Family Practice Forum

Adverse Drug Reaction Reporting and the Family Physician

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A recent article in this journal, "Gynecomastia Associated With Theophylline"[1] and a follow-up inquiry to the Food and Drug Administration's Spontaneous Reporting System (SRS) pointed up a possible defect in the knowledge base of family physicians. The purpose of this communication is to clarify the reporting of adverse drug reactions and the role and responsibility of the family physician.

My inquiry to the SRS revealed that the adverse reaction reported in this journal had not been reported to the SRS. Further, the only other report of such a reaction with this specific drug had occurred in the early 1970s. Thus, this reaction might be an isolated incident or the beginning of a new adverse finding that might have potential clinical significance, or it might represent a problem with the production of the drug product. That it had not been reported identifies a potential weakness in the reporting chain.

The reporting and collection of adverse reactions first began about 30 years ago with the association of aplastic anemia and chloramphenicol.[2] By 1968 the FDA's Spontaneous Reporting System for adverse drug reactions had become established, and it now serves as the prime point of collection for such information about all drugs. (A similar system is in place for collection of device information.) The basic purpose of the system is simply to collect data in order to efficiently monitor drugs currently in the marketplace for the protection and benefit of both the patient and the physician.

Before new drugs are introduced into the marketplace, they are tested under a carefully designed and time-tested system, and the sponsor, usually a pharmaceutical firm, is required to submit a Notice of Claimed Investigational Exemption for a New Drug, commonly referred to as an IND. Through this process the new drug is usually tested in several thousand patients, a procedure that generally detects the most common side effects and adverse reactions. However, as evidenced by the recent withdrawals from the marketplace of such drugs as ticrynafen (Selacryn) and benoxaprofen (Oraflex), not all adverse reactions are identified through the early experimental testing because some reactions may occur only once in 10,000 times. Testing in only a few thousand patients will statistically miss these infrequent reactions. (The alternative is more extensive testing and delays in introducing new drugs.) Thus, the family physician, because of his unique role in being often the first and sometimes the only person to see the drug reaction, plays a key role in reporting adverse reactions. (In fact, one could speculate that if more family physicians could be relied upon for earlier reporting of adverse drug reactions, we might see an earlier release of new drugs.)

If a physician notes a new or unexpected reaction to a drug not listed in the labeling, or notes a serious, life-threatening, or fatal drug reaction, this reaction should be reported to the FDA. In

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addition, congenital anomalies that might be associated with drugs taken during pregnancy should also be reported. Further, if a physician notes a series or cluster of commonly noted reactions, these, too, should be reported. Finally, a series of cases of nonresponse to a drug should also be reported, for such nonresponse might indicate a manufacturing defect. The suspected reaction should be reported to the FDA on the Drug Experience Report Form.* A letter (FDA, Rockville, MD 20857), however, or even a telephone call to the local FDA office (listed in the white pages) will start the reporting procedure. In all cases confidentiality of both patient and physician will be maintained.

In some cases the FDA has found that physicians may be reluctant to report a case or series of cases because they are planning to publish an article or a case report. This reluctance stems from the misinterpretation of the "Inglefinger Rule" (named after the late editor of *The New England Journal of Medicine*, who stated that he would not publish material in that journal if it had received prior publicity). Although it is true that many editors are reluctant to publish articles or case reports that are first released through other media channels, such is not the case with adverse reactions reported to the FDA. Authors who delay reports to the agency are not guilty of any crime, as reporting is strictly voluntary, but they certainly have abandoned their responsibilities to their colleagues and the public.

References

1. Dardick KR: Gynecomastia associated with theophylline. J Fam Pract 1984; 18:141-142
2. Lee B, Turner WM: Food and Drug Administration's adverse drug reaction monitoring program. Am Hospital Pharmacy 1978; 35:929-932

*Form FDA 1639 is available from the Department of Health and Human Services, Food and Drug Administration, Rockville, MD 20857 (Telephone 301/443-4580).