

# Meaningful Toxicology\*

ROBERT V. BLANKE, Ph.D.

*Associate Professor of Clinical Pathology, Medical College of Virginia  
Health Sciences Division of Virginia Commonwealth University, Richmond*

Before discussing this subject in a "meaningful" way, we must have some agreement as to what is meant by the term "toxicology." Toxicology includes such widely diverse areas as the chemistry of toxic substances, the signs and symptoms elicited by such substances, the detection and identification of toxic substances in a wide variety of specimens, the interpretation of analytical results and the treatment of toxic episodes. Although in recent years, toxicology has dealt with the problem of drug overdosage almost exclusively, it must be appreciated that any chemical substance, when absorbed in sufficient quantities to produce an adverse effect, is toxic. This would include common substances such as ordinary table salt and range through substances generally recognized as poisonous such as strychnine. In addition, the broad field of toxicology is concerned with the effects of acute overdosage of toxic agents as well as the effects of long-term, chronic exposure to these agents. The scope of toxicology, therefore, may extend from the study of a single element such as lead to a complex, chemically uncharacterized substance such as snake venom; from an overdose of heroin to the effects of long-term exposure to low levels of pesticides on anticonvulsant therapy. For the purpose of this discussion, we shall narrow the limits of the broad field of toxicology considerably, but it is important to be aware of the breadth and depth to which toxicology may at times extend.

Clinical toxicology laboratories generally have two main functions. The first and most apparent is the identification and quantitation of toxic substances in specimens from patients brought to the

Emergency Room after a possible acute toxic episode. In general, the clinician needs the laboratory results promptly in order to answer questions such as: What toxic substance, if any, is present? If present, is the quantity consistent with the signs and symptoms displayed by the patient? Will the quantity of toxic substance present influence the choice of the treatment? Do the laboratory findings confirm the history, diagnosis or clinical impression?

The second general function of the clinical toxicology laboratory is to monitor certain chemical substances in patients. This may be done for the purpose of maintaining therapeutically effective drug levels such as in epileptic patients, or for the purpose of determining the effectiveness of a treatment procedure in reducing levels of toxic agents. A relatively recent area of interest may also include the determination of metal levels in cases of industrial exposure or when alteration in metal metabolism may be associated with a clinical condition.

Both of these general functions utilize common laboratory facilities and personnel, so that it is reasonable that the clinical toxicology laboratory be engaged in both activities. Since the goals to be achieved by these two functions are quite different, the approaches to the achievement of these goals must be considered separately. In general, in order to fulfill its role in dealing with the emergency situation, the toxicology laboratory must provide 24-hour service and utilize reliable, rapid methods resulting in a short turn-around time to be of maximum use to the clinician. The monitoring of chemical substances in patients can usually be achieved within a normal workday using dedicated procedures on a relatively continuous basis. Ideally, of course, with unlimited facilities, personnel and support, these goals can easily be achieved. Since most laboratories can never hope to enjoy this luxury, a more prag-

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matic approach must be taken which involves compromises between the ideal and the practical.

Since there are literally thousands of toxic substances which may be encountered in clinical toxicology, it is absolutely essential at the outset that these substances be examined realistically, making a selection of those which are commonly encountered in the community served by the clinical laboratory. Some substances are common to almost all treatment facilities while others may be unique to a particular locality. Rural and urban communities, for example, may differ as to the relative importance of problems relating to narcotics and pesticides. An important industry in a specific area may present specific toxicological problems which would not usually be encountered elsewhere.

It is commonly acknowledged that good communication between the clinician and the laboratory facility is essential for the production of meaningful laboratory results. Unfortunately, the gap between acknowledging this truism and its implementation is difficult to bridge. Lines of communication between the clinical toxicology laboratory and the clinician can be established initially by identifying the priority by which new toxicological procedures should be made available. It is essential that the laboratory understand the problems of the clinician and that the clinician understand the problems of the laboratory. For example, it may be important in a specific case to identify whether a patient has ingested an overdose of lysergic acid diethylamide (LSD). It is possible to assay LSD levels by radioimmunoassay, but does the need occur often enough to justify the expenditure of funds for equipment and personnel to make this assay procedure available on a "STAT" basis? Conversely, the laboratory may have an elegant method for measuring fluoride levels in serum, but is it of practical use to the clinician when 24 hours are required to obtain test results?

It is better for a clinical toxicology laboratory to conduct a relatively small number of tests by reliable methods in reasonable time periods than to attempt to handle all types of situations which might arise. Once having agreed upon a basic nucleus of tests, the laboratory can adapt and evaluate published procedures to give the clinician results which are meaningful both in reliability and in turn-around time.

It is essential that once lines of communication are opened, they be maintained in both directions. It is the responsibility of the laboratory to inform the

clinician as to what can or cannot be done within the constraints imposed upon it in a given situation. It is the responsibility of the clinician to request reasonable and specific tests, supplying sufficient information to permit the laboratory some leeway in establishing priority with which specimens will be processed and to provide proper and adequate specimens for analysis.

The "unknown" toxic agent is always a difficult problem to handle. Again, good communication can help to partially resolve the problem. Most clinical toxicology laboratories have the ability to conduct a variety of screening tests. None of these is all-inclusive and most of them are chiefly of value when they are negative. Some screening tests are of the spot-test type, which can be conducted on urine or gastric contents after a minimum of handling. Others can be used to screen for metals, alcohol, other volatile substances or narcotic drugs. The simple request for "toxicological screening" or "test for poisons" presents a dilemma to the clinical toxicology laboratory. Should the screening tests be directed toward detecting drugs of abuse or heavy metals? Should pesticides be considered or is the patient a known alcoholic? Valuable time can be saved and costs minimized by a brief history or clinical summary of the patient's condition. If nothing else, this would indicate to the toxicology laboratory what substances are not likely to be present.

Ideally, a clinical toxicology consultant should be available to contribute personal expertise in the resolution of these difficult problems. Many toxicology laboratories have the experience and necessary resource material to aid the clinician in making a proper evaluation. Additionally, there are other resources available provided they are utilized. The poison control center, drug information center, and specialists in specific areas can make important contributions to patient management. Thoughtful planning and interdepartmental or interagency support can significantly assist, provided arrangements can be made in advance to utilize these resources properly. Obviously, an emergency at 2:00 a.m. is not the time to decide where to look for help or how to carry out a difficult laboratory test.

The development of a regional poison control center has been found to be the most effective way to resolve these problems in many communities. Properly coordinated, such a regional center could supply information, treatment and laboratory facili-

ties to a large area. This would ensure that costly equipment and skills could be most effectively used to serve a large geographic area. Costs for a specific test, for example, which may be difficult to justify due to infrequent occurrence in a given institution, might be practical if the frequency of occurrence were increased by serving a larger area.

Functioning lines of communication are also important in deriving meaningful toxicological data from laboratory procedures not related to the emergency room. Frequently, the toxicology laboratory is requested to develop or add to the armamentarium of tests available, a procedure identifying a specific drug in serum. The fact that the laboratory may have a certain instrument or procedure available does not necessarily enable the laboratory to apply that instrument or procedure to a specific test. Since the development of gas-liquid chromatography which now makes possible the detection of a vast number of drugs, it is frequently assumed that this is the answer to all drug analyses. Frequently, it is not possible in a practical manner, to modify a gas chromatograph, in order to shift it from a routine, smoothly operating procedure to a special application. Not only will the parameters of the new test be somewhat different but sample preparation is almost always the major problem. One of the difficulties confronting the toxicology laboratory is removing the toxic agent from the specimen submitted in such a manner and in such a state of purity that a particular instrumental procedure can be used for its identification and quantification. In addition, many substances which are rapidly metabolized may not even be detected in biological specimens. Thus, although the parent drug may be easily identified in a standard solution, the presence or absence of that

drug in biological material may be a much more complex problem. Detection and estimation of metabolites may be the only method by which the original drug can be detected. These and similar problems should be discussed between the clinician and the toxicology laboratory in order that both may understand the usefulness or limitations of a given analytical procedure.

Finally, in order for the toxicology laboratory results to be meaningful to the clinician, some interpretation of the results is necessary. Tables of normal values are of little use since frequently there are no "normal" values for toxicological analyses. In the case of drugs, therapeutic levels may be available but these must be interpreted cautiously, since some patients may develop tolerance to a given drug after prolonged therapy and others may exhibit a hypersensitivity to very low levels of drugs. It is becoming increasingly common that drug combinations may be present and little information is now available as to drug interactions. Here, again, the clinical toxicologist and those sources of information previously mentioned can be utilized, so that the clinician may benefit more from the services of the toxicology laboratory.

In summary, "meaningful" toxicology can be realized only when the clinical toxicology laboratory provides more than a place where tests are run. Thoughtful and well-planned coordination of the laboratory's efforts with the efforts of the clinician can be provided by establishing and maintaining good communication between the parties. Outlining the proper procedure for establishing this communication is relatively simple. Making it work requires a constant, willful expenditure of effort in both directions.