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Death from Intravenously Administered Narcotics: A Study of 114 Cases

The attempt to explain the pathophysiology of deaths from intravenously administered narcotics has been hindered in the past because of the small number of fatal cases reported annually in most areas of the United States and relatively insensitive toxicological methods. A sudden and dramatic increase in deaths attributed to intravenously administered narcotics together with improved and sensitive methods for the identification and quantitation of the major metabolite of heroin in tissues have provided the forensic pathologist with the necessary tools to re-evaluate this type of fatality.

Before 1969 in Orange County, Calif., the number of deaths attributed to narcotics taken intravenously was less than five annually. From 1969 through 1972, 20 to 25 fatal cases were certified annually by the coroner. In 1973, 61 cases were recorded, a drastic increase. Thirty-six additional deaths due to heroin were certified in the first six months of 1974. Similar statistics indicating a significant increase of fatal cases have been reported from other areas of the United States [1-4].

Data will be presented on 114 cases investigated by the Orange County, Calif., sheriff-coroner's office over a 30-month period and certified as heroin-induced or heroin-related deaths. Additional data from seven cases involving addicts who died of causes other than intravenously administered narcotics will also be presented.

Toxicological Methods

In all cases, toxicological screens were performed for the detection of acidic, neutral, and basic drugs as well as for volatile compounds. For drugs other than morphine, ultraviolet spectrometry and thin-layer and gas chromatography were used. Morphine, the major metabolite of heroin, was determined by fluorescence spectrophotometry [5]. In each case, confirmation was by thin-layer chromatography or, when concentrations were low, by gas chromatography.

The absolute sensitivity of the fluorometric procedure is about 0.1 μg . The limiting concentration for the specimen is approximately 1 $\mu\text{g}/100\text{ ml}$ for blood, 1 $\mu\text{g}/100\text{ g}$ for brain and lung, and 10 $\mu\text{g}/100\text{ ml}$ for urine and bile.

The usual specimens analyzed consisted of 15 ml blood, 15 g brain, 15 g lung, 20 ml urine, and the total contents of the gall bladder. The urine and bile specimens were hydrolyzed before extraction; one tenth of each of these two samples was used for the fluorometric method and the remainder for confirmation. The other specimens were

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extracted without hydrolyzing. Many of the specimens were also analyzed by an independent laboratory with immunochemical techniques.

Anatomic Findings

Complete gross autopsies and microscopic examinations were performed on all cases. The pathological criteria are well documented in the literature and need not be repeated here [4,6-10]. The characteristic criteria of refractile crystalline granulomas in the lung and skin, increased lymphocytic infiltrates in the portal and periportal areas, and benign lymphoid hyperplasia (particularly about the porta hepatis) are not diagnostic.

The range of severity of tissue reactions is not constant. Cases of 20 to 30 years' addiction may show minimal tissue response, while younger addicts with a much shorter addiction period may produce more well-developed tissue criteria. Variations in the types and amounts of adulterants most likely account for these inconsistencies.

Only two cases presented crystalline granulomas of the brain, liver, spleen, and kidney. Since this is rare, the findings must represent a cardiopulmonary shunt to escape the alveolar capillary filter.

Discussion

For convenience, the drug concentrations that were measured and pertinent history for each case are provided in tabular form (Tables 1-9). In 40 cases morphine was the only drug found (Table 1). These cases represent 35% of the total and are composed of 33 males (83%) and 7 females (17%); the average age is 25 years. The blood concentrations in these cases range from none detected to 140 $\mu\text{g}/100$ ml. In general, higher values are most often found with cases of short time duration between injection and death, but this is not consistent. There appears to be very little relationship between concentrations and the duration of life after the injection of heroin.

Morphine in combination with ethanol was present in 39 cases (Table 2). This represents 34% of an all-male population with an average age of 28. The blood concentration in these cases range from none detected to 200 $\mu\text{g}/100$ ml.

In 25 cases morphine was found in combination with sedative/hypnotics (Table 3). This represents 22% of the series, predominantly male (84%), with an average age of 24. The range of blood morphine concentration is from none detected to 60 $\mu\text{g}/100$ ml.

In three cases, in addition to morphine, amphetamine was found (Table 4). In one case amphetamine was not in a detectable concentration in the blood or liver and may not have been significant; however, in the other two cases, both amphetamine and morphine concentrations were high and the cause of death was due to the effects of the drugs in combination.

In seven cases, morphine was found in combination with ethanol and other drugs (Table 5). The average age is 27, and the population is all male. This represents too few cases for a range of blood morphine concentrations to be meaningful.

In seven cases death in addicts was due to causes other than narcotics taken intravenously (Table 6). It is apparent even from these few cases that tissue concentrations in the tolerant subject may be very similar to those found in fatal cases.

In 23 cases the terminal episode was considered well documented by both coroner and police investigators (Table 7). In all cases death occurred in less than two hours after injection and the blood morphine concentration ranged from 2 to 200 $\mu\text{g}/100$ ml. In at least one case there was strong evidence that the decedent died shortly after using heroin for the first time. In this case (and in several other cases cited in Table 7) no morphine was detected in the bile or urine. Since morphine is excreted in the urine within 6 min after heroin injection [11], an explanation for this lack of morphine in the urine is a sudden and intense cardiovascular collapse with a lack of perfusion of liver

TABLE 1—Morphine concentrations found in fatal cases attributed to heroin use.

Age	Sex	Morphine, $\mu\text{g}/100$ ml or 100 g					Remarks
		Blood	Brain	Lung	Bile	Urine	
33	M	140	...	50	70	500	described by wife as intoxicated when he left house; found dead in street 1½ hours later
19	M	5	800	200	found dead in camper in park
18	M	6	...	30	1 400	+	body found in vacant lot
19	M	1	...	+	700	20	spoon and syringe found near body in residence
21	M	2	...	10	2 000	700	found dead in bathroom, "outfit" beside body; addicted at least 5 years
20	M	ND	...	6	800	200	came home intoxicated; found in bed next morning
27	M	1	1 300	700	wife found husband (an M.D.) ill after heroin injection. She gave him 0.4 mg Narcan®; he survived less than 2 h after the medication
37	F	4	...	10	300	NA	found seated in chair in hotel room by maid; recent needle mark; history of suicide attempts
32	M	ND	...	20	1 400	ND	loud and labored breathing when found; DOA at hospital less than 2 h later
22	M	ND	...	ND	800	400	history of drug abuse; found unconscious, responded to cold bath; put to bed and observed; lived 13 h
23	M	9	...	70	1 000	1 600	found sitting at desk; tourniquet on arm; outfit on desk
30	F	50	...	90	ND	ND	allegedly given injection by boyfriend; lived less than 30 min
25	M	20	...	20	300	NA	became comatose immediately after injection; friends gave him milk intravenously; died in less than 30 min
27	M	3	...	20	3 000	NA	found face down on bathroom floor with spoon in hand, syringe nearby; taken to hospital; lived 1 h after admission
27	M	20	...	60	1 600	600	snoring heavily when roommates left for work; dead when they returned 8 h later
25	M	ND	...	8	2 000	2 800	recent needle marks and numerous old marks
22	M	ND	...	4	1 400	1 400	injected during afternoon; again early evening, in coma 2 h; regained consciousness and went for walk; found later in street
22	M	20	...	30	80	ND	DOA at hospital; friends stated he injected heroin and collapsed immediately; bundle in pocket contained 28% heroin

TABLE 1—*Morphine concentrations found in fatal cases attributed to heroin use—Continued.*

Age	Sex	Morphine, $\mu\text{g}/100\text{ ml or }100\text{ g}$					Urine	Remarks
		Blood	Brain	Lung	Bile			
37	M	5	...	80	700	600	found in bathroom by police after anonymous phone call; balloon on body contained 14% heroin	
29	M	6	6	10	800	10	found in coma; DOA at hospital	
27	M	20	28	60	300	ND	friend found decedent and another man unresponsive in car; the other man survived after hospital treatment; estimated decedent lived less than 1 h after heroin injection	
21	M	10	60	30	30 000	12 000	decedent and friend "shot up" at friend's home; decedent returned home and went to sleep on couch; survived approximately 3 h	
23	M	20	41	80	2 000	400	recently released from drug rehabilitation center; visited with parents and went into bathroom; they heard strange sound and found him collapsed on floor; outfit found; lived less than 1 h	
22	M	7	4	3	250	1 300	lived in commune; two recent needle marks	
19	M	7	9	7	5 200	2 400	marital problems; left suicide note; "hype kit" found by body	
22	F	6	3	4	1 000	NA	body abandoned in vacant lot; fresh needle marks and "tracks"	
28	M	20	30	200	3 000	NA	history of heroin use since 1966; two prior overdoses with heroin; syringe and balloon found, the latter containing 2.7% heroin	
26	F	9	8	24	650	ND	fresh needle marks and tracks	
38	F	26	21	75	10 600	ND	long history of heroin use; tracks on both arms; survived less than 1/2 h after injection	
27	M	16	11	10	570	70	addicted since age 13; went into bathroom and was not checked for more than an hour; needle was still in vein	
21	M	110	60	420	2	+	addicted for more than 2 years; fresh needle marks	
18	M	61	45	90	NA	ND	found in bathroom; belt (tourniquet) still on arm; syringe and kit by body; survived less than 30 min	
21	F	1	5	21	150	NA	recent injection sites (2); no other indication of intravenous injection history; argument with husband; he left house and decedent was found 3 h later	
20	M	4	13	11	1 100	760	body found in vacant lot	
19	M	2	20	12	2 600	730	injected heroin at party about	

TABLE 1—Morphine concentrations found in fatal cases attributed to heroin use—Continued.

Age	Sex	Morphine, $\mu\text{g}/100$ ml or 100 g					Urine	Remarks
		Blood	Brain	Lung	Bile			
33	F	1	31	59	3 500	1 000	10:30 p.m.; DOA at medical center about 1½ h later	
22	M	+	3	7	1 800	940	addict since 1963; recently released from jail for possession; found on rear seat of auto found in bed by co-worker; outfit on bedside table	
25	M	13	8	22	2 100	960	injected; fell into deep sleep; died about 4 h later	
35	M	14	10	8	27	NA	found in his auto in isolated area; fresh needle marks; no outfit found	
22	F	2	2	2	200	NA	injected late afternoon; retired about midnight; probably survived about 12 h after injection	

NA = not available
 ND = none detected

TABLE 2—Deaths attributed to the combined effects of heroin and ethanol.

Age	Sex	Morphine, $\mu\text{g}/100$ ml or 100 g					Urine	Blood Ethanol, mg/100 ml	Remarks
		Blood	Brain	Lung	Bile				
28	M	2	...	10	300	50	200	found on floor of kitchen; fresh needle mark; tracks on both arms	
36	M	2	...	30	ND	ND	60	ex-addict; had recently begun using heroin again	
29	M	15	...	100	ND	ND	210	drinking in bar all afternoon; went to rest room and did not return; outfit found by body; heroin packets in wallet	
39	M	4	...	500	600	ND	110	collapsed in bathroom at home; outfit on floor	
21	M	ND	...	ND	3000	400	130	"snorted" heroin; retired for night; found dead next morning	
26	M	4	...	5	4800	ND	40	body found in vacant lot wrapped in blanket	
29	M	2	...	+	200	4	200	body found in ditch	
30	M	QNS	...	+	2300	NA	70	found dead in residence	
27	M	5	...	16	200	ND	220	drank beer during p.m., then shot up; drank more beer then became comatose; survived 2 h after injection	
22	M	200	...	400	20	NA	30	shot up in service station restroom; body and outfit found by attendant; survived less than 1 h after injection	
20	M	2	...	10	2200	20	30	found in back of van in parking lot; estimated to	

TABLE 2—Deaths attributed to the combined effects of heroin and ethanol—Continued.

Age	Sex	Morphine, $\mu\text{g}/100$ ml or 100 g					Blood Ethanol, mg/100 ml	Remarks
		Blood	Brain	Lung	Bile	Urine		
27	M	20	...	50	2300	80	200	have been dead at least 2 days found in residence; outfit near body
36	M	ND	...	3	1900	400	260	found in car; two recent needle marks
22	M	7	...	17	9000	15	110	found staggering after injection, later went into coma; survived approximately 2 h
41	M	3	...	20	NA	100	50	in coma about 14 h after injection
32	M	3	...	5	NA	100	160	friends brought decedent home in state of gross intoxication; wife found him dead 3 h later
26	M	20	27	30	40	50	150	shot up in truck behind service station; tourniquet near left arm; outfit on floor of truck; packet in pocket contained 23% heroin
42	M	3	10	7	100	100	80	found on floor of residence bathroom, outfit on floor; residue powder contained 4% heroin
29	M	9	+	70	30	ND	150	found at home; had been drinking heavily for 3 days before death; addicted to heroin for years
23	M	2	13	70	30	ND	80	according to witness, shot up, then collapsed; DOA hospital; survived less than 1 h
40	M	1	3	190	70	60	250	found in hotel room; syringe still in hand
24	M	ND	ND	5	920	120	120	drinking at party before heroin injection; found next morning
29	M	1	9	50	20	ND	160	found in bathroom of residence; outfit together with packets of heroin (4.6% heroin, 4.2% procaine)
28	M	+	+	30	170	50	130	found in parked car
29	M	100	40	80	NA	260	100	allegedly a weekend user; suspected by friends of being a police informer; collapsed immediately on injection and died in less than 30 min; outfit not found, but police suspect a "hot shot"

TABLE 2—Deaths attributed to the combined effects of heroin and ethanol—Continued.

Age	Sex	Morphine, $\mu\text{g}/100$ ml or 100 g					Urine	Blood Ethanol, mg/100 ml	Remarks
		Blood	Brain	Lung	Bile				
23	M	1	4	5	1700	NA	130	found staggering in hall; placed in bed and observed; he died approximately 5 h later	
23	M	6	12	17	490	90	100	according to witnesses, survived about 2 h after injection	
19	M	8	10	14	2100	660	150	found comatose in car; partially full bottle of vodka on seat	
23	M	1	2	1	12	16	80	survived about 4 h after injection	
25	M	43	39	+	ND	ND	180	drank 2 pints of bourbon with neighbors; went home, injected, and collapsed; survived about 20 min	
26	M	1	6	17	90	30	80	went home intoxicated; found by wife next morning, approximately 7 h later	
26	M	16	35	62	2400	950	100	survived less than 1 h after injection; outfit contained 1% heroin, 3% procaine	
41	M	26	20	42	NA	33	250	survived less than 3 h after injection	
35	M	41	34	17	77	ND	80	professional man, addicted for 15 years; had been on methadone program but discontinued about 4 months before death; found in residence bathroom; died in less than 30 min; packet of heroin in pocket determined to be 10%	
28	M	24	24	43	ND	NA	210	drinking all day with friends; found on bathroom floor	
22	M	3	5	21	1400	13	80	left in car in front of emergency room at hospital; driver fled	
24	M	1	12	8	1600	4	100	body found in vacant lot	
20	M	21	16	7	500	NA	170	body found in isolated area	
37	M	6	...	14	trace	NA	70	checked into motel with unidentified female; found dead 4 days later; drug pusher	

NA = not available

ND = none detected

QNS = quantity not sufficient

TABLE 3—*Death attributed to the combined effects of heroin and other drugs (excluding ethanol).*

Age	Sex	Morphine, $\mu\text{g}/100$ ml or 100 g					Other Drugs, mg/100 ml or 100 g			Remarks
		Blood	Brain	Lung	Bile	Urine	Drug	Blood	Liver	
21	M	60	...	3	900	150	secobarbital	0.3	1.3	recent and old needle marks
22	M	20	...	20	30	70	secobarbital	0.3	1.0	outfit found near body; rapid death
21	M	+	...	100	100	400	secobarbital	0.3	1.0	outfit found at scene; recent and old needle marks
20	M	ND	...	ND	1 900	100	secobarbital	ND	0.8	occasional user of heroin; observed after injection; survived 7 to 8 h
19	M	12	...	800	300	NA	phenobarbital	0.3	...	found in apartment; DOA at hospital; no needle marks found on body
21	M	30	...	140	7 500	600	secobarbital	ND	0.3	rapid death; outfit found on floor near body; cocaine metabolite found in urine
20	M	ND	...	20	1 400	700	amobarbital pentobarbital	0.1	0.4	came home intoxicated and was put to bed; snored loudly for about 5 h, then died
24	M	4	...	6	3 800	800	secobarbital	0.3	1.4	death attributed to aspiration of gastric contents; recent and old needle marks
27	M	2	...	1	800	40	amobarbital	0.4	1.0	found in truck in parking lot; fresh needle marks; outfit on seat
20	M	ND	...	ND	800	200	secobarbital	0.8	2.3	came home ill and went to bed; told family he had been on drugs all weekend; found dead next morning
23	M	20	...	20	400	300	secobarbital	0.1	0.7	found on floor of residence; outfit by body; recent and old needle marks
28	M	15	200	260	160	+	phenobarbital	1.9	...	injected heroin into webbing of hand; suffered reaction and told girl friend to call ambulance; died in less than 20 min
25	F	3	2	10	NA	9 600	chlordiazepoxide	0.1	...	body abandoned in vacant lot; member of motorcycle gang; no needle marks observed
24	M	3	7	9	2600	1 400	phenobarbital	0.3	...	wife said he shot up after argument; probably survived about 5 h
30	F	2	9	5	170	NA	diazepam	0.1	0.6	abandoned at hospital emergency room;

TABLE 3—Death attributed to the combined effects of heroin and other drugs excluding ethanol—Continued.

Age	Sex	Morphine, $\mu\text{g}/100$ ml or 100 g						Other Drugs, mg/100 ml or 100 g			Remarks	
		Blood	Brain	Lung	Bile	Urine	Drug	Blood	Liver			
25	M	10	14	40	1	100	NA	diazepam	0.1	...	given Narcan® and epinephrine; survived 12 h	
17	M	ND	2	...	NA	300	chlordiazepoxide diazepam	0.1 0.2	abandoned at hospital in coma; lived less than 1 h; recent and old needle marks	
25	F	22	NA	NA	50	NA	secobarbital/ amobarbital	0.7	1.5	1.5	collapsed after injection; died in less than 30 min	
28	M	ND	ND	ND	30	10	pentobarbital	0.3	0.5	0.5	found choking and gagging; DOA at hospital	
23	F	5	6	6	NA	+	chlordiazepoxide diazepam	0.5 0.1	found in coma; DOA at hospital	
26	M	3	14	10	720	330	phenobarbital	2.6	2.4	2.4	came home intoxicated; observed by parents for about 9 h at which time he quit snoring; ambulance called; DOA at hospital	
23	M	1	8	45	13	000	+	amobarbital/ secobarbital	0.4	1.2	1.2	addicted for 5 years; flew in from East; appeared "high"; went to bed at 6 p.m.; died approximately 8 to 9 h later
33	M	1	2	ND	NA	100	secobarbital propoxyphene	0.4 0.2	1.9 4.2	1.9	asked girl friend to pick him up at party due to illness; DOA at hospital an hour later; had been on "propoxyphene maintenance" program for addiction for 22 days; daily dosage 900 mg	
29	M	ND	8	18	140	NA	amobarbital/ secobarbital	0.4	0.9	0.9	body abandoned in vacant lot	
25	M	12	35	61	NA	540	diazepam	0.08	decedent and two friends shot up at 4:00 p.m.; all became unresponsive; one regained consciousness at 6:30 p.m. and called ambulance; decedent was dead; other two survived	

NA = not available
 ND = none detected

TABLE 4—Deaths in which morphine and stimulants were found in combination.

Age	Sex	Morphine, $\mu\text{g}/100\text{ ml or }100\text{ g}$				Amphetamine, $\mu\text{g}/100\text{ ml or }100\text{ g}$			Remarks	
		Blood	Brain	Lung	Bile	Urine	Blood	Liver		Urine
27	M	2	1000	300	100	600	...	decedent was "high" on amphetamines; injected heroin to "come down"; rapidly became comatose; DOA hospital
32	M	1	12	11	900	500	400	weekend user of heroin; more frequent user of amphetamine; became comatose soon after injecting heroin; substance in one packet analyzed: 4.7% heroin
19	M	3	6	11	1690	2800	3	118	...	decedent rapidly became comatose after heroin injection; a friend admitted giving him 8¢ worth of amphetamine intravenously, which we are told is about 250 mg

and kidney. In other cases, morphine was found in the bile but not detected in the urine. There is a much longer perfusion time for excretion in bile, and morphine would be expected to remain there for several hours. Therefore, the presence of morphine in the bile and its absence in the urine suggests a prior injection not related to the most recent injection. Conversely, presence in the urine and absence in the bile strongly suggests that this was the first injection for several days.

A summary of morphine concentrations found in fatal cases is provided in Table 8. The concentration range and average do not appear to provide as much information as does a median value. In those cases attributed to heroin only, a median of $6\ \mu\text{g}/100\text{ ml}$ blood is found. The median falls to $4\ \mu\text{g}/100\text{ ml}$ in those cases in which heroin was used in addition to ethanol and to $3\ \mu\text{g}/100\text{ ml}$ in those cases in which heroin was used in conjunction with sedative/hypnotics and other depressant drugs.

Rarely is the investigator able to find packets of heroin on the body of the decedents. In only ten cases reported here were these packets found (Table 9). According to Orange County crime laboratory analysts, confiscated heroin (found in packets at the scene or on the body) analyzed in their laboratory ordinarily runs at 4 to 8% in purity. The percentage of heroin in half these cases ranged from 1 to 4.7%. In the case in which 1% heroin was found the individual survived less than 1 h, and the morphine blood concentration was quite high. It is unknown whether multiple packets were injected. In the other five cases, the percentage of heroin ranged from 10 to 30%. In three of these cases observers reported a rapid death.

This study tends to confirm the opinion of other investigators that certification of death in cases of intravenously administered narcotics is dependent on a number of factors: adequate history, thorough scene investigation, the absence of other significant causes of death, and supportive toxicological findings.

Perhaps the higher blood concentrations are self-explanatory and most probably represent a degree of tolerance in the individual involved. The high concentration combined with a known short time duration between injection and demise would corroborate the probability of an overdose. In the 22 cases reported by Garriott and Stumer [6] in which death occurred within 3 h after the intravenous administration of

TABLE 5—Death attributed to the combined effects of heroin, ethanol, and other drugs in combination.

Age	Sex	Morphine, $\mu\text{g}/100\text{ ml}$ or 100 g					Other Drugs, $\text{mg}/100\text{ ml}$ or 100 g			Remarks	
		Blood	Brain	Lung	Bile	Urine	Drug	Blood	Liver		Alcohol
22	M	+	...	500	+	NA	diazepam	0.2	...	80	transient; fresh needle mark; no history; body found in vacant lot
18	M	24	16	32	8	NA	phenobarbital	0.5	3.1	140	body found in vacant lot
29	M	36	24	92	880	30	diazepam	0.006	...	90	body found in motel room
24	M	28	72	45	NA	NA	meprobamate	0.6	...	50	body found in alley
33	M	30	30	20	10	NA	imipramine	0.16	0.36	40	found in car; packet on body contained 30% heroin
27	M	26	56	NA	NA	NA	methadone	150	found in laundromat bathroom by customer; on methadone maintenance program; urinalysis showed trace methadone
39	M	15	22	23	60	16	diazepam	0.15	0.5	90	truck driver; history of "chipping"

NA = not available

TABLE 6—Deaths in addicts from causes other than drug use.

Age	Sex	Morphine, $\mu\text{g}/100$ ml or 100 g							Other Findings	Cause of Death
		Blood	Brain	Lung	Bile	Urine				
30	M	1	...	20	400	3000	homicide—gunshot stab victim; survived 16 h in hospital	
39	M	7	...	30	1400	+	traffic fatality; on methadone	
33	M	ND	...	4	100	NA	blood alcohol: 60 mg/100 ml	blood alcohol: 60 mg/100 ml	fatally shot during robbery	
26	M	5	7	20	300	300	meprobamate: blood, 1.9 mg/100 ml	meprobamate: blood, 1.9 mg/100 ml		
25	M	ND	...	ND	700	NA	liver, 1.6 mg/100 g	liver, 1.6 mg/100 g	death due to injuries sustained in fall during police chase; survived 28 h in hospital	
40	M	1	9	290	3800	1800	diazepam: blood, 0.15 mg/100 ml	diazepam: blood, 0.15 mg/100 ml	suicide—gunshot	
63	M	10	27	62	1300	NA	liver, 0.5 mg/100 g	liver, 0.5 mg/100 g	coronary occlusion; addict for more than 40 years	

NA = not available

ND = none detected

TABLE 7—Fatalities from heroin with a short survival time after injection.

Age	Sex	Morphine, $\mu\text{g}/100$ ml or 100 g					Survival Time ^a
		Blood	Brain	Lung	Bile	Urine	
35	M	41	34	17	17	77	>30 min
29	M	100	...	40	80	NA	>30 min
25	F	22	NA	NA	50	NA	>30 min
39	M	4	...	500	600	ND	>30 min
28	M	15	200	260	160	+	>30 min
30	F	50	...	90	ND	ND	>30 min
25	M	43	39	+	ND	ND	>30 min
25	M	20	...	20	300	NA	>30 min
29	M	15	...	100	ND	ND	>30 min
18	M	61	45	90	NA	ND	>30 min
22	M	200	...	400	20	NA	>1 h
21	M	30	...	140	7500	600	>1 h
23	M	2	13	70	30	ND	>1 h
26	M	20	27	30	40	50	>1 h
39	M	15	22	23	60	16	>1 h
27	M	20	28	60	300	ND	>1 h
26	M	16	35	62	2400	100	>1 h
23	M	6	12	17	490	100	>2 h
22	M	20	...	20	30	70	>2 h
23	M	9	...	70	1000	1600	>2 h
19	M	2	20	12	2600	730	>2 h
27	M	16	11	10	570	70	>2 h
27	M	5	...	16	200	ND	>2 h

NA = not available

ND = none detected

^a Based on history

heroin, the concentration of free morphine in the blood was quite high (10 to 93 $\mu\text{g}/100$ ml).

In addition to tissue concentrations in fatal cases reported by Garriott and Sturner, studies have been published by Robinson and Williams [12] and by Johnson et al [13]. In the latter report, body distribution studies in eight addicts revealed a free morphine blood concentration ranging from 0 to 100 $\mu\text{g}/100$ ml. In the former study, 22 cases of sudden death due to intravenously administered narcotics were reported in which the range of free morphine found in the blood was 0 to 100 $\mu\text{g}/100$ ml. The cause of death in some of those cases was attributed to causes other than the narcotics.

High blood concentrations of morphine supported by evidence of paraphernalia on or near the body and packet content of higher than usual street value should justify certification of death due to intravenously administered narcotics. Moreover, in those cases in which blood concentrations are low but combined with alcohol or other drugs, death may be due to the combined effects.

This, however, does not explain those cases with low or nondetectable blood concentrations in which alcohol or other drugs are not found. These cases have caused speculation. Allergic response has been proposed to explain this phenomenon, but there is no apparent tissue eosinophilia to support this theory [8]. Adulterants such as quinine have been alleged to cause cardiac irregularities which may be a mechanism for sudden deaths in addicts [14]. Recently, Brashear et al [15] have suggested that histamine released after heroin use may be a contributing factor. In general, all these discussions center on the idea of an acute reaction of the body produced by a foreign substance.

The human body responds in some fashion to all foreign materials introduced into it. One of the major factors in the control of these foreign substances is the immune

TABLE 8—Summary of morphine concentrations in fatal cases (in $\mu\text{g}/100\text{ ml}$ or 100 g).

	Death Attributed to Heroin Only			Death Attributed to Heroin and Alcohol in Combination			Death Attributed to Heroin and Other Drugs Excluding Alcohol		
	Average	Median	Range	Average	Median	Range	Average	Median	Range
Blood	16.4	6	0 to 140	37.0	4	0 to 200	9.0	3	0 to 60
Brain	19.1	11	0 to 60	16.0	11	0 to 40	23.6	8	0 to 200
Lung	44.9	20	0 to 420	54.6	17	0 to 500	68.4	10	0 to 800
Bile	2192.8	1000	0 to 30 000	1045	200	0 to 9000	1795	760	0 to 13 000

TABLE 9—Comparison of tissue concentrations of morphine in cases in which heroin packets were found at the scene.

Morphine, $\mu\text{g}/100\text{ ml}$ or 100 g					Heroin, %	Remarks
Blood	Brain	Lung	Bile	Urine		
20	NA	30	80	ND	28	only morphine found in tissue; immediate collapse after injection
20	27	30	40	50	23	rapid death; blood alcohol, 150 mg/100 ml
3	10	7	100	100	4	blood alcohol, 80 mg/100 ml
5	NA	80	700	600	14	only morphine found in tissue
20	30	200	3000	NA	2.7	only morphine found in tissue
1	9	50	20	ND	4.6	blood alcohol, 160 mg/100 ml
41	34	17	77	ND	10	blood alcohol, 80%
1	12	11	900	500	4.7	amphetamine in urine
30	30	20	10	NA	30	blood alcohol, 40 mg/100 ml; imipramine in therapeutic concentration
16	35	62	2400	950	1	lived less than 1 h after injection; blood alcohol, 100 mg/100 ml

NA = not available

ND = none detected

mechanism. Either an overreaction or an insufficient reaction of this immune mechanism may prove fatal and certainly produces a host of disease processes in man, with new disease entities being added daily to the literature.

It is our theory that a relatively short-acting immunoglobulin may be specifically produced toward heroin or adulterants. It would have to be a relatively short-acting component because of the time duration involved in most cases of this type. As long as there is a relatively constant intake of heroin or adulterants this specific globulin would be produced. With abstinence from heroin or adulterants this specific globulin would continue to be produced for several months, increasing the amount of available circulating globulin due to the lack of a specific binding substance. The re-introduction of heroin or adulterants could produce a massive, perhaps fatal, tissue reaction.

Summary

A careful study of more than 100 fatal cases due to intravenously administered narcotics provides further evidence of the complexity involved in the certification of death. The wide range of blood morphine concentrations found in these cases indicates that tissue concentrations alone will not always provide the necessary information. High concentrations of morphine, the major metabolite of heroin, in blood and other tissues may be consistent with overdose. But in those cases involving very low concentrations at the time of death, other criteria must be considered.

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