Analysis of Results of Toxicological Examinations Performed by Coroners' or Medical Examiners' Laboratories in 2000 Drug-Involved Deaths in Nine Major U. S. Cities

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Data were collected on 2000 deaths in which psychoactive drugs were involved. The data were submitted by medical examiners or coroners in nine U. S. cities from their case files. The 2000 cases comprise a representative sample from each of these cities of deaths from psychoactive drugs between 1972 through 1974. This report details inter-city differences in methods and practices of the toxicological examination as well as in the type and numbers of drugs reported. Even when the same analytical method was used in various cities, there were differences in extraction solvent and extraction pH. Of the 3909 drugs detected, 2945 were quantitated; the number of drugs quantitatively measured per case studied ranged from a low of 0.82 for New York to a high of 2.20 for Washington, D. C. The number of different drugs quantitatively measured varied from 16 for New York to 30 for San Francisco; however, New York qualitatively assayed for the presence of a total of 25 drugs. The number and type of drugs found per case varied. Methadone, for example, was found in 60% of the cases reported by New York and in 49% of the cases reported by New York, D. C., but in only about 10% of cases reported by Philadelphia, Dallas, Miami, and San Francisco, and in less than 1% of Los Angeles and Cleveland cases; it was not reported by Chicago. Phenmetrazine-caused deaths were reported only by Dallas (one case) and Washington, D. C. (29 cases). From the data as a whole, information is presented for 33 drugs as to the concentration in physiological tissues and fluids. Analysis of single psychoactive drug cases and single-drug-plus-ethanol cases shows that, in the presence of ethanol, the toxic blood concentration of imipramine, amitriptyline, meprobamate, thioridazine, morphine, propoxyphene, methaqualone, and all barbiturates was decreased by an average of 50%.

Our research group, under the auspices of the National Institute on Drug Abuse, has collected extensive data on 2000 psychoactive drug-involved deaths from nine major United States cities. The U.C.I. Reporting Form for Drug-Involved Deaths, developed by this group (7), was used to obtain the data (2). It consists of about 135 items of inquiry in such areas as biographic, demographic, on-site investigation, toxicological examination, postmortem examination, treatment before death, and suicide.

This paper deals solely with the toxicological examinations as reported by the cities on the U.C.I. Reporting Form for Drug-Involved Deaths. Analysis of these data clearly demonstrates large variations among cities in procedures, methods, test results, and drugs tested for.

Methods of Data Collection

A collaborative working relationship was first established with the medical examiner or coroner in each of the nine cities and with his associated toxicological laboratory. “Psychoactive drug-involved death” was defined as any death referred to a medical examiner or coroner in which psychoactive pharmacological agents were considered to be related to or involved in the fatal event. Instances in which ethanol was the sole chemical agent involved in the death were not acceptable for this study, but instances in which ethanol in combination with other psychoactive chemical substances was involved with the death were acceptable.

The National Institute on Drug Abuse limited this study to the collection of psychosocial and biomedical data on 2000 cases from nine cities (one laboratory per city), which included such large cities as New York, Chicago, Los Angeles, and Philadelphia, a well as the smaller cities of Cleveland, Dallas, Miami, San Francisco, and Washington, D. C.

Based on 1970 census figures, quotas were set for each urban jurisdiction on the basis of the ratio between its population and that of the others. Thus, if City A had twice the population of City B, City A would be expected to contribute about twice as many cases. Smaller cities were assigned smaller quotas, but slightly more than their share so that there would be enough data for valid statistical analysis. In the opinion of each medical examiner or coroner, the cases reported are representative of all such cases occurring in each city during 1972–1974. We assumed that, when cases were gathered at different time intervals from different cities within the total time-frame, month-to-month biases arising from seasonal influences were negligible or nonexistent. This assumption was considered warranted by all participating data-collection centers.

All cases selected for this series had to be, in the opinion of the referring medical examiner or coroner,
a psychoactive drug-involved death in which the drug—alone, in combination with another psychoactive drug or alcohol, or in combination with a pre-existing medical disease or an external circumstance (auto accident or gunshot)—led to a fatality. Each data-collection center was also advised to select consecutive cases on which all data necessary to complete the forms were available.

These data on 2000 psychoactive drug-related deaths are most likely not representative of the entire United States during 1972–1974, but probably give a fair picture of urban America, and certainly allow a meaningful and accurate analysis of regional variations in characteristics of the toxicological examination.

Results

The toxicological laboratories of these cities tested for a total of 3909 drugs (1.95 per case). Of these, 2945 were quantitated, traces or no drugs were found in 159, and 805 drugs were simply reported as being present. Table 1 lists the type of result reported by the laboratory of each city. Definite patterns of toxicological examination clearly emerge. Washington, D. C., quantitated all of the drugs detected. In contrast, New York quantitated 33.8%, reported a qualitative “present” for 59.5%, and found a trace or no drug for 6.7% of the drugs that were tested for. The other cities lay somewhere between these two extremes. Qualitative presence was reported by Miami for 17%, by Philadelphia for 24.4%, and by Cleveland for 26% of their tested drugs. Chicago, Dallas, Los Angeles, and Washington reported a qualitative presence for less than 2% of their drugs. The same four cities reporting high percentages of drugs as qualitatively present also reported higher percentages of zero or traces found, as follows: Miami, 4.2%; Cleveland, 4.4%; New York, 6.7%; and Philadelphia, 14.2%. The other five cities reported less than 2% zero or traces.

Another way to view these differences is to look at the number of quantitated drugs per case studied. By this analysis, New York and Philadelphia were clearly different from the other seven laboratories in the number of drugs quantitated per case: 0.82 and 1.06, respectively. A middle group of cities reported quantitation of drugs per case as follows: Miami, 1.43; Cleveland, 1.44; Chicago, 1.58; San Francisco, 1.72; and Los Angeles, 1.76 drugs per case, while Dallas and Washington quantitated 2.14 and 2.20 drugs per case, respectively.

Chicago, Los Angeles, San Francisco, Dallas, and Washington quantitated in their toxicological laboratories practically all the drugs found, and the number of drugs reported per case nearly equals the number of drugs quantitated per case. On the other hand, more drugs were reported per case than were quantitated by Cleveland (1.14-fold), Miami (1.27-fold), and Philadelphia (1.63-fold). New York reported per case three times as many drugs as they quantitated.

Alcohol (ethanol), diazepam, morphine, barbiturates (phenobarbital, amobarbital, pentobarbital, and secobarbital), and propoxyphene comprised 68% of the total drugs quantitated by the nine cities, as shown in Table 2. The percentages of the total comprised by these drugs ranged from a low of 38.2% for Washington, D. C., to a high of 85.2% for Los Angeles. These same drugs accounted for 89% of the qualitative assays performed by New York. Miami’s low percentage for these drugs (47.7%) was due to a relatively large number of glutethimide, ethchlorvynol, and methaqualone assays. New York showed an overwhelming proportion of methadone assays, more than three times the proportion of the other cities combined. Philadelphia showed a relatively high number of amphetamine, methamphetamine, and methadone assays, and Washington a large number of methadone, methamphetamine, qui-
nine, and phenmetrazine assays. Among all the cities, only Washington (29 cases) and Dallas (one case) reported phenmetrazine cases.

The number of different drugs quantitated by the cities varied as well, from a low of 16 drugs for New York to a high of 30 for San Francisco. New York, however, qualitatively assayed for 25 drugs.

Table 3 summarizes the laboratory results for five drugs, listing in each cell the number of tests performed quantitatively or qualitatively, the percentage of the total drugs reported, and percentage of cases positive for the drug for each city. There were large differences among cities. In New York and Washington, methadone represented 24.5% and 22.1%, respectively, of all drugs tested for and was found in 60% of the cases for New York and 49% of the cases for Washington—very high percentages indeed. In contrast, methadone was found in much smaller proportions in Philadelphia, Dallas, Miami, and San Francisco, in less than 1% of cases reported by Los Angeles and Cleveland, and was not reported at all by Chicago.

Morphine was found in significant numbers by all cities, ranging from a low of 3.6% of total drugs (reported by Miami) to a high of 27.2% of total drugs (reported by Los Angeles). Morphine was found in 48.3% and 43.1% of the cases reported by Los Angeles and Chicago, respectively, and in only 6.6% of Miami cases. Quinine was not reported in four cities, including both Chicago and Los Angeles, the leaders in percentage of cases containing morphine. It was reported found in about 30% of the cases in New York, Washington, and Philadelphia. These northeastern seaboard cities seemed to observe a very high incidence of methadone- and morphine-related cases, much more so than the rest of the participating cities. In contrast, Washington alone among the nine cities found a substantial number of cases of phenmetrazine-involved death, 20% of their cases. Washington and Philadelphia showed the greatest proportion of amphetamine-involved deaths. About 15% of the cases reported by these cities were found to involve amphetamine, whereas the average for the other cities was 1.2%.

One possible source of the differences would seem to be the drug-analysis methodology used by each city. If, for example, Los Angeles had used a more specific and accurate method for measuring morphine, and the other cities had used other, less-specific or less-reliable methods, this might explain the large representation of morphine-involved deaths in Los Angeles. Unfortunately, the methodologies used by the various cities for morphine assays were quite similar: gas–liquid chromatography predominated, followed by spectrofluorometry, immunoassays, fluorescent assays, and color tests. Perhaps the chief difference was not in the final assay method, but in earlier steps of the assays—in the extraction procedure, the extraction solvent, or the pH used in the extraction. One can use gas–liquid chromatography to measure a drug after it has been concentrated from the specimen by a wide variety of extraction methods and solvents. Therefore, though the final assay methods were similar, the earlier steps might have been different. The answer to this question must await further data collection and analysis. The other clear possibility is that these are genuine epidemiological differences.

Table 4 lists in Part A the total number of drugs detected in various body tissues and fluids and the percent of the grand total for all sites. Of this total, 93% was on the blood, urine, bile, liver, or stomach contents. The frequency of tests on other body fluids or tissues depends largely on the city and on the drug in question. Phenothiazines, amphetamine, metaamphetamine, and quinine are preferentially assayed in urine; bile is the preferred specimen for morphine assays.

Part B of Table 4 lists the five major drugs tested for in each tissue or physiological fluid and the percent of the total per site. Morphine was the most commonly tested-for drug in the blood, urine, and bile, closely
followed by methadone in these same three fluids. Methadone, however, was the most commonly assayed-for drug in all tissues and fluids, possibly representing the large number of methadone treatment programs in the northeastern seaboard cities, New York, Philadelphia, and Washington. D. C. These three cities represented 45% of all drugs reported, and from Table 3 it can be seen that they showed much larger percentages of morphine and methadone than did the other cities combined. The data on phenmetrazine in Table 4 were primarily due to reports by Washington. Part B of Table 4 would hardly be different if only New York, Philadelphia, and Washington were considered.

Table 5 lists the drugs most commonly found, representing more than 90% of the drugs reported. Some drugs were detected by the laboratory more often then they were listed as being involved in the death in another part of the form, indicating that in some instances the presence of a drug in body fluid or tissues was judged not to be a factor in the death.

The first three columns of Table 5 list the number of cases, the type of specimen studied, the mean concentration found, and the standard deviation of the concentration reported for these drugs. The large number of cases and the standard deviations presented in Table 5 add immeasurably to the usefulness of the data, giving a range—for some drugs a rather wide range—of toxic concentrations. This table complements other tabulations of toxic concentrations (3, 4).

The remainder of Table 5 gives data on the concentration of only those drugs that were found alone and the concentration of those drugs found in combination with alcohol. With the possible exception of diazepam, methadone, and glutethimide, all the other drugs when present alone show a higher toxic blood concentration than when they are present in combination with ethanol. Such synergism not only involves barbiturates, but also includes a great variety of drugs such as imipramine, amyttriptyline, meprobamate, thioridazine, morphine (in blood and bile), propoxyphene, and methaqualone. The decrease in toxic concentration when the drug was present in combination with ethanol was usually considerable; only about half as great a concentration was toxic.

The exceptions noted above, upon further investigation and collection of data, may not really disagree with the trend. Diazepam, for example, appeared in these data in concentrations only slightly greater when in combination with alcohol than when alone, diazepam in combination with alcohol was reported in only five cases, and glutethimide in combination with alcohol in only three. Data on more cases may easily alter the pattern for these two drugs. Methadone is a different story: its concentration in blood when present in combination with ethanol was more than 20-fold that when it was present alone. The standard deviation for this combination is more than three times the mean, indicating a very wide range of results (Table 5). On further inspection of these data, one finds that New York represents 70% of the cases of blood methadone reported, whether alone or in combination. New York, however, did not report assays for methadone in urine. The results for methadone in urine, alone and in combination with alcohol, contrast sharply with the results for blood. For all cities, the mean concentration of methadone in urine when present alone was 10.3 mg/liter (n = 27; SD = 11.9 mg/liter), but when methadone was present in combination with alcohol, the mean was 4.5 mg/liter (n = 13; SD = 2.7 mg/liter). These results for urine imply that ethanol is toxicologically synergistic with methadone and that New York's large influence on the blood data obscures possible synergism in blood. In contrast to the pattern in drug combinations with alcohol, the concentration of a drug in blood when it is present alone or when in combination (Table 5, first six columns) does not seem to follow any clear pattern.

A toxicology proficiency survey was done concurrently with the data collection (5). The analysis of the toxicological examinations performed on 2000 drug-involved deaths by the nine participating cities demonstrated a wide interlaboratory variance in the quality of the toxicological examinations from these cities.

In summary, it is clear that definite and potentially significant differences exist in the toxicological examinations performed by the various laboratories to give rise to the disparities noted. Regional psychosocial and biomedical differences have also been found (6). A question that must be asked about the interlaboratory toxicological differences in psychoactive drug-involved deaths presented to medicolegal offices is: to what extent are these true differences, representing regional epidemiological differences, and to what extent do these differences represent toxicological, instrumental, and methodological availability or sophistication, personal or forensic laboratory departmental emphasis, personnel training, case load, resource limitations, or other factors? This is a critical question and needs to be considered in interpreting drug-death statistics and related toxicological findings.

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References


