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Toxicology and Sudden Infant Death

Sudden infant deaths, like all sudden deaths, come under the jurisdiction of the local medical examiner or coroner. The cause of death is then determined by a process of investigation and a postmortem examination, not necessarily autopsy.

In contrast to adult cases of sudden death, toxicology is much less frequently used in the final determination of the cause of infant death. By definition, the diagnosis of sudden infant death syndrome requires a proper investigation and thorough autopsy. Although toxicological examination is not necessitated under this definition, a recently heard criticism of the handling of sudden infant deaths is that without toxicology other possible causes of death, such as poisoning, have not been excluded [1]. In a report of three cases of sudden infant death in children of methadone-maintained addicted mothers, toxicology results were available in only one case and were negative [2]. Furthermore, a noted expert in child abuse recently included repeated poisoning as one of the eleven examples of the battered child syndrome [3].

Wayne County, Michigan, with 2.7 million residents, encompasses both urban and semirural populations. A large drug subculture that uses both "hard" and "soft" drugs exists within the city of Detroit. The rate of deaths from the use of narcotics ranks as one of the highest in the United States. In 1975, 341 deaths resulting from narcotic abuse were examined by the office of the medical examiner. A widely used rule of thumb estimates the number of addicts as 200 for every recorded death [4]. Thus, approximately 65 000 narcotic addicts reside in Wayne County, many of them women in the childbearing age. The possibility of narcotic-addicted parents administering drugs to infants was another factor which this study intended to assess.

Furthermore, it was considered advisable to evaluate the role of agents such as prescription and over-the-counter medications, as well as alcohol, since these substances are often available in the home.

Commencing in December, 1975, and continuing through November, 1976, 130 consecutive cases of sudden deaths of infants between 48 h and one year of age were examined according to a comprehensive toxicological protocol to determine if unsuspected cases of infant poisoning were occurring within Wayne County. Included within the total of 130 cases were 103 cases of sudden infant death syndrome (SIDS). The other cases are outlined in Table 1.

Methods

One hundred and thirty consecutive cases of sudden deaths of infants under one year of age, including natural and unnatural deaths, were examined at the facilities of the

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TABLE 1—*Classification of sudden infant deaths in Wayne County, Michigan, from December, 1975, through November, 1976.*

Cause	<i>n</i>
Natural	
SIDS	103
Other	14
Accident	8
Homicide	5
Total	130

Office of the Medical Examiner of Wayne County. The autopsy procedure [5] included careful assessment of all possible sites of infection, including the middle ears, both grossly and microscopically. Blood, urine, and tissue (liver and kidney) samples were obtained from each case and analyzed by the following techniques.

Ethanol

Blood samples were screened for volatile alcohols by the colorimetric Conway microdiffusion method [6]. This technique detects ethanol, methanol, and isopropanol. The sensitivity for ethanol is approximately 0.02% (w/v) when a 1-ml sample is employed. Positive samples were quantitated by gas chromatography by using the Perkin-Elmer Model F-40 Head Space Analyzer [7] with a 0.4% Carbowax 1500 on Carbowax A column.

Barbiturates

Blood samples were analyzed by gas chromatography [8], and tissue samples were analyzed by ultraviolet spectrophotometry [9]. The sensitivity for blood is approximately 0.1 mg/dl when a 1-ml sample is employed.

Salicylate

Blood samples were analyzed by ultraviolet spectrophotometry [10], and urine samples were screened by a spot test employing ferric chloride [11]. The sensitivity for blood is approximately 2 mg/dl when a 1-ml sample is employed.

Organic Bases

Tissue samples were hydrolyzed in hydrochloric acid, made alkaline, and extracted for organic bases (phenothiazines, antihistamines, and narcotics). The final extract was analyzed by ultraviolet spectrophotometry and thin-layer chromatography. For most organic bases the thin-layer chromatographic technique can detect 3 to 6 μg of drug. Typically, a 10-g sample was analyzed. All positive results were confirmed by gas chromatography employing two different columns.

Opiates

After adjusting the pH of the alkaline tissue (from the organic base procedure) to 8.5, the hydrolyzed tissue was extracted for opiates (morphine and codeine). The final extract was divided into two portions. One portion was prepared for fluorometric analysis [12], and any positive result was confirmed by submitting the second portion to thin-layer

chromatography. The fluorometric technique can detect approximately 100 ng of morphine, and the thin-layer chromatographic technique can detect approximately 3 to 6 μg of morphine.

Tests for carbon monoxide were carried out in selected cases but not routinely because of a lack of evidence of possible furnace or other heating device malfunction. No deaths occurred in automobiles.

Case Reports

Drugs were detected in 6 of the 130 cases studied (Table 2). The substances present in 5 of these cases had been prescribed by physicians for illnesses such as "colds," vomiting and diarrhea, restlessness, and convulsive disorder. In the remaining case methadone was detected. Details of these cases are given below.

In Case 1, phenobarbital was present in blood and liver and had been prescribed for restlessness. The levels were not considered toxic. The autopsy findings were consistent with SIDS.

In Case 2, pheniramine was present in liver and kidney in minute amounts. This was a component of medication prescribed for a mild cold. Autopsy findings were consistent with SIDS.

In Case 3, salicylate was present in the blood. This drug had been prescribed for treatment of a febrile illness complicated by vomiting and diarrhea. Autopsy findings confirmed a diagnosis of acute enterocolitis.

In Case 4, methadone was present in both the blood and liver. This infant was born to a former heroin addict being maintained on methadone. At birth the infant weighed 5.5 lb (2.5 kg) and at death 5.2 lb (2.4 kg). The autopsy findings were those of an underweight, undernourished infant, otherwise nonspecific, and a diagnosis of failure to thrive was made. The subsequent toxicology findings resulted in the diagnosis being changed to methadone intoxication.

In Case 5, salicylate was present in the blood and kidney and had been administered for a mild fever. However, autopsy revealed no evidence of significant respiratory tract or other system disease and supported a diagnosis of SIDS.

In Case 6, the infant developed a convulsive disorder related to birth trauma. A barbiturate had been prescribed and was present in blood, liver, and kidney. Evidence of a skull fracture and intracerebral hematoma was present at autopsy.

Discussion

The possibility of not detecting cases of poisoning is an ever-present concern of medico-legal investigators. Present toxicological laboratories in most modern medical examiner facilities greatly increase the likelihood of detecting this type of "hidden homicide" in adult deaths. However, relatively little attention has been paid to the involvement of drugs in sudden infant death. Certainly drugs may be involved in a deliberate, homicidal manner, but probably of more importance to the field of SIDS is the fact that chemicals administered by normal, concerned adults may play a significant role in altering the infant's vulnerable neurophysiological system, resulting in malfunction and respiratory or cardiac arrest.

Of 130 consecutive cases of infant death studied at this institution, 6 were found to contain identifiable drugs (see Table 2). In 5 of the 6 cases the drugs found had been prescribed by physicians for certain ailments, and their presence supported the history obtained prior to autopsy. Three of these cases proved to be SIDS since the levels of the drug present were judged not to be contributory to these infants' deaths [13].

In the sixth case, the infant exhibited definite evidence of maldevelopment and was found to have significant levels of methadone in his body. It was later learned that the

TABLE 2—Cases of sudden infant death with positive toxicological findings.

Case	Age, weeks	Sex	Race	Place of Death	Cause of Death (Certified)	Sample	Toxicological Findings	
							Drug	Concentration
1	9	m	w	crib	sudden infant death syndrome	blood	phenobarbital	0.5 mg/dl
2	9	m	w	bassinette	sudden infant death syndrome	liver	phenobarbital	1.5 mg/100 g
3	11	m	w	crib	acute enterocolitis	kidney	pheniramine	positive
4	5	m	b	crib	drug (methadone) intoxication	blood	pheniramine	positive
						blood	salicylate	7.0 mg/dl
						kidney	methadone	0.04 mg/dl
5	8	m	b	bassinette	sudden infant death syndrome	liver	methadone	not detected
						blood	methadone	positive
						kidney	salicylate	17.0 mg/dl
6	3	f	w	crib	craniocerebral injury	blood	salicylate	13.3 mg/100 g
						liver	phenobarbital	0.9 mg/dl
						kidney	phenobarbital	positive
							phenobarbital	positive

mother, a known narcotic addict being maintained on methadone, had been breast-feeding the baby. The fact that narcotics, including methadone, are secreted in the breast milk is well recognized [14], and instructions against this feeding method are routinely given by the prenatal clinic for addicted mothers.

Included in the 103 cases of SIDS were the infants of 12 drug-addicted mothers. In contrast to the case described in the preceding paragraph, each of the other 11 infants exhibited a normal pattern of development and typical findings of SIDS. Furthermore, toxicological studies were negative in each case. Other workers [2] reported three sudden infant deaths in children of methadone-addicted mothers. Toxicological tests were performed in only one of these cases, and the negative result obtained parallels the findings in our 11 cases.

These results were especially significant in view of the large drug addict population existing in our community. Drug-addicted parents are viewed with considerable suspicion and often hostility by the lay and professional communities when one of their children dies suddenly. If a prenatal history of drug addiction is obtained during the investigation, it is advisable to carry out toxicological studies to eliminate the possible accusations that the parents may face.

The significance of the proportion of infants of drug-addicted mothers dying of SIDS will not be dealt with in the context of this paper.

This study does support the authors' opinion that toxicology is not an essential component in the criteria for the early diagnosis of SIDS. If the investigation and autopsy findings are consistent with SIDS, a provisional diagnosis should be made immediately. This can be changed if subsequent laboratory tests (microbiology, histology, toxicology) yield significant results. Unfortunately, we are aware of too many offices that cause unnecessary anguish to parents of SIDS victims by delaying the diagnosis for up to several weeks while toxicological studies are being completed.

In our experience, individuals, including physicians, have voiced their suspicions of poisoning being an important consideration in the examination of sudden infant death. Furthermore, references to this phenomenon have recently appeared in the medical literature [3]. Certainly the medical examiner's office is obligated to investigate any suspicious case; but it is somewhat unrealistic to anticipate a result which would contradict a good investigation and a thorough autopsy.

This study of 130 cases of sudden infant death includes 103 cases of SIDS in which toxicological studies yielded negative or noncontributory results and, therefore, did not affect the final diagnosis. Our conclusion is that toxicological studies should be carried out when indicated by the facts provided from the investigation. If routine toxicological testing is done on all cases of sudden infant death, it is unlikely to change the initial diagnosis of SIDS established by investigation and autopsy. The authors do not wish to discourage toxicological examinations in infant deaths if such facilities are readily available. We must, however, emphasize that these studies should not delay the early diagnosis of SIDS when appropriate.

Summary

One hundred thirty cases of sudden infant death occurring in Wayne County, Michigan, (population 2.7 million) were analyzed for possible drugs. The toxicological protocol has been outlined. Six cases were found to be positive, and in five of these the drugs found had been prescribed for a variety of illnesses. In one case methadone was found in the blood of an infant whose mother was undergoing methadone treatment for drug addiction, the drug being transmitted through breast milk. In none of the 102 cases of sudden infant death syndrome (SIDS) included in the study did the toxicological results affect the diagnosis. In our study, toxicological analyses never contradicted an initial diagnosis

of SIDS, and, therefore, we feel that this diagnosis should be made promptly based on investigative and autopsy findings.

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