*, Ross Zumwalt,M.D.
Patricia McFeeley,M.D. Office of the Medical Investigator, State of New Mexico.
Nancy Wohlenberg, B.S., Scientific Laboratory Division, Health and Environment Department, State of New Mexico, Albuquerque, New Mexico.

Two cases involving overdoses of Carisoprodol are descibed. Toxicological analysis of biological specimens in both cases revealed significant concentrations of carisoprodol and its major metabolites, meprobamate and hydroxymeprobamate(Table 1). Quantitative results were determined by gas chromatography/mass spectrometry.

Table 1. Distribution of Carisoprodol and Its Metabolites, Meprobamate and Hydroxymeprobamate.

	CARISOPRODOL		MEPROBAMATE		HYDROXY-MEPROBAMATE	
	CASE		CASE		CASE	
Specimen	1	2	1	2	1	2
	mg/L		mg/L		mg/L	
HEART BLOOD	39.4	14.0	40.1	18.9	ND	ND
FEMORAL BLOOD	39.3	6.5	51.9	20.5	ND	ND
URINE	12.6	-	61.0	-	POS	-
VITREOUS	18.9	8.7	45.9	50.2	ND	ND

ND - none detected
Case 1 - no other drugs were detected
Case 2 - verapamil was detected (Blood - 13.8mg/L)

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A QUICK AND RELIABLE SCREENING TECHNIQUE FOR CYANIDE USING CYANTESMO PAPER AND THE CONWAY DIFFUSION DISH. Michael I. Schaffer, Ph.D.* and Mark Bloom, M.S. Office of the Medical Examiner, Cook County, 2121 W. Harrison St., Chicago, Il.

Cyantesmo paper (Machery-Nagel, West Germany) was used to screen ME cases for the presence of cyanide/HCN. A 1" ribbon was placed in the center well of the Conway dish. A 1 mL sample of blood or other liquid biological fluid, or 1 gram of solid tissue was placed in the outer well. Two mls of 10% sulfuric acid was then added to the outer well, and the dish was then sealed. A 1 and 4 micrograms/ml cyanide standard along with a blank were also analyzed. Two blood samples were placed in each dish; each 1 ml. The dishes were stored at room temperature for 1 hour before viewing. The expected colors for the blank, the 1 and 4 micrograms/ml standards were pale green, pale blue and dark blue, respectively. The manufacturer specifies a 0.2 microgram/ml level of detection. Attempts to obtain a 0.25 and 0.5 microgram/ml level of detection met with negative results after 24 hours. We have been using this technique for several years in our general screening, followed by the pyridine-barbituric acid color test for quantitation purposes. Gastric contents may also be tested after ensuring that the sample is sufficiently acid. Analysts usually note a smell of bitter almonds, an ammonia type of odor or another unusual type of smell which is characteristic but difficult to describe.

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A KINETIC MODEL OF COCAINE AND BENZOYLECGONINE DISPOSITION

John Ambre, M.D., Ph.D. Northwestern University Medical School, Chicago, IL

A kinetic model can be used to characterize the time course of drug/metabolite disposition. The model may in turn be used to make general, quantitative predictions that may form the basis for interpretation of analytical data on isolated samples.

We have developed a model of cocaine (C) and benzoylecgonine (BZ) disposition based on data from studies in intravenous cocaine users (plasma levels and excretion rates for C and BZ after intravenous injection and/or infusion of C). Kinetic analysis was done with the CONSAM 29 computer program. Model parameters indicated:

The elimination clearance of C is dose dependent within the range of dose commonly reported by users. There is no significant effect of dose on the volume of distribution of C. The halftime for urinary excretion of BZ averaged 4.5 hours, as found previously. A halftime for formation of BZ of 1.5 hours suggests that renal processing rather than formation is the rate limiting step determining the appearance of BZ in the urine. There is no effect of dose on BZ formation rate. The distribution volume of BZ is 49 liters, one third that of C.

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PHENCYCLIDINE-RELATED DEATHS IN NEW JERSEY DURING 1987 AND 1988.

*Reng-lang Lin, Ph.D., and Robert Goode, M.D. New Jersey State Medical Examiner Office, Newark, New Jersey 07103

Thirty-three phencyclidine-related deaths were reported in 1987 (18 cases) and 1988 (15 cases). It was about 4% of the total annual toxicology cases. Phencyclidine was extracted from tissues and body fluids using the typical double basic extraction procedure with hexane as the solvent and quantitated by GC-NPD using a 3% OV-101 column with the internal standard method. All positive cases were confirmed by GC-MS. Phencyclidine concentrations in blood range from 0.01 to 0.46 mg/L. There was no case where the death was caused by acute overdose of phencyclidine alone. Although multiple drug intoxication was cited as the most frequent cause of death, especially in combination with morphine, other causes included drowning, motor vehicle accident, gunshot, stabbing, etc. The manner of death was mostly accident with some homicide and suicide. Other drugs such as ethanol, cocaine, morphine, cannabinoids, etc., were found in most cases. Only in three cases was phencyclidine detected as the sole drug. The majority of victims were young males under the age 30. The racial distribution was 20 white, 12 black and 1 hispanic. Details of the results will be discussed along with the case histories.

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METHODS FOR QUANTITATIVE ANALYSIS OF COMMON PRESERVATIVES IN BLOOD AND URINE FORENSIC ALCOHOL SPECIMENS

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Methods for the quantitative analysis of sodium fluoride and mercuric chloride are described. Sodium fluoride testing utilizes an ion-selective fluoride electrode and a milliVolt meter for the potentiometric determination of fluoride concentration. After diluting 50 ul of blood, urine or control in 50 ml CDTA buffer solution, mV measurements are taken and a standard semilog curve generated. A 0.18% NaF control run by various technicians over a period of six months yielded a SD of 0.02 with a CV of 11.2% (N=62). The method is designed to detect NaF levels between 0.05% (0.5 mg/ml) and 2.0%.

Mercuric chloride analysis is performed using a cold vapor method and a mercury analyzer. A 10 ul sample is diluted 1:1000 in water, treated with nitric and sulfuric acids and potassium permanganate to oxidize the mercury, then reduced with stannous chloride to metallic mercury. The resulting mercury vapor is bubbled through a Buck 400 Mercury Analyzer and absorbance is measured and plotted directly using a standard curve generated with each test batch. A CV of 14.2% (N=29) was obtained for a 0.14 mg/ml control (SD=0.02) tested over six months by different analysts. Target range for the method is 0.05 to 1.0 mg/ml mercuric chloride.

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"THE EFFECTS OF SOLVENTS ON THE INTOXILYZER 4011AS-A"

C. N. Hodnett*, E. Spratt, S. Ferrand; Westchester County, NY, Dept. of Laboratories & Research

The response of the intoxilyzer 4011AS-A to common solvents was investigated by introducing dry solvent vapor samples into the instrument during the "test subject" step and observing if any "alcohol concentration" was displayed or the "interference" circuit was activated.

Solvent vapor samples with and without ethanol were used in this study. They were prepared by adding known quantities of the solvents to teflon gas bags containing a known volume of air at ambient temperature and atmospheric pressure.

Solvents containing methyl functions produced "alcohol concentrations". Common chlorinated solvents produced no or weak responses. The presence of carbon chain branching or carbonyl groups in the solvent's structure increased the probability that the "interference" circuit would be activated.

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PERINATAL MORBIDITY IN INTRAVENOUS (IV) VS OTHER FORMS OF DRUG ABUSE (DA). S. Aduana, E. Berman, S. Pyati, R.S. Pildes.* Div. of Neonatology and Laboratories, Cook County Hospital, Chicago.

We studied the impact of IV vs other routes of DA on perinatal outcome during the course of an anonymous 5 month HIV surveillance of 2510 neonates. We identified 182 (7.3%) DA: 37 (1.4%) IV, 122 Non-IV (5%) and 23 (0.9%) unknown route. Demographic and lab data were collected and recorded within 72 hours after birth. Statistical analysis were done by Chi-square analysis and Fisher's exact test. Mothers and babies were identified by historical data at time of admission for delivery. Of those tested, the %age confirmed by urine tox. in mothers and babies of IV was not sig. different from that of NIV (74%, 81% vs 71%, 49% respectively): 23 were identified by urine toxicology and no history. Maternal data are shown in Table:

	Race %			Age(yr)%		Smoking	Alcohol	+VDRL
	B	H	W	<20	>30	%	%	%
IV	91	3	6	0	32*	91	44	16*
NIV	94	3	2	11	17	93	35	4
NDA	53**	39	4	29***	16	4.3**	0.9***	1***

Fetal and neonatal mortality and morbidity are listed below:

	≤1000g	≤2500g	NICU Admiss %	Still-birth/ 1000T.B.	Mort. < 72hr/ 1000L.B.	+HIV %
IV	9	38	29	0	29	24**
NIV	5	37	26	16	16	0
NDA	2	11***	10***	9.8	8	.17

We concluded: 1) IV ↑ morbidity above that seen in NIV by sig. ↑ in **($p<0.01$) HIV-Pos. and *($p<0.05$) +VDRL. 2) Both IV and NIV DA differed markedly ***($p<0.001$) from NDA mothers. 3) 1 of 5 admissions to NICU were newborns of DA.

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INSTRUMENT PERFORMANCE EVALUATION, John T. Cody, Ph.D.*, Air Force Drug Test Laboratory, Brooks AFB TX 78235-5000

Gas chromatography/mass spectrometry (GC/MS) is recognized as the most definitive method for the analysis of unknown compounds in the area of forensic toxicology. Recent developments in the area of analytical instrumentation and computers have given rise to sophisticated and relatively inexpensive analytical systems which match capabilities of far more expensive and complex instruments. A wide variety of criteria may be used to evaluate the performance of the system, but which ever criteria are used, it is important that any GC/MS system be evaluated before data are collected using the instrument.

The most common procedure to evaluate the current status of a mass spectrometer is tuning. Most systems use PFTBA to tune the instrument. This is an ideal compound because it covers a range of masses typically encountered in forensic toxicology and is used by most laboratories. While this is an important and fundamental process, evaluation of other parameters is useful for evaluation of instrumental performance. Significant advantage can be gained by using several diagnostic procedures to ensure the system is performing properly and is consistent with previous analyses. Use of such performance checks can save a great deal of time and effort by diagnosing problems or differences prior to beginning analyses of samples.

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QA/QC STANDARDS AND CONTROLS IN FORENSIC GC/MS; NORMAN A. WADE, 4949 BROADWAY, SACRAMENTO, CA 95820

BECAUSE GAS CHROMATOGRAPHY/MASS SPECTROMETRY HAS BEEN DEFINED AS THE "GOLD STANDARD" FOR CONFIRMATION OF DRUGS AND/OR POISONS IN BIOLOGICAL SPECIMEN IT HAS BECOME IMPERATIVE TO THE FORENSIC TOXICOLOGIST TO RECOGNIZE AND IDENTIFY THE NEEDS OF QUALITY ASSURANCE AND QUALITY CONTROL IN THIS ANALYTICAL TECHNIQUE. DEFINITIONS OF WHAT IS MEANT BY THE TERMS QUALITY ASSURANCE AND QUALITY CONTROL IN GC/MS WILL BE DISCUSSED. IN PARTICULAR, EXAMPLES WILL BE GIVEN FOR RECOMMENDED METHODS FOR ASSURING THE QUALITY OF THE ANALYTICAL PRODUCT PRODUCED BY THE FORENSIC TOXICOLOGY LABORATORY TO BE THE HIGHEST ATTAINABLE. BECAUSE FORENSIC URINE DRUG TESTING ANALYSIS IS ONLY ONE THIRD OF THE TYPES OF FORENSIC TOXICOLOGY CURRENTLY BEING PRACTICED BY OUR LABORATORIES AND IT HAS BEEN FULLY COVERED BY THE DEPARTMENT OF HEALTH AND HUMAN SERVICES GUIDELINES AND BY THE COLLEGE OF AMERICAN PATHOLOGISTS GUIDELINES THIS DISCUSSION WILL FOCUS ON POST-MORTEM AND HUMAN PERFORMANCE TOXICOLOGY AS RELATED TO GC/MS QUALITY ASSURANCE. CRITERIA WILL BE GIVEN FOR GOOD LABORATORY PRACTICES FOR GC/MS IN A TYPICAL FORENSIC TOXICOLOGY LABORATORY.

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SHOULD GC/MS DRUG CONFIRMATIONS BE BASED ON FULL-SCAN OR SIM MASS SPECTRAL DATA?
Rodger L. Foltz*, Connie O. Sakashita, and Kim M. Monti, Center for Human Toxicology, University of Utah, 417 Wakara Way, Salt Lake City, Utah 84108.

The question posed by the title of this talk continues to be debated. Advocates of GC/MS confirmations based upon a full-scan mass spectrum argue that it provides a more detailed "fingerprint" identification than does a selected ion monitoring analysis, and therefore it constitutes a more rigorous confirmation. Proponents of confirmations based on selected ion monitoring (SIM) analysis claim that it provides greater sensitivity and better quantitative accuracy. The validity of each of these points will be examined by comparing full-scan and SIM data obtained on the same body-fluid extracts. Additionally, data from both a Hewlett-Packard Mass Selective Detector (MSD) and a Finnigan Ion Trap (ITS-40) will be compared in an attempt to identify the strengths and limitations of each instrument.

CRITERIA FOR IDENTIFICATION BY GC-MS:
WHEN IS A POSITIVE A POSITIVE?
Michael A. Peat, Ph.D, CompuChem Corporation
Research Triangle Park, N.C.

The use of GC-MS for identification and quantitation is now widespread. Ion abundance ratioing is often used as criteria for defining a positive. If this is used what criteria should be established for identification purposes?

For historical reasons a +/- 20% range is widely applied but this may not be applicable at low concentrations where the amount injected on column is small causing larger variations in ion abundances. A laboratory should establish its own range depending on the assay, the concentration range expected, the ionization method and instrumentation used.

What if the ratio is +21% from target - does this mean that the sample is negative? One should not forget other factors such as extraction procedure and retention time in defining the criteria for a positive indentification. The same arguments can obviously be applied to full spectra comparisons.

The experience and training of an analytical toxicologist must be available when reviewing GC-MS data, if a realistic answer to the question of when is a positive a positive can be made. It is possible that the use of rigid rules will result in a positive being reported as a negative.

ADMINISTRATIVE PROBLEMS IN GC/MS
Michael I. Schaffer, Ph.D., Nancy B. Wu Chen, Ph.D. and MaryAnn Suero,M.S., Office of The Medical Examiner, Cook County,Il.

Performing GC/MS analyses as part of an investigation within a Medical Examiner/Coroner system, requires more than state of the art technology, properly identified and qualified tissue specimens and well trained GC/MS operator(s). When all these routine functions have been properly resolved, there are still problems with definitions such as administrative cutoff, limit of detection, limit of quantitation, limit of sensitivity, criteria for identification, either in full scan or SIM mode, use of de facto ion ratios, and acceptable criteria for purely qualitative identification.

Reporting values which are below your administrative cutoff, but which are above your documented lowest reproducible value on a standard curve, may be questionable, but often practiced. Qualitative identification may be required in certain instances, and may be acceptable within certain defined criteria. Single tissue determinations, when the specimen amount is limited, may be the greatest source for concern. Most GC/MS analyses are not performed in duplicate; is that necessary? Do you apply the same criteria when performing multiple sample types; i.e., blood, liver, vitreous, etc.? These and other issues will be reviewed for your consideration.

WORKSHOP II

CLINICAL APPROACH TO THE POISONED PATIENT
Daniel Hryhorczuk, Section of Toxicology, Division of Occupational Medicine, Cook County Hospital

The clinical approach to the poisoned patient consists of 1) support of vital functions; 2) prevention of further absorption; 3) identification of the toxin; 4) enhancement of elimination; and 5) antidotal therapy. Identification of the toxin relies on the history, physical examination, and laboratory analysis. Combinations of signs and symptoms called toxidromes provide clues to the diagnosis. Techniques of gastric decontamination include use of ipecac, lavage, activated charcoal, cathartic, and whole bowel irrigation. Elimination of some toxins may be enhanced through repetitive oral dosing of charcoal, diuresis, hemodialysis, or hemoperfusion. Specific antidotes are available for relatively few poisons.

THE LABORATORY APPROACH TO THE POISONED PATIENT
Eleanor Berman, Ph.D. Head, Toxicology Section Biochemistry Division, Cook County Hospital, 1825 W. Harrison Street, Chicago, IL.

In his approach to an apparently poisoned patient, the laboratorian follows an analytical protocol not unlike that employed by his colleagues in forensic laboratories. However, he is cognizant of the possibility that the presenting problem may not be caused by an extraneous toxic substance, but, in fact, be due to a metabolic disorder, an infective process, a trauma, or non-compliance with a therapuetic regimen. Therefore, his contribution to the resolution of the situation is also guided in part by the patient's physical signs and symptomatology. Data obtained from routine biochemical and hematological investigations play a role, also.

Pertinent case histories illustrating a clinical laboratorian's approach to the poisoned patient will be presented.

WORKSHOP II ----------

The Toxicology of Chemical Asphyxiant Gases
Anne Krantz, Division of Occupational Medicine, Cook County Hospital, Chicago, Ill.

The presentation and clinical course of workers exposed to hydrogen sulfide gas will be presented, followed by a discussion of the toxicities of the chemical asphyxiants carbon monoxide, hydrogen cyanide and hydrogen sulfide. The pathophysiology, cellular mechanisms, and clinical presentation for each gas will be reviewed. The laboratory investigations used to aid in diagnosis of toxicity, dose-response characteristics, and pharmacokinetis for each gas will be discussed Finally, guidelines for therapy will be outlines for each of the three gases.

COCAINE ABUSE AND TOXICITY

Timothy Erickson, MD: Toxikon Consortium Cook County Hospital, Chicago, IL

Following a brief case presentation of acute cocaine toxicity, introductory comments will cover the early history of abuse along with the drugs current manufacturing process and methods of illegal smuggling.

Discussion will then follow regarding the physiologic effects, metabolism, routes of administration, lab analysis, and acute management of cocaine toxicity. Finally, aspects of chronic addiction and fetal toxicity will be presented.

EXACERBATION OF LEAD POISONING IN CHILDREN FOLLOWING DELEADING OF THEIR HOMES

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"Deleading" the homes of children with lead poisoning is a necessary step to terminate the child's exposure to lead. Lead poisoning as a result of lead exposure during the process of deleading has occurred in deleading workers but has not been well documented among children whose homes are deleaded. We treated four children with classes I through III lead poisoning (range of blood lead [Pb-B] level, 1.6 to 2.75 umol/L [33 to 57 ug/dL]) who had significant elevation of their Pb-B levels (range, peak 4.34 to 6.27 umol/L [90 to 130 ug/dL]) following deleading of their homes. The methods used for deleading included scraping, sanding, and burning of the paint. Symptoms included irritability (n=3) and vomiting (n=1). The elevation of Pb-B levels was detected early, allowing prompt chelating therapy. Because exacerbation of lead poisoning may occur in children following deleading of their homes, safer approaches of deleading should be determined.

Acute Toxicity of Organic Solvents

Stephen M. Hessl, MD MPH*

On April 4, 1986 a worker was assigned to remove oil tank sludge from a 7 & 32 foot underground "oil" storage tank. The worker wore an air purifying respirator and protective garments and entered the tank. After ~55 minutes in the tank, a second worker joined him. Soon thereafter, the first worker became light-headed and lost consciousness. The second worker attempted to carry the first worker out but a rope ladder broke and an additional ~50 minutes transpired before fire department paramedics removed the workers. The second worker developed dizziness but did not lose consciousness.

Analysis of blood for volatile organic solvents several days later revealed detectable levels of several solvents which appeared to correlate well with the ingredients found on subsequent analysis of the tank residuals.

Neuropsychological assessment of these workers revealed strong evidence for central nervous system injury to the first worker.

The presentation, diagnosis, and treatment of acute organic solvent toxicity will then be discussed.

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