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CASE REPORT

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Toxic or Tolerant: Chloral and the Drug Dilemma

Chloral hydrate, discovered in 1832, is considered to be the first synthetic organic compound effectively used as a hypnotic [*1*]. Its relative safety gained it great popularity, and reports of administering up to 25 g in a 20-h period have been published [*2*]. Dependency potential was recognized early, and many notable individuals including the philosopher Nietzsche became habituated. Individual case histories have documented persons taking almost 25 g nightly over prolonged periods of time [*3*] but little has been published on actual blood concentrations in such apparently tolerant individuals. The following case exemplifies some of the problems encountered in certifying a death in a person using relatively large amounts of chloral hydrate.

Case History

O. B. was a 65-year-old, 110-lb (50-kg), semi-invalid woman found dead in bed by a friend with whom she shared an apartment. There was a glass filled with purple liquid and a vermouth bottle containing similar liquid on the bedside stand (later identified as a nonalcoholic beverage). The previous evening O.B. had called the local suicide prevention center—a frequent occurrence. Verbal suicide threats had been common and were no longer taken very seriously. Prior to retiring she had been given her usual medications by the roommate; these consisted of one Empirin® with codeine, six 500-mg chloral hydrate capsules, and two Excedrin®. The Empirin and Excedrin were found on the bedside stand. The roommate stated that O.B. would sequester and pilfer chloral hydrate, frequently taking more than the usual 3 g at bedtime.

Past history revealed hospitalizations for a fracture of the hip with subsequent surgical procedures. While hospitalized she was given 4.0 g of chloral hydrate at bedtime without problem.

Pathology and Toxicology

The most significant anatomic finding in this case was severe coronary arteriosclerosis with numerous areas of occlusion and recanalization. Myocardial fibrosis was not evident grossly but was identified microscopically. The kidneys were markedly shrunken from chronic renovascular disease. Pulmonary congestion and edema were moderate. Results of toxicological analysis are shown in Table 1.

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TABLE 1—*Results of toxicologic examination.*[a]

Phenobarbital	1.0 mg/100 ml blood
Trichlorethanol	10.7 mg/100 ml plasma
Salicylates	13.9 mg/100 ml blood
Codeine	0.4 mg/100 ml urine

[a]Performed by the Institute of Forensic Sciences, Oakland, Calif.

Discussion

The case presented demonstrates the potential for error present when dealing with "toxic" concentrations of drugs. The plasma trichlorethanol (a metabolite of chloral hydrate) concentration of 10.7 mg/100 ml is significantly above the published therapeutic range [*4*] and could conceivably be interpreted as a cause of death. The strong history of suicidal ideation would tend to support this conclusion. The excessive use of the drug in the case presented and the knowledge of the tolerance possible with abuse make such a conclusion much less secure. Further doubt concerning the role of the drug is raised by the presence of natural disease of sufficient severity to account for the death.

The certification of death is frequently associated with some degree of uncertainty, and caution must be exercised whenever blood or tissue levels of drugs are used to establish the cause or mode of death. For some drugs, therapeutic and toxic levels may have been adequately established. Unfortunately, data are far from complete for many drugs, and physiologic tolerance produces an overlapping of lethal and nonlethal levels. Difficulties are often encountered in establishing a medical cause of death when drugs are present, and differentiation between natural, accidental, and suicidal modes of death may not be possible. To indicate the uncertainty in this case, the cause of death was listed as "Undetermined (potentially lethal blood level of trichlorethanol with history of chronic excessive intake and probable tolerance; severe coronary arteriosclerosis present)." "Chronic renal disease, moderate to severe" was entered as another significant condition. The mode of death is "Undetermined," and all drug levels have been included on the certificate of death.

Summary

The role that a drug or combination of drugs plays in the causation of death cannot always be stated with certainty. Drugs associated with the development of tolerance create a particular problem, and there is need for additional data concerning tolerable concentrations achieved by drug abusers. The common drug chloral hydrate falls into this category, and a case of possible chloral hydrate intoxication has been presented.

References

[*1*] Butler, T. C., "The Introduction of Chloral Hydrate into Medical Practice," *Bulletin of the History of Medicine,* Vol. 44, No. 2, 1970, pp. 168–172.

[*2*] Hawes, A. J., "Safety of Chloral," *British Medical Journal,* Vol. 2, No. 2, 1968, p. 627.

[*3*] Robinson, J. T., "A Case of Chloral Hydrate Addiction," *International Journal of the Society of Psychiatry,* Vol. 12, No. 2, 1966, pp. 66–71.

[*4*] Baselt, R. C., Wright, J. A., and Cravey, R. H., "Therapeutic and Toxic Concentrations of More Than 100 Toxicologically Significant Drugs in Blood, Plasma, or Serum: A Tabulation," *Clinical Chemistry,* Vol. 21, No. 1, 1975, pp. 44–62.

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