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Some Observations Concerning Blood Morphine Concentrations in Narcotic Addicts

Progress in the development of analytical methods has enabled the forensic toxicologist to detect and quantitate morphine in blood from the deceased narcotic addict. Techniques such as gas chromatography [*1,2*], radioimmunoassay [*3–5*], and spectrophotofluorometry [*6,7*] are adequate in terms of sensitivity and specificity. A comparison of three methods has also appeared [*8*].

Interpretation of the quantitative data is as significant as the development of adequate methods, and several workers [*2,8–13*] have presented their findings. Some of these data are summarized in Table 1. In addition to reporting blood morphine concentrations,

TABLE 1—*Summary of blood morphine concentrations in narcotic addicts.*

Reference	Cases,[a] *n*	Range, μg/dl	Method
2	8	33–40	gas chromatography
9	22	3–93	fluorometry
10	66	18–200	radioimmunoassay
11	22	10–100	ultraviolet spectrophotometry

[a]Refers to the total number of cases studied. In some cases the blood morphine concentration was negative or not reported.

Garriott and Sturner [*9*] correlated the survival time after the last injection with the concentration of free morphine in the blood. In 22 cases they found that if the survival time were short (less than 3 h) the blood morphine concentration ranged from 10 to 93 μg/dl. An intermediate survival time (3 to 24 h) resulted in a blood morphine concentration of 3 to 10 μg/dl.

All of the above workers dealt mostly with fatal episodes of heroin injections. This discussion explores the blood morphine concentration in narcotic addiction deaths further and adds to these data what must be considered nonlethal blood morphine concentrations. The source of the latter samples was homicide victims who were narcotic addicts, and these blood morphine concentrations are compared with individuals who died from narcotic addiction. In addition, the presence and significance of other drugs detected in narcotic addiction deaths are discussed.

Sample Selection and Methods

All blood samples were obtained from the heart at autopsy. Morphine and quinine were

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identified in appropriate biological samples by spectrophotofluorometry [7] and thin-layer chromatography [14]. Morphine was quantitated in blood (nonhydrolyzed) by spectrophotofluorometry [7], and quinine by ultraviolet spectrophotometry [15]. Diazepam (Valium®) was quantitated in blood by spectrophotofluorometry [16] and ethanol by automated headspace gas chromatography [17] employing the Perkin Elmer Multifract F-40 gas chromatograph. As in the case of a recent publication [13] no attempt was made to evaluate the pathological findings.

Results and Discussion

Table 2 summarizes the comparison of blood morphine concentrations in narcotic addiction and homicide deaths. For convenience, the data are grouped into ranges of blood morphine concentrations.

TABLE 2—*Comparison of blood morphine concentrations in narcotic addiction and homicide deaths.*

Morphine, μg/dl	Narcotic Addiction Deaths	Homicide Deaths
Negative	3	3
1-9	7	15
10-19	5	8
20-29	2	1
30-49	2	0
50-99	1	0
100-199	2	0
200-299	1	0
Total	23	27

A qualitative evaluation of these data indicates that the frequency of detecting morphine in the blood of the homicide victim (88% of the cases) is about the same as that of the narcotic addiction death (83% of the cases). A reasonable conclusion from this observation is that even if morphine is detected in the blood in a narcotic addiction death, this qualitative information is insufficient to determine if this were an acute overdose episode.

For this reason one must attempt to evaluate the quantitative data. None of the homicide victims had a blood morphine concentration greater than 25 μg/dl. One concludes from this observation that for most narcotic addicts this is probably a nonlethal concentration. This is in reasonable agreement with the conclusion of Felby et al [18] that the minimal lethal blood morphine concentration in man is 20 μg/dl.

The interpretative problem one has, however, is that most of the blood morphine concentrations in narcotic addiction deaths fall within this same range (less than 25 μg/dl). Certainly it would be misleading to apply the word "overdose" to these deaths based solely on the blood morphine concentration. Factors such as tolerance and the time interval between the last injection and death certainly affect the postmortem blood morphine concentration, but in only a few instances did this value exceed 25 μg/dl. The assumption that these particular individuals died rapidly after the fatal injection is apparently contrary to the pattern of death of most narcotic addicts.

In a few instances adequate history is available to substantiate the assumption of a rapid death subsequent to a heroin injection. In one instance (blood morphine concentration, 51 μg/dl), a person who was incarcerated was given heroin by a visitor, and death occurred less than 3½ h after the injection. In another instance a person who had bail posted by an individual known to be involved in drugs was found dead the next day with a syringe still in his arm. The blood morphine concentration in this instance was 230 μg/dl.

The blood morphine concentration of a person who had an argument with his girl friend and was seen going to bed, but was found dead the next morning with a syringe in his hand, was 112 μg/dl.

The data illustrated in Table 2 were obtained during the latter part of 1974. The determination of morphine in the blood of homicide victims was discontinued, but quantitative analysis of the blood in narcotic addiction deaths is performed in every instance where morphine is implicated.

In 1975 a record 341 narcotic addiction deaths were recorded in Wayne County. Factors such as prolonged hospitalization, advanced body decomposition, and narcotic deaths not involving heroin precluded a meaningful blood morphine analysis in every case, but this test was performed in 268 of these deaths. The blood morphine concentrations that were obtained are shown in Table 3.

TABLE 3—*Blood morphine concentrations in narcotic addiction deaths, 1975.*

Morphine, μg/dl	Cases, *n*
Negative	28
1-9	97
10-19	76
20-29	34
30-49	20
50-99	12
100-199	1
Total	268

The results obtained from these cases are not very different from those previously discussed. In only 10.4% of the cases was morphine not detected in the blood, and in 87.3% of the cases the concentration was less than 30 μg/dl. Employing the results previously obtained with homicide victims as a guideline, one must conclude that in the great majority of cases death was not a result of a toxic quantity of morphine in the blood. Lack of tolerance is a factor which is often argued, but it is unlikely that nearly 9 of 10 deaths in this county occur for this reason.

The months of July and August, 1975, deserve special consideration. During this two-month period, 100 narcotic addiction deaths occurred, and morphine was detected in 86 of these cases. Blood morphine analyses were performed in 81 instances, and in 6 cases morphine was not detected. In only 10 individuals was the concentration greater than 30 μg/dl, the highest level being 93 μg/dl. An unusually strong heroin preparation being sold on the streets was highly suspect during this period, but the blood morphine concentrations obtained postmortem would appear to discredit such a possibility. In addition, chemical analyses by the Detroit Police Laboratory of material confiscated during this time period revealed nothing extraordinary, either in terms of heroin content or diluents.

In 1976 the number of narcotic deaths in Wayne County decreased to 203, and morphine was detected in 171 of these deaths. These data do not warrant special tabulation; however, the trend was consistent with that of the previous year. In 9.4% of the cases morphine was not detected in blood from the deceased, and in 83.6% of the cases the concentration was less than 30 μg/dl.

The presence and contribution of other drugs to narcotic addiction deaths have not been discussed up to this point. The previously discussed data represent all deaths involving morphine, regardless of the presence or absence of other drugs. The following data represent cases where either morphine or morphine and one or two other drugs were detected in the blood of the deceased narcotic addict. It should be emphasized that these are the

same narcotic addiction death cases previously discussed, but they are now categorized by the presence of other drugs.

Deaths in which only morphine was detected are detailed in Table 4. In nearly 79%

TABLE 4—*Blood morphine concentrations in deaths involving only morphine.*

Morphine, μg/dl	Cases, *n*
1-9	26
10-19	15
20-29	7
30-49	5
50-99	6
100+	2
Total	61

of these cases the morphine concentration was less than 30 μg/dl, which is considered a nontoxic level for most individuals [*18*]. The cases in which the blood morphine concentration was greater than 100 μg/dl could represent acute overdoses of the drug, since this concentration is five to six times that which is most often found. This, however, would account for only approximately 3% of these deaths. Even if one assumes that an overdose occurred in all cases where the morphine concentration was greater than 30 μg/dl, only 21% of these deaths would be involved.

Since cases in which only morphine is present are the least complicated to interpret, it may be contributory to speculate further on these cases. Certainly the frequency of injection and the time interval between the last injection and death are two important factors affecting the postmortem blood morphine concentration. Added to these is the biphasic half-life of morphine [*4*]. In spite of these factors, however, it is conceivable that an injection of heroin can produce respiratory depression and coma, in which case the blood morphine concentration would continue to decrease until death and the postmortem concentration would most likely be in an intermediate range (50 to 80 μg/dl). In a few instances "difficulty in breathing" has been a symptom described by individuals who have witnessed fatal episodes of heroin injections. Therefore, acute respiratory depression is a probable mechanism of death for some narcotic addicts.

Table 5 summarizes 69 cases in which only ethanol was found in combination with morphine. Although the mean concentration of ethanol is fairly constant throughout the range of blood morphine concentrations, the maximum value of 420 mg/dl at a blood morphine range of 1 to 9 μg/dl is significantly higher than any value observed at higher blood morphine concentrations. In this particular group three individuals had a blood ethanol concentration greater than 300 mg/dl, and a good possibility is that these persons died from

TABLE 5—*Deaths involving morphine and ethanol.*

		Ethanol, mg/dl	
Morphine, μg/dl	Cases, *n*	Range	Mean
1-9	35	20-420	140
10-19	15	20-220	150
20-29	8	40-220	100
30-49	6	50-210	140
50-99	5	50-290	130
Total	69	...	...

the combined central nervous system (CNS) effects of ethanol and morphine. As the blood morphine concentration increases the quantity of ethanol that can be tolerated decreases, and this factor may be involved in deaths involving the higher blood morphine concentrations and ethanol.

Quinine is the adulterant most commonly employed in the Detroit area, and the cases involving only morphine and quinine are shown in Table 6. The cardiovascular effects of

TABLE 6—*Deaths involving morphine and quinine.*

		Quinine, μg/dl	
Morphine, μg/dl	Cases, *n*	Range	Mean
1-9	18	1.1-9.0	2.9
10-19	22	1.0-6.9	4.0
20-29	22	1.2-9.9	3.1
30-49	10	0.4-5.6	3.6
50-99	2	1.8-8.5	5.2
Total	74	...	...

quinine have been demonstrated [*19*] and it is impossible to exclude this mechanism in any narcotic death involving morphine and quinine. If one evaluates the quinine toxicity in these cases based on the blood concentration, however, only in a few instances is the quinine concentration somewhat elevated. Therapeutic concentrations are considered to be 3 to 5 μg/ml and lethal concentrations, greater than 30 μg/ml [*20*]. Although the blood concentration of an oral administration is not directly comparable to that resulting from an intravenous injection of drug [*21*], in no instance did the blood quinine concentration exceed 10 μg/ml. Perhaps the most meaningful observation from these data is that higher blood concentrations of quinine were consistently obtained at the higher blood morphine concentrations, probably indicating an acute episode of heroin exposure and death resulting from the combined effects of these drugs.

Table 7 summarizes cases involving morphine, quinine, and ethanol. The trend ob-

TABLE 7—*Deaths involving morphine, ethanol, and quinine.*

		Ethanol, mg/dl		Quinine, μg/ml	
Morphine, μg/dl	Cases, *n*	Range	Mean	Range	Mean
1-9	47	30-500	180	0.5-7.7	2.5
10-19	35	10-360	130	1.0-5.9	3.7
20-29	13	40-380	140	1.3-11	3.4
30-49	11	40-220	110	1.8-8.6	5.0
50-99	6	30-180	95	1.2-7.3	4.8
Total	112	...	...	...	...

served with the combination of these three substances parallels that which was obtained when only ethanol and quinine were present. At increasing morphine concentrations the ethanol values decreased slightly, and the quinine concentrations increased. Although some deaths probably resulted from the combined effects of morphine and ethanol, it is unlikely that a lethal level of quinine was involved in any of these cases. Pharmacologically, quinine is not a CNS depressant, so its effect is not additive to that of morphine and ethanol. For this reason the contribution of ethanol to these deaths is probably more significant than that of the quinine.

Cases involving morphine and diazepam (Valium) are shown in Table 8. It should be mentioned that the fluorometric method employed to quantitate diazepam measures total

TABLE 8—*Deaths involving morphine and diazepam* (n = *12*).

Morphine, μg/dl	Diazepam, μg/ml
2	1.1
3	4.8
5	0.6
7	3.7
9	3.2
9	2.9
10	1.2
10	3.6
12	3.0
18	1.5
26	7.4
31	4.3

benzodiazepine, that is, diazepam plus its major metabolites. Since the metabolites are biologically active, however, this is justified and toxicologically more meaningful than measuring only the parent drug.

The contribution of diazepam to any drug death is always a debatable point, but by most criteria the blood concentrations obtained in these narcotic addiction death cases would be considered elevated. It has been reported [*22*] that after the administration of 40 mg of diazepam per day the maximum blood concentration to be expected is 2.0 μg/ml. Only four of the narcotic addicts had blood concentrations less than this value. After 5 or 10 mg of diazepam, the blood concentrations range from 0.2 to 0.5 μg/ml. None of the narcotic addicts had a blood concentration less than 0.5 μg/ml. Some addicts apparently abuse diazepam as well as the narcotic, and the combined depressant effects of these drugs should be considered when evaluating a death involving these drugs.

Summary

Blood samples from deceased narcotic addicts were analyzed for morphine, and the results from persons who died from narcotic addiction were compared with those from homicide victims. In most instances morphine was detectable in both types of death, and usually the values obtained were less than 30 μg/dl. Narcotic addiction deaths involving only morphine, or morphine plus a combination of ethanol, quinine, or diazepam (Valium), were also evaluated. In some cases high quantities of ethanol were present, and death could be attributed to the combined CNS depressant effects of morphine and ethanol. The quinine levels would not normally be considered toxic, however, and it could not be ascertained that the quantity of this drug present contributed to death. Diazepam was present in elevated concentrations, and its depressant effect may have been a factor in some narcotic addiction deaths.

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