

Correspondence

Clinical Forensic Medicine: Do It Well for the Patient

Sir:

Since the publication in JFS of Smock and co-workers' article on Clinical Forensic Medicine, other publications have addressed the issue of incorrect diagnosis or documentation of gunshot wounds (entry versus exit, size, shape, location, etc.) by clinicians (1–3). These publications have discussed the potential adverse effect of inadequate wound documentation on criminal investigations and on the adjudication of criminal cases, but a very important issue has not been mentioned—that incorrect or incomplete diagnoses may lead to inappropriate or ineffective diagnostic or therapeutic procedures. For example, in some cases, thoracotomy or laparotomy might have been avoided if the gunshot wound patterns were more thoroughly and adequately interpreted prior to surgery (4). As another example from personal experience, medical personnel interpreted ragged wounds on the knee of a man found lying in the street as pedestrian impact wounds and then treated the man for assumed internal injuries. He died in the emergency room of hemorrhage from a shotgun blast to the knee which showed distinctive cutaneous wounds and shotgun pellets on X-ray. It is understandable that incorrect diagnoses will occur when time is of the essence during emergency treatment, especially when adequate history is lacking. But cases such as this one illustrate that a major reason for training in clinical forensic medicine relates to the need to improve patient care, not only because of possible problems during criminal investigations and legal proceedings.

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Randy Hanzlick, M.D.
Atlanta, Georgia

Drug Enforcement Administration (DEA) Chemists Erred in Calculating Quantity of Methadone that Could Be Synthesized from Precursor Chemicals

Sir:

I was recently called upon to review a matter involving the illicit synthesis of methadone. It became apparent that the DEA office handling this case was using an incorrect formula for calculating the amount of methadone that could be synthesized from

the amount of diphenylacetoneitrile seized; the amount calculated by the DEA needed to be adjusted by at least 50%. I wish to take this opportunity to alert the forensic science community to this problem, including the chemists at other DEA centers who may be using a similar formula.

The synthesis of methadone (Amidone) was first described in 1945 (1). Soon thereafter, it became evident that this method of synthesis results in the production of equal amounts of two isomeric aminonitrile intermediates, *only one of which eventually produced methadone* (2, 3). The chemical explanation for the production of the two isomers has been delineated (4, 5). A different procedure for the synthesis of methadone which avoids the production of two nitriles has been published (6), but this method results in low yields.

The illicit synthesis of methadone which produces two isomeric nitriles uses, among other chemicals, dimethylamino-2-propanol, thionyl chloride, and diphenylacetoneitrile in the presence of sodamide, similar to the method first described (1). The production of the two isomeric nitriles is known to law enforcement agencies (7). In the present case, the DEA determined the potential amount of methadone hydrochloride that could be synthesized from the quantity of diphenylacetoneitrile seized by using a "molar ratio" factor of 1.78 (should be 1.79); that is, one molecule of diphenylacetoneitrile will yield one molecule of methadone hydrochloride weighing 1.78 times as much. However, because only one of the two nitrile intermediates derived from diphenylacetoneitrile yields methadone, multiplying the entire weight of the diphenylacetoneitrile seized by this factor is not correct and must be reduced by 50%.

Also, the use of the 1.78 factor by the DEA assumes that the ingredients used in the synthesis of methadone, subsequent to the diphenylacetoneitrile reaction, are present in sufficient quantity and will not, therefore, limit the potential yield of methadone hydrochloride. If, in fact, the quantity of moles of any one of the ingredients is less than that of diphenylacetoneitrile, then it would not make sense to use the 1.78 factor. Thus, the quantity of each ingredient seized must be determined and calculated on a molar basis.

The chemical reactions are not 100% efficient. In the present case, the DEA did calculate the final yield of methadone hydrochloride using an efficiency of 79%. Using scientifically controlled conditions, the yield of the two isomeric nitriles following the diphenylacetoneitrile/sodamide reaction has been reported at 79% (3), but a lower efficiency of 71% has also been reported (8). An alternate step in the synthesis of methadone using potassium tertiary butoxide instead of sodamide results in a yield of mixed nitriles of 92% (3).

The efficiency of the final reaction in the synthesis of methadone must also be considered. The conversion of the intermediate nitrile to methadone involves a Grignard reaction. The yield of product following this reaction has been reported at 83% (8) and at 85% (6). Thus, the yield of methadone hydrochloride from the

diphenylacetoneitrile/sodamide reaction could be the amount of diphenyl-acetonitrile seized $\times 1.79$ (the molar ratio of methadone hydrochloride to diphenylacetoneitrile) $\times 0.79$ (yield of both nitrile intermediates) $\times 0.50$ (only one nitrile isomer leads to methadone) $\times 0.85$ (final yield after Grignard reaction), or it could be $1.79 \times 0.71 \times 0.50 \times 0.83$. Other combinations of these yields are possible.

All of the above factors should be taken into consideration in the final determination of the amount of methadone hydrochloride that could be produced from the amounts of chemicals seized.

Finally, for the purpose of sentencing the defendant, it is the weight of methadone that determines the length of the sentence. Because the molecular weight of methadone is about 10% less than that of methadone hydrochloride, using the above factors is detrimental to the defendant, and a factor of 1.60 rather than 1.79 should be used to determine the theoretical yield of methadone from diphenylacetoneitrile, along with all of the other factors discussed above.

References

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Morris S. Zedeck, Ph.D.
Pharmacologist/Toxicologist
Zedeck Advisory Group, Inc.
245 East 80th Street
New York, NY 10021