

Pitfalls in Unqualified Acceptance of Laboratory Data*

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One can never be absolutely certain that any single laboratory report is correct. As a general rule, therefore, do not undertake potentially serious action on behalf of any patient solely because of a single laboratory report. This is especially important if the result is unexpected or not in harmony with the rest of the clinical information available.

What are the reasons for this seemingly deplorable situation and how can it be remedied? The reasons are legion and I do not foresee the day when they can be remedied to the point where no errors ever occur. On the other hand, the situation has improved considerably during the past decades and there are reasons to hope for further improvement. Such improvement will require greater effort from physicians ordering the tests as well as those working under their professional supervision, greater effort on the part of reagent, laboratory-ware and instrument manufacturers and greater effort on the part of laboratory personnel.

Let us begin with specimen collection. I fear that even in these days, when each hospital patient has a wrist band with his name and identifying number on it, and when hospital rules usually forbid two patients with the same last name being placed in the same room—or even on the same floor in some cases—mistakes are occasionally made in patient identification. The errors arise in various ways. The blood collector may not check the wristband and a new patient may have been placed in the room, or the blood collector may have entered the wrong room. The collector may have asked, “Are you Mrs. Jean Jones?” and have been answered, “Yes” by Mrs.

Sally Smith who didn't understand the question and who always answers questions positively. I have heard that this is not an uncommon reaction among patients, who wish to please those who are taking care of them. Or the patient may actually be Mrs. Jean Jones, but the collector may have picked up Mrs. Sally Smith's pre-labeled slips and collection containers. Pre-labeling, while time saving, can generate problems, since it makes this sort of mistake easier. I have seen a nurse hand a sputum jar to a patient about to undergo gastric lavage for suspected tuberculosis and be told by the patient that the name on the slip was not his own. Once such an incorrectly identified specimen reaches the laboratory the error is hardly likely to be caught.

Almost no other clinical feat appears more difficult than obtaining an accurate 24-hour urine collection. Bottles continually arrive in the laboratory bearing on the laboratory slip the information that the patient's collection started at 8 a.m. on the morning of the first day and terminated at 8 a.m. on the morning of the second day. Nonsense! I'll bet not one in one hundred patients voids on the hour exactly. A nurse or nurse's aide has probably pre-labeled the containers and slips and left them with the patient with rapid-fire oral instructions or a neat little card bearing written directions which the patient can't read, doesn't read or doesn't understand. It is essential that someone who really understands the procedure explain it to the patient in simple terms. It is not important that the collection start and stop on the hour or that it be exactly 24 hours—a fact which in my experience seems to escape most medical students and probably most nurses. It is important that the time be known exactly, that the first specimen at the beginning of the collection

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period be discarded and that all of the urine be collected during the following collection period, uncontaminated by feces. Patients often forget when they use a bed pan that urine passed along with the bowel movement also counts. As a matter of fact, errors in 24-hour urine collections are so universal that many laboratories will not report results per 24 hours, but merely the volume of the urine and the results per 100 ml or per milliliter, in order not to return ridiculous results.

The type of container and what it contains is also important. I know of an expensive study of calcium and phosphorus metabolism conducted some years ago at a famous clinic which was invalidated because of improper cleaning and rinsing of the urine containers. Heparinized blood used for collection for blood ammonia determinations may be unsatisfactory as some heparins contain significant amounts of ammonia. I know of a case in which a fibrinogen band on electrophoresis of what was thought to be serum was interpreted as a monoclonal gammopathy or *M* peak when plasma was inadvertently substituted for serum. Nonsterile containers are often used to collect and transport specimens for bacteriologic study. Containers not chemically cleaned are often used to collect specimens for trace metal analysis. Manufacturers have suddenly, without prior notification, introduced changes such as siliconizing a widely used brand of blood-collection tube and consequently wreaked havoc with unsuspecting hematology laboratories using the tubes for whole blood clotting times! The wrong anticoagulant can make the interpretation of a peripheral blood smear difficult or impossible. Improper preparation of the patient is also a common cause of unreliable laboratory results. Glucose tolerance tests on patients who have been on starvation or reducing diets in the days preceding the specimen collection are not reliable for purposes of diagnosing diabetes mellitus. Serum lipids may be misleadingly normal if the patient has been losing weight or has been on a starvation or fat restricted, low calorie diet. It is not possible to interpret the 24-hour urine calcium, if the calcium content of the diet prior to the collection is not known.

Inappropriate specimen handling and inadequate preservation also causes error. Glucose rapidly metabolizes if plasma or serum is allowed to sit in contact with red cells. Although variable, the average rate of reduction of blood glucose at 37°C is 15 mg/100 ml/hr. Bilirubin is oxidized rapidly when

exposed to direct sunlight or even to fluorescent lighting. Ammonia generation starts immediately following withdrawal of the blood sample. The pH rises if blood is exposed to air. There is a paradoxical rise in serum alkaline phosphatase (as much as 10%) when serum is refrigerated overnight.

Hemolysis of the sample can interfere with many laboratory procedures by different mechanisms including absorbance by hemoglobin at the wavelength used, inhibition of enzyme activity by hemoglobin (lipase) or contribution of intracellular substances present in higher concentration in red cells than in serum (potassium, LDH). Turbidity of the serum may also interfere, particularly in photometric procedures.

The problem of drug interference is so formidable that I hesitate even to mention it. Drugs may interfere by altering the patient's biochemical and physiological processes or by interfering with the analytic procedures. This may result in raising or lowering test results significantly or only slightly, or may render the specimen totally unfit for testing. The entire October 1972 issue of *Clinical Chemistry*, the journal of the American Association of Clinical Chemists is devoted to a computer printout of laboratory tests and drugs affecting them. It represents 9,000 filed entries developed in the Clinical Pathology Department of the Clinical Center of the National Institute of Health and over 250 pages are devoted to this problem in that one issue. It is beyond the capability of the human mind to remember even a fraction of such a list. Even if it were not, the lack of quantitative data concerning the degree of interference and its consistency and the innumerable possible combinations and their varying effects would cause this to be an almost unsolvable problem. Even so, major effects of the commonest medications on the frequently used laboratory tests should be kept in mind. Examples of interference by physiologic mechanisms are the effect of "the pill" on thyroid function tests, and of morphine or codeine on serum amylase. Examples of interference with chemical analyses directly include the effect of administration of iodine containing substances on the serum protein bound iodine (PBI) and the effect of bromide on the ferric iron cholesterol methods.

If the patient has been properly prepared, the specimen properly collected and preserved and the patient has received no interfering medications, many potential pitfalls still await the procedure within the laboratory. Once again, there is the pos-

sibility of misidentification of specimens. I know of no completely foolproof specimen identification system, although in recent years improved systems have been evolved.

There is the ever present problem of unacceptable error originating in the actual laboratory procedure. First, let us acknowledge the hard fact that no human act—or even the act of any machine (although machines may come closer)—is perfectly reproducible. There is an irreducible minimal variation inherent in the actions of the technologists, in the limitations of glassware, reagents and instruments with which we must all live. It is the business of the clinician to acquaint himself with this variability as estimated by his own laboratory for each of its laboratory procedures, so that he may decide whether two tests on the same patient can reasonably be judged to be different. A simple, somewhat oversimplified rule of thumb is not to consider two test results which are within three standard deviations of each other (the standard deviation in this case estimated from daily quality control samples) to be significantly different—or to indicate a possible laboratory error—unless they *should* be different and do not appear to be. There are two general sorts of analytic error—those that effect all the unknowns in the batch in the same direction (bias) and those that strike randomly. The systematic error or bias can result from deteriorating standards, a bad reagent, improper instrument setting or operation. All laboratories have or should have an adequate daily control program whose primary purpose is to detect this sort of error, so that it can be corrected before erroneous results are reported. Random errors, on the other hand, are generally not detected by the usual quality control program. They can result from pipetting errors, an intermittent instrument failure, a random calculation error or from the lack of specificity of the tests coupled with an abnormal concentration of some other substance in the sample. They can be minimized by good procedures, good instruments, good instrument maintenance and well-trained, careful technologists. All calculations should be performed independently by two different laboratory workers and results should, whenever possible, be compared with previous results on the same patient or with other tests performed for the same patient on the same day with an eye to their compatibility. Unfortunately, since errors can be in either direction and of any magnitude, there is really no greater reason to subject abnormally high or low

results to closer scrutiny than normal results (unless results are incompatible with life or ridiculously abnormal). There does exist the possibility of greater liability of significant inappropriate therapeutic intervention on the basis of abnormal laboratory results, but lifesaving intervention not initiated because of an erroneously reported normal laboratory value can be similarly threatening. The physician ordering the test can be of assistance by informing the laboratory if, judged by other information available to him, it appears likely that a laboratory error has occurred. The laboratory director should encourage this type of feedback and should see that each instance is investigated thoroughly. The laboratory should indicate a willingness to repeat the test on a freshly collected sample without additional charge—certainly if the first result was erroneous, and probably even if the first one was not in error, provided, of course, that the clinicians do not abuse this opportunity.

Even if the analytic procedure is reasonably specific and the result is accurate, there are still pitfalls awaiting the unwary interpreter. These pitfalls result from intra- and interpatient variability and the many unsolved problems related to normal values and interpretation of laboratory test results.

In summary, numerous pitfalls await anyone brash enough to accept laboratory data in an unqualified fashion. Errors result from improper patient preparation, improper specimen collection and preservation or identification, drug interference and technologist, glassware, reagent or instrument failure. Errors can be minimized by education, interest and cooperation among clinicians, laboratory directors, nurses, technologists and all others involved. Such errors cannot ever be completely eradicated. It bears repeating, therefore—*never undertake potentially serious action on behalf of a patient solely on the basis of a single laboratory test result.*

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