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Site to Site Variability of Postmortem Drug Concentrations in Liver and Lung

ABSTRACT: We evaluated postmortem diffusion of gastric drug residue into tissues and blood in eight suicidal overdoses. Analyses were performed on liver (five sites), lung (four sites), spleen, psoas muscle and kidney (left and right), blood (peripheral and torso), vitreous, pericardial fluid, bile and, urine as well as residual gastric contents. Standard anlytical techniques and instrumentation gas chromatograph/mass spectrometer and high performance liquid chromatography (GC-MS and HPLC) were used throughout. These case studies confirm previous studies of an animal and human cadaver model of gastric diffusion, in that in several instances there was drug accumulation in the left posterior margin of the liver and, to a lesser extent, the left basal lobe of the lung. Uncontrollable variables, such as postmortem interval, refrigeration before autopsy, and position of the body appear to influence significantly drug accumulation in a specific site. We suggest that autopsy sampling techniques should be standardized on blood taken from a ligated peripheral (preferably femoral or external iliac) vein, and liver from deep within the right lobe.

KEYWORDS: forensic science, forensic toxicology, postmortem redistribution, liver, lung, skeletal muscle, benzodiazepines, propoxyphene, paracetamol, amitriptyline, gastric residue

An animal model of postmortem drug redistribution showed postmortem diffusion of gastric drug residue into liver and lung (1). A human cadaver model (2) and an isolated case report (3) suggest that this may pose a significant problem in the interpretation of drug concentrations in case material. To evaluate this issue further, we performed toxicological analyses on multiple samples of liver and lung, as well as other tissues and body fluids in cases of acute poisoning.

Methods

Suspected cases of drug poisoning were identified before autopsy. The details of the eight cases are summarized in Table 1. The autopsy protocol allowed for multiple sampling of body fluids and tissues. Samples of vitreous humor, bile, urine, and blood were obtained by needle puncture. Before obtaining blood samples, the vessels were ligated or crossclamped. Pericardial fluid was sampled and the pericardial sac swabbed dry before obtaining blood samples from the heart and great vessels. Blood samples

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were obtained from the femoral veins, aortic arch, right atrium, left atrium, and inferior vena cava (IVC), with, in some cases, separate samples from the suprarenal and infrarenal portions of the IVC. Tissue samples were obtained from the right and left kidneys, right and left psoas muscles, five areas of the liver (left anterior margin, left posterior margin, caudate lobe, right anterior margin and right posterior margin), and four areas of the lungs (left and right upper lobe apices, and left and right lower lobe posterobasal). The volume of the gastric contents was measured and a representative sample was obtained for analysis.

Analytical Methods

All samples were stored at −20°C until analysis. From the tissue samples, 5.0 g were accurately weighed. The sample was finely chopped with scissors and homogenized with a blender (Ultra Turrax T25, Janke and Kunkel, IKA Labortechnik) for 1 min at 8500 rpm, and then subsequently at 9500, 13,500, 20,500, and 24,000 rpm for 1 min each. The homogenate was added to 20 mL of distilled water. The liquid samples were diluted four times with distilled water. Quantities of 4 mL of homogenate or 4-mL-liquid sample solution were used for extraction. All analyses were performed in duplicate to within 5% of the mean value. The assays used follow the standard investigative procedures used and developed within the laboratory to determine drug concentration in various body fluids and tissues. Quantitation is performed using a six point calibration curve for each drug with a minimum acceptable correlation coefficient of 0.99.

For benzodiazepines analysis, 10 μL of internal standard solution (1-mg/mL prazepam) and 1 mL of phosphate buffer (pH 7.4) were added to the extraction sample and mixed briefly on a vortex mixer. A 4-mL-quantity of diethyl ether was added and mixed for 15 min (Spiramix 10, Denley, UK). The organic layer was separated and 4 mL of diethyl ether was added to the extraction sample and mixed again. The combined organic layer was evaporated to dryness at 50°C under a stream of dry air. The extracts were further purified by partition between 1 mL of acetonitrile and 2 mL of heptane. The acetonitrile layer was separated and evaporated to dryness. The residue was resuspended in 100 μL of methanol and 20 μL of this solution was injected into the high performance liquid chromatography (HPLC) system. The HPLC conditions were as follows: instrument, Perkin-Elmer isocratic LC pump 250 with Perkin-Elmer ultraviolet spectrophotometric detector C 90 (wavelength 240 nm) and Waters autoinjector 712 WISP, column, Apex II ODS 5 μm, 150 by 4.6 mm with guard column 20 mm; mobile phase, 180 mL of 10mM phosphoric acid, 20 mL of 10mM disodium hydrogen phosphate, 200 mL of acetonitrile, and 100 mL of

TABLE 1—*Case data for the eight cadavers sampled.*

Cases	Age/Sex	Height/ Weight‡	History/Autopsy Notes	Postmortem Interval (h)*	Refrigeration (h)	Body Positions†
1 (379/93)	49 F	59/170	Depression	>19	15	Prone
2 (315/94)	41 M	47/173	Depression, BAC = 187 mg%	28–37	23	Prone, crouched
3 (100/95)	37 F	56/156	Depression, tablet residue in duodenum	21	16	Supine
4 (76/93)	31 M	55/162	Depression, tablet residue in stomach	71–77	16	Seated in car
5 (380/93)	26 M	81/180	Depression, early putrefaction, tablet residue in stomach	43–61	Nil	Prone
6 (117/95)	33 F	96/160	Depression, resuscitation attempted	22	20	Supine
7 (128/95)	49 F	65/160	Depression, alcoholism, tablet debris in stomach	24–32	20	Prone
8 (138/95)	37 M	90/173	Depression, alcoholism, hiatus hernia, gastric material in airways/oesophagus	28–38	25	Prone

*Using the best estimate of time of death based upon anamnestic data.
†Body position as found from information in police report and distribution of lividity; subsequently refrigerated supine.
‡Height in centimetre, weight in kilograms.

TABLE 2—*Concentration (μg/mL or μg/g) of the drugs temazepam, paracetamol, and propoxyphene in blood, fluid, tissue samples, and in gastric contents, mg/mL (case one; 379/93).*

Samples	pH	Temazepam	Paracetamol	Propoxyphene
Blood:				
Femoral vein	3.0	157	2.9	
IVC*	4.1	202	3.1	
Aorta	3.2	186	4.7	
Right atrium	2.9	165	3.6	
Left atrium	2.5	177	4.6	
Vitreous:	ND†	73	3.0	
Pericardial fluid	13.5	277	11.9	
Urine	1.4	351	9.0	
Bile	8.0	315	11.7	
Psoas muscle:				
Left	6.8	3.0	76	20.6
Right	6.2	3.1	88	26.3
Kidney:				
Left	6.9	5.4	300	26.5
Right	6.8	5.4	327	14.8
Liver:				
Left anterior margin	6.1	9.1	342	66.4
Left posterior margin	6.4	37.0	1410	66.1
Caudate lobe	6.1	6.3	228	82.4
Right anterior margin	6.2	6.9	180	65.1
Right posterior margin	5.9	6.5	186	50.5
Lung:				
Left upper lobe	6.8	4.6	78	40.3
Left lower lobe	6.7	10.1	542	87.8
Right upper lobe	6.9	6.4	151	37.4
Right lower lobe	6.9	4.7	134	36.1
Gastric contents (300 mL)	5.1	0.31	65	2.24

*IVC = inferior vena cava.
†ND = not detected.

methanol were mixed; flow rate 1.0 mL/min. Under these conditions, the retention times for nitrazepam, oxazepam, temazepam, nordiazepam, diazepam, and prazepam were 3.5, 3.8, 4.8, 6.6, 8.5, and 14.5 min, respectively. The calibration ranges of each compound were from 0.1 to 10 μg/mL.

For paracetamol analysis, extraction was done by the same procedure as the benzodiazepines. As internal standard, 2-acetoamidophenol (200 μg/mL) was used. The extracted residue was resuspended in 1 mL of methanol and 20 μL of this solution was injected into the HPLC system. The HPLC conditions were as follows: wavelength, 255 nm; mobile phase, 100 mL of acetonitrile, 50 mL of acetic acid diluted to 1000 mL with distilled water. Under these conditions, the retention times for paracetamol, and 2-acetoamidophenol (I.S.) were 3.3 and 6.4 min, respectively. The calibration range was from 2.0 to 200 μg/mL.

For dextropropoxyphene analysis, 10 μL of 1 mg/mL amitriptyline solution, as internal standard, and 2 mL of 0.5 N sodium hydroxide were added to the extraction sample. A 4-mL quantity of' heptane: isoamyl alcohol (98.5:1.5) was added and mixed for 15 min. The organic layer was separated and another 4 mL of heptane: isoamyl alcohol (98.5:1.5) was added to the extraction sample and rotated similarly. The combined organic layer was backextracted with 2 mL of 0.1 N sulfuric acid. The acid layer was made alkaline with 1 mL of 1.0M carbonate/bicarbonate buffer (pH 9.0) and extracted with 2 mL of toluene: isoamyl alcohol (85:15) by mixing for 15 min. The organic layer was separated and evaporated to dryness. The extract was resuspended in 100 μL of ethyl acetate and 1 μL of this solution was injected into the gas chromatograph connected to a mass spectrometer (GC-MS). The GC-MS conditions were as follows: instrument, Fisons GC 8000 series equipped with quadrapole mass analyser MD 800; column, HP-1 30-m by 0.25-mm I.D. with a 0.25 μm film thickness; temperature program, initial temperature, 100°C (1 min hold), ramped at 20°C/min to 300°C (3 min hold); injection port temperature, 250°C; carrier gas, helium (linear velocity 35 cm/s); ionization energy, 70 eV; ion source temperature, 200°C; transfer line temperature, 250°C. Under these conditions, the retention times for dextropropoxyphene and amitriptyline (I.S.) were 8.9 and 10.5 min, respectively. The calibration range was from 1.0 to 100 μg/mL.

For cyclizine, prothiedin, dipipanone, and paroxetine analysis, extraction was done by the same procedure as for dextropropoxyphene. Retention times were 9.0, 10.8, 11.4, and 11.8 min, respectively.

Peaks corresponding to drugs of interest were identified by a combination of their full mass spectra and retention times. Quantitation of both sample peaks and standard peaks was performed using the total ion current (TIC), except dextropropoxyphene, in which m/z 58 was monitored. The peak area ratio was normalized

TABLE 3—*Concentration (μg/mL or μg/g) of the drugs temazepam and diazepam, and their metabolites oxazepam and nordiazepam, in blood, fluid, tissue samples, and in gastric contents (case two; 315/94).*

Samples	pH	Temazepam	Oxazepam	Diazepam	Nordiazepam
Blood:					
Right femoral vein		1.3	<0.1	<0.1	<0.1
Left femoral vein		0.9	<0.1	<0.1	<0.1
IVC* (suprarenal)		2.4	<0.1	<0.1	<0.1
IVC* (infrarenal)		1.9	<0.1	<0.1	<0.1
Aorta		1.4	<0.1	<0.1	<0.1
Right atrium		3.0	<0.1	0.2	<0.1
Left atrium		1.9	ND†	<0.1	<0.1
Vitreous		<0.1	<0.1	ND†	ND†
Urine		0.1	<0.1	<0.1	<0.1
Psoas muscle:					
Left	6.2	0.9	<0.1	<0.1	<0.1
Right	5.5	0.8	<0.1	<0.1	<0.1
Kidney:					
Left	6.9	2.8	<0.1	0.2	0.2
Right	6.3	3.0	<0.1	0.2	0.2
Liver:					
Left anterior margin	6.4	8.0	<0.1	0.5	0.4
Left posterior margin	6.5	19.4	<0.1	1.7	0.5
Caudate lobe	6.2	5.9	0.1	0.3	0.3
Right anterior margin	6.0	4.2	<0.1	0.2	0.2
Right posterior margin	5.9	4.2	<0.1	0.2	0.4
Lung:					
Left upper lobe	7.1	2.5	<0.1	0.1	<0.1
Left lower lobe	7.0	3.6	<0.1	0.2	<0.1
Right upper lobe	7.1	2.7	<0.1	0.2	<0.1
Right lower lobe	7.2	2.7	<0.1	0.1	0.1
Gastric contents (50 mL)	6.4	300	ND†	6.7	ND†

*IVC = inferior vena cava.
†ND = not detected.

TABLE 4—*Concentration (μg/mL or μg/g) of the drugs nitrazepam, dipipanone, and cyclizine in blood, fluid, tissue samples, and in gastric contents (case three; 100/95).*

Samples	pH	Nitrazepam	Dipipanone	Cyclizine
Blood:				
Femoral vein		ND†	0.1	0.2
IVC*		ND†	0.1	0.2
Aorta		ND†	0.3	7.5
Right atrium		ND†	0.2	2
Left atrium		ND†	0.3	11.7
Vitreous		ND†	0.2	0.2
Pericardial fluid		ND†	1.8	4.2
Bile		0.45	0.2	7.3
Urine		ND†	ND†	ND†
Psoas muscle:				
Left	5.9	0.6	0.4	1.4
Right	6	0.2	0.1	0.4
Kidney:				
Left	6.7	ND†	0.3	4.6
Right	6.5	ND†	0.5	4.4
Spleen	5.7	0.48	0.5	6.3
Liver:				
Left anterior margin	6	ND†	34.8	744
Left posterior margin	6	0.1	34.4	759
Caudate lobe	6	0.4	12.9	482
Right anterior margin	6	ND†	23.1	876
Right posterior margin	6	ND†	19.7	960
Lung:				
Left upper lobe	6.2	0.4	4.4	122
Left lower lobe	6.3	0.6	2.4	190
Right upper lobe	6.3	0.3	3.8	108
Right lower lobe	6.4	0.7	3.2	153
Gastric contents (50 mL)	5	6	0.9	17.6
Duodenal contents	5.1	16.8	309	521

*IVC = inferior vena cava.
†ND = not detected.

TABLE 5—*Concentration (μg/mL or μg/g) of the drug amitriptyline and its metabolite nortriptyline in blood, fluid, tissue samples, and in gastric contents (cases four, five, and six; 76/93, 380/93, 117/95).*

Samples	Case four (76/93)			Case five (380/93)			Case six (117/95)		
	pH	Nor*	Ami†	pH	Nor*	Ami†	pH	Nor*	Ami†
Blood:									
Femoral vein		1.8	5.5		1.6	2.3		2.3	3.9
IVC‡		3.9	10.9		3.4	15.3			
IVC‡ (suprarenal)								3.6	17.8
IVC‡ (infrarenal)								3.0	13.0
Aorta					2.4	2.3		4.7	24.4
Right atrium					2.3	3.1		1.7	18.3
Left atrium								5.5	51.2
Vitreous					1.6	1.6		0.5	0.9
Pericardial fluid					5.0	5.3		2.7	5.0
Bile		4.7	17.0					14.0	66.7
Psoas muscle:									
Left				5.4	5.4	11.2	5.8	5.4	11.3
Right				6.2	4.8	7.5	5.8	5.7	11.2
Kidney:									
Left				6.9	5.7	12.6	6.2	21.2	10.5
Right				7.0	5.7	10.9	6.3	13.7	6.7
Spleen							5.9	8.9	19.8
Liver:									
Left anterior margin	5.8	21.2	66.2	5.8	18.3	19.7	5.7	12.8	45.2
Left posterior margin	5.9	23.2	122	5.8	16.6	25.2	5.5	12.2	98.5
Caudate lobe	5.8	20.3	73.9	6.1	19.5	19.9	5.6	14.9	57.5
Right anterior margin	5.8	27.4	99.3	5.9	15.8	16.8	5.6	12.4	52.3
Right posterior margin	5.8	26.3	85.4	5.9	16.5	17.9	5.6	12.6	44.8
Quadrate lobe	5.8	21.8	75.6						
Right lobe deep	5.9	23.0	69.8						
Right lobe deep	5.9	20.5	88.1						
Lung:									
Left upper lobe	6.2	47.2	85.9	6.8	15.1	18.3	5.5	23.4	59.7
Left lower lobe	6.3	35.5	52.2	6.7	29.4	26.7	5.9	21.3	82.3
Right upper lobe	6.2	59.8	117	6.6	22.8	20.3	5.6	24.1	52.9
Right lower lobe	6.1	41.3	68.8	6.5	23.6	21.9	5.8	27.5	37.5
Gastric contents (500, 50 mL)	6.6	4.9	314	4.4	5.3	84.1	4.7	1.5	882

*Nor = nortriptyline.
†Ami = amitriptyline.
‡IVC = inferior vena cava.

to the internal standard and the sample drug concentration calculated from the relevant linear calibration curves.

For amitriptyline and nortriptyline, extraction was done by the same procedure as for dextropropoxyphene with the exception that doxepin (100 μL; 400 μg/mL) was used as the internal standard, and the evaporated sample was resuspended in 100 μL of methanol. The HPLC system was injected with 20 μL of this extract. The HPLC conditions were as follows: wavelength, 254 nm; mobile phase, 300 mL of phosphate buffer, pH 3.0, 600 μL *n*-nonylamine, 200 to 250 mL acetonitrile. The calibration range was from 0 to 400 μg/mL. Retention times under these conditions were 4.48 min for amitriptyline, 3.70 min for nortriptyline, and 2.99 min for doxepin.

Results

All eight cases were suicidal poisonings, and the relevant case data are summarized in Table 1. In five of the eight cases, there was visible tablet residue in either the stomach or the duodenum. The analytical results together with tissue pH are summarized in Tables 2 to 7, inclusive. Table 5 combines three cases involving amitriptyline and in one of these (case 4), eight liver samples rather than the usual five were taken.

Discussion

It is well recognized that drug levels in blood may be unstable postmortem as a consequence of redistribution artefact (4), whereby drugs diffuse from reservoirs of high concentration, such as liver and lung into the blood. Similarly, drugs can be expected to diffuse from gastric residue into blood, liver, lung, and other nearby organs. Rats killed and then subjected to gastric instillation of amitriptyline showed drug diffusion into the liver from 5 h post dosage at room temperature (1). Over time, highest concentrations were reached in liver lobes adjacent to the stomach with significantly lower levels in the right lobe. Similar studies on human cadavers used amitriptyline, paracetamol, and lithium in quantities representing 10 tablets of each drug (2). After 48 h at room temperature, drug diffusion affected the left lobe of the liver, and to a lesser extent, the caudate lobe and variably the right lobe posteriorly (with the cadaver supine). In the lungs, the left was more affected than the right and the base more than the apex, although this was not always true. The present study confirms that similar changes occur in case material. It was found that the greatest accumulation of drug was in the left posterior margin of the liver (Tables 2 and 5, for benzodiazepines, paracetamol, and amitriptyline), and to some extent, the caudate lobe (Table 7, for propoxyphene and paroxetine). It was also apparent that drug concentrations were greater

TABLE 6—*Concentration (µg/mL or µg/g) of the drugs paracetamol, propoxyphene, prothiadin in blood, fluid, tissue samples, and in gastric contents (case seven; 128/95).*

Samples	pH	Propoxyphene	Prothiadin	Paracetamol
Blood:				
Femoral vein		0.8	5.1	44.3
IVC*		1.1	6.6	52.9
Aorta		0.7	5.1	52.9
Right atrium		1.1	4.9	68.4
Left atrium		0.9	4.6	46.6
Vitreous		ND†	ND†	11.5
Pericardial fluid		1.3		26.4
Bile				
Urine		17.7	6.6	358
Psoas muscle:				
Left	6.2	0.5	8.3	53.3
Right	6.2	0.5	6.2	32.1
Kidney:				
Left	6	0.8	43.2	552
Right	6	0.9	39.6	356
Spleen	5.9	0.7	42.4	81.5
Liver:				
Left anterior margin	6.1	1.2	103	114
Left posterior margin	6	1.9	155	133
Caudate lobe	6	2.3	135	102
Right anterior margin	6.1	1.2	182	115
Right posterior margin	6.1	1.9	217	80.2
Lung				
Left upper lobe	6.2	1	76.8	68
Left lower lobe	6	0.9	96.4	64.6
Right upper lobe	6.2	1.4	146	52.1
Right lower lobe	6.2	0.9	114	69.12
Gastric contents (150 mL)	4.9	5.6	82	3190

*IVC = inferior vena cava.
†ND = not detected.

TABLE 7—*Concentration (µg/mL or µg/g) of the drugs propoxyphene, paroxetine, and paracetamol in blood, fluid, tissue samples, and in gastric contents (case eight, 138/95).*

Samples	pH	Propoxyphene	Paroxetine	Paracetamol
Blood:				
Femoral vein		1.3	N.D.†	116
IVC* (suprarenal)		1.9	N.D.†	131
IVC* (infrarenal)		1.5	0.4	148
Aorta		N.D.†	N.D.†	131
Right atrium		1.7	N.D.†	128
Left atrium		5.2	0.6	161
Vitreous		0.5	0.2	
Pericardial fluid		3.5	N.D.†	139
Bile		8.9	2.4	217
Urine		7.3	N.D.†	217
Psoas muscle:				
Left	5.9	4.2	2.3	87.3
Right	6.1	3.1	0.9	103
Kidney:				
Left	6.4	5.7	2.4	217
Right	6.4	4.9	3.3	207
Spleen	6.4	7.1	2	173
Liver:				
Left anterior margin	6	7.6	8.2	388
Left posterior margin	6	8.4	11.6	298
Caudate lobe	5.9	9.4	17.4	265
Right anterior margin	6	7.8	14.1	265
Right posterior margin	6	7.4	12.6	240
Lung:				
Left upper lobe	6.5	9.7	17.4	139
Left lower lobe	6.5	8	17.2	104
Right upper lobe	6.5	9.8	16.1	242
Right lower lobe	6.4	8.4	18	198
Gastric contents 500 mL	5.3	11.7	16.1	1360

*IVC = inferior vena cava.
†ND = not detected.

in the left basal lobe of the lung compared with other regional sites within this organ (Tables 2, 3, and 4 for benzodiazepines and cyclizine).

It has been suggested that quantitation of liver tricyclic antidepressant levels is superior to blood levels in distinguishing between acute overdose and therapeutic ingestion (4) because of the problem of artefactual postmortem elevation of blood drug levels (5). This case series, a previous case report (3) and experimental studies (2) indicate that there may also be artefactual differences in drug concentration between liver samples. The liver blood drug ratio has been proposed as a measure of the acuteness of drug ingestion (6). However, the site of origin of the blood sample and the liver sample may have a profound influence on the ratio, as a result of postmortem redistribution. Before these approaches can be validated, there is a need to standardize sampling. The best liver sample for toxicological analysis is probably one from deep within the right lobe. A blood sample should be peripheral blood and a femoral or external iliac) venous sample obtained by needle puncture from a proximally clamped/ligated vessel is recommended. That blood samples for toxicological analysis should be obtained from peripheral vessels and not from the cardiac chambers or large vessels of the torso is well accepted in European practice (7).

Skeletal muscle has been advocated as a routine alternative specimen to blood for drug analysis (8), and some workers (9) have used the psoas muscle as the standard. An experimental study (2) suggested that psoas muscle may be suspect due to diffusion

artefact from gastric residue. The present case data lendsome support to this view (Table 4, Case 5 in Table 5). For this reason, skeletal muscle samples should be obtained from a limb.

An experimental model has previously illustrated postmortem diffusion of ethanol (10) and drugs (2) into pericardial fluid from gastric residue. In the present case data, this possibility is best evaluated by contrasting pericardial fluid drug levels with femoral blood and vitreous. Significantly higher drug levels in pericardial fluid may reflect gastric residue diffusion (e.g., Table 2 and propoxyphene in Tables 6 and 7). An alternative possibility is drug diffusion from lung reservoirs (5 either directly or via pulmonary vessels. Nevertheless, because pericardial fluid is a relatively clean specimen, it may be useful for qualitative screening. Diffusion of drug from the stomach into the bile was demonstrated in a cadaver model (2) and is not surprising in light of the extent of drug diffusion into the liver. It is not possible to evaluate this in case material, but it is unlikely to be of practical importance, if only because drug quantitation in bile is rarely the basis of opinion.

A study (10) of alcohol diffusion from the stomach suggested that diffusion in mortuo is markedly inhibited by refrigeration at 4°C and is otherwise directly proportional to time. This is in accord

with basic concepts of diffusion. The cases used in our study covered a wide range of postmortem interval with variable refrigeration time (Table 1) as would be expected in routine case work. There was also variability in body position before refrigeration with some subjects prone or seated, whereas experimental work has been confined to supine cadavers (2,10,11). Consequently, temperature, time, and body position are uncontrolled variables in this study. The results from this study suggest that these factors have a significant confounding influence, in that although a general trend of artefactual diffusion has been identified, the extent of drug accumulation within specific sites is variable.

It is apparent that drug diffusion in a cadaver is an important and complex phenomenon that can affect a wide range of organs as well as blood. Therefore, knowledge of sampling site and sampling technique is a prerequisite for an informed interpretation of analytical results. To facilitate this, pathologists should formalize their protocols for toxicological sampling at autopsy. We recommend that: (a) a blood sample should be obtained by needle puncture of the external iliac or femoral vein following proximal ligation/clamping at the start of the autopsy, (b) a liver sample should be obtained from deep within the right lobe, and (c) any lung sampling should be from the apex rather than the basal lobes.

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