Perspective on the Clinical Laboratory: New Uses for Informatics

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Enhanced capabilities of modern information systems will have a major impact on the way that clinical laboratories generate diagnostic information and transmit that information to their physician clients. This article provides a perspective on how some of the most imminent changes in informatics are likely to alter laboratory

practices and to create new roles for the clinical laboratory through the ability to manage vast quantities of information. The areas covered include utilization of laboratory services, process control in the laboratory, interpretation of test results, and laboratory economics. *J. Clin. Lab. Anal.* 13:53–58, 1999. © 1999 Wiley-Liss, Inc.

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INTRODUCTION

The intention of this article is to generate insight into some of major challenges facing clinical laboratories today for which vastly improved information systems promise solutions. Modern information systems have the potential to restructure how physicians access and use physiologic information from their patients. This discussion elaborates on one of the themes developed in the editorial that appears in this issue by Robert M. Nakamura, M.D., on the future direction of the clinical laboratory (1).

This article focuses on several different aspects regarding the generation and dissemination of diagnostic information. They include physician utilization of laboratory services, process control in the analytic laboratory, interpretation of test results for individual patients and for larger population groups, and stabilization of laboratory economics. These areas correspond roughly to pre-analytic, analytic, and post-analytic activities plus an additional category of billing and collecting fees for providing the clinical information derived from laboratory testing. Attention is also given to some of the major challenges now facing clinical laboratories for delivering services while remaining in compliance with changing regulations.

PHYSICIAN UTILIZATION OF LABORATORY SERVICES

The use of laboratory services by physicians really begins as a conceptual process (pre-pre-analytic phase) during the formulation of a differential diagnosis and a diagnostic plan (Table 1). The physician often decides which tests to order based in part on what is abnormal from history and physical examina-

tion; however, much testing is done because the physician is uncertain about the patient's condition and needs more objective information to arrive at a diagnosis. Physicians vary markedly in their use of laboratory testing at this stage. Consequently informatics has the opportunity to make physicians more effective as diagnosticians by prompting them to order the most appropriate tests for an individual patient while steering them away from other tests that will yield information that is either redundant or has no value for that particular patient.

Utilization extends further through confirmation of a diagnosis and subsequent visits to monitor the effects of treatment. It may last many years or even life-long for monitoring drugs such as digoxin, coumadin, etc., which may be administered for the rest of a patient's life. Efficiency of ordering laboratory tests over the long term may also be improved through use of an information system to guide physician choices. In this context, it is important to distinguish between having a computer making choices and having the computer present to the physician a list of choices ranked according to potential benefits and costs. The latter approach is preferable because it maintains physicians as decision makers and draws on their years of clinical experience while operating under standard protocols to optimize care.

The area of wellness testing provides an excellent example of how advances in information systems could improve medical care by keeping track of a complex set of testing guide-

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TABLE 1. Physician Utilization of Laboratory Services

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- Pre-pre-analytic phase/conceptualization
 - Wellness testing
 - Practice parameters
 - Expectation for good quality care
 - New procedures evaluated through patient outcomes
 - Information systems
 - Laboratory
 - Hospital
 - Billing
 - Ranking of tests by true medical utility
-

lines. The two basic strategies in wellness testing are: (1) screening all individuals; and (2) testing only those persons who present to a physician for some other reason (i.e., case-finding method). A common example of screening is fecal occult blood testing on an annual basis for an entire adult population, a maneuver that has been shown to reduce mortality from colorectal carcinoma by one third due to early detection of curable cancer (2). An example of recommended case finding is to test thyroid function (by measurement of TSH and free thyroxine) in any woman aged 50 years or older who visits a physician for any reason (such as an upper respiratory infection). Even though there may be no apparent link between the presenting condition and the disease being tested for, the resulting yield of positive cases is more efficient than that from screening an entire population.

Recently the College of American Pathologists (CAP) published a practice parameter that lists laboratory procedures for which consensus exists among several different medical societies for performing tests to detect predisease states in asymptomatic individuals (3). The full list of testing recommended by the CAP practice parameter includes screening the general adult population for total cholesterol, high-density lipoprotein cholesterol, serum iron and transferrin saturation, cervical cytology, and stool for occult blood. For adults the practice parameter recommends a case finding approach for blood glucose in pregnant females, in persons with demonstrated hypercholesterolemia, and in other selected patients; thyroid function tests in selected adults and for demonstrated hypercholesterolemia, serum creatinine and urea nitrogen for demonstrated hypercholesterolemia; and prostate-specific antigen with digital rectal examination. Subsequently the American Diabetes Association issued an updated guideline to screen for diabetes mellitus and gestational diabetes which lowered the upper limit of normal blood glucose to correspond to concentrations at which diabetic complications begin. It also expanded the population base for recommended testing (4). Implementation of all these recommendations is complicated, and some are likely to be forgotten without prompting from an information system.

Practice parameters are important because they establish the minimum of good care that physicians are expected to provide for their patients. Adherence to these expectations is now monitored by insurance companies (e.g., health mainte-

nance organizations) to guarantee that the physicians they pay actually provide the minimum of good quality care. On the other hand, insurance companies do not wish to pay for medically unnecessary services that do not have values for detecting diseases (especially ones for which no successful treatment exists). And yet new procedures are constantly being introduced through research, and new commercial assays are being cleared by the Food and Drug Administration and sold. How are the payers for medical services to know which of the new procedures and which of the long-established ones are worth supporting? The most deliberate way to answer this question is to examine large numbers of patient outcomes based on the procedures in question. This type of evaluation requires information that typically resides in many different data bases: a laboratory information system has patient test results; a hospital information system has clinical findings, diagnoses, and treatments from both inpatient and outpatient encounters; and a billing/accounting information system provides financial data regarding the costs of laboratory and other medical services. The challenge is to integrate all of these different data collections over a large enough patient base (preferably at multiple medical centers) so that the efficacy of any particular procedure can be adequately judged.

The long-term payoff from this type of statistical examination will be to distinguish laboratory procedures and to rank them according to their true medical utility. The alternative is to allow individual physicians to continue ordering tests according to their own preferences which are generally influenced and weighted by their most memorable clinical experiences rather than by a thorough examination of all outcomes from all patients. Fully informed decision making may be achieved by using all the relevant data bases with very powerful information systems that can let physicians know just how useful procedures can be in any particular clinical situation.

PROCESS CONTROL IN THE ANALYTIC LABORATORY

Clinical laboratories have very complex and comprehensive protocols for monitoring the quality of analysis in testing patient samples for individual analytes (Table 2). These procedures are exemplified by Levey-Jennings control charts and the Westgard rules which set conventional criteria for accepting or rejecting patient results according to accompanying measurements of quality control samples with previously determined target values (5). The Westgard rules established reasonable and readily adhered-to criteria to detect not only major shifts in analytic precision but also to anticipate deterioration of an assay by monitoring its long-term drift (6). The wide acceptance of these rules and others for monitoring quality control has made the analytic event on automated instrumentation probably the most regulated step in the clinical laboratory. Accordingly the analytic precision of most automated chemistry, hematology, coagulation, therapeutic drug

TABLE 2. Processes for Improvement in Specimen Handling Through Informatics

Analytic quantitation
<ul style="list-style-type: none"> • Quality control on instrument • Quality control between different instruments/different locations • Quality control for point-of-care testing • Record keeping for distributed testing
Specimen identification
<ul style="list-style-type: none"> • Collection (includes proper samples) • Transportation to the laboratory • Processing and aliquot formation • Tracking specimen/aliquot movements within the laboratory • Analytic phase on instrument • Results verification • Storage • Retrieval for repeat/add-on testing • Disposal vs. long-term retention

monitoring, immunology, and other instruments is no longer a major priority for improvement in clinical laboratories.

The new challenge for many laboratories is to establish consistent results between different institutions that have been linked operationally through various business relationships ranging from outsourcing some fraction of testing to complete mergers between laboratories at different hospitals. In these cases, it is desirable to have identical reference ranges for the same analytes even though they may be measured on different instruments or even on similar instruments at different sites. Physicians who practice at multiple locations strongly desire this level of continuity to avoid making errors in diagnosis or treatment that may arise due to a misunderstanding of reference ranges from site to site. Thus information systems should have the capability of relating quality control results from different laboratories and judging what degree of deviation from expected target values should prompt corrective action.

A further extension of this scenario is evident in the proliferation of bedside and other point of care testing (POCT). The majority of patient and quality control results generated by POCT probably resides on individual pieces of paper and so is not integrated into a comprehensive data base such as an electronic permanent patient medical record. Preliminary efforts have attempted to collect POCT results by interfacing these instruments directly to large laboratory information systems (7). This task can be monumental when considering recent growth in the number of inpatient and outpatient locations where POCT is practiced. Furthermore, even though many POCT procedures such as glucose, electrolytes, blood gases, and coagulation can be done on hand-held or mobile instruments that can be interfaced electronically, other assays such as dipstick urinalysis, pregnancy testing, bacterial antigen tests, and fecal occult blood, are manual. Those results must be entered by hand into a computer if they are to be captured for long-term care purposes.

With analytic error minimized through extensive use of

quality control and cross-instrument checks, one of the next most important improvements to make in clinical laboratory processes will be in reducing the number of mislabeled specimens. Improvement in specimen identification begins at the time of collection and extends throughout the various steps of transportation to the laboratory, processing, testing, and specimen disposition.

It is desirable to label a specimen uniquely with the following elements: patient name, medical record number, location, time and date of collection, tests ordered, and physician name. Many institutions still use patient-specific labels that are printed in batches for multiple purposes including pharmacy, radiology, and others in addition to the laboratory. This process requires an additional requisition form to travel with the labeled sample to distinguish it from all other samples collected from that patient. Additional paper leads to more work and more opportunities for error in transcription or for bundling forms with the wrong samples. Unfortunately, most specimens collected at sites distant from the testing laboratory follow this mode of labeling with a separate requisition form, which greatly increases the overhead for handling those samples. A specimen-specific label should contain all the elements necessary to identify the specimen uniquely, thus obviating the need for an additional requisition sheet. A modern information system should be capable of printing labels using some modality such as bar coding for unique identification (8).

Most so-called laboratory errors probably occur at the time of collection due to labeling errors or inadequate attention to proper venipuncture technique. Laboratory-directed employees have a far lower rate of unacceptable specimens due to mislabeling, improper tube, clotted blood, etc., compared with other personnel such as nurses and doctors (9). Better performance by laboratory personnel in the collection phase may be due to the expertise of staff dedicated to that task. It also may be due in part to the feedback that specimen collectors get from their peers and supervisors who see the immediate impact of unacceptable specimens in the laboratory. An information system could provide similar feedback to all medical personnel who collect specimens. Without critical review of their performance, most persons will assume they are doing an adequate or even excellent job; shortcuts that impair specimen quality will be learned and passed on to others if no negative feedback occurs. Thus total monitoring of specimen quality starting from the point of collection should be a goal for modern information systems.

Unique specimen identification is essential for the entire sequence of events following collection. The specimen must be routed through the most appropriate means (e.g., pneumatic tube, manual transport, courier between buildings) and required conditions (e.g., ambient temperature, refrigerated, frozen, warm, protected from light) and to the correct location. Thus transportation with destination and mode of travel should be sorted out by an information system and linked directly to specimen identification.

Upon arrival at the laboratory, accessioning is tremendously accelerated by scanning bar code labels. Automated aliquot formation should be controlled by an information system that generates labels for those aliquots that correspond exactly to the unique identifying label on the primary collection tube. New robotic systems from several manufacturers show promise to deliver those samples or aliquots directly to analyzers without operator intervention unless special handling circumstances arise (10,11). Patient results may be automatically verified by an information system if they are within established limits, or they may be rerun with an automatic prompt. Samples and/or aliquots are generally stored for several days after testing to allow for physician requests to repeat or add on other tests. Most institutions have inadequate procedures for storing and retrieving samples and much labor is expended in finding old samples. An information system should organize and direct this process. And finally, when outdated samples are to be disposed of, should they be discarded or should some be retained for research, for validation testing of new assays, or for medical-legal purposes (e.g., the primary tube of an HIV positive result)? The information system should use preset criteria to direct the disposal/retention process. In summary, tracking the overall movement of specimens and aliquots throughout a laboratory should be the domain of a powerful information system that prioritizes and directs the flow of analytic processes and specimen handling.

INTERPRETATION OF TEST RESULTS

Clinical laboratories are in the information business; they generate test results and sell that information to physicians. The ease with which physicians can access and comprehend clinical diagnostic information may influence their choice of which laboratory to use. Information systems that enhance these functions will have a competitive market advantage. A new generation of information systems also should have the ability to sift through an enormous amount of clinical laboratory data and to add value to each result by putting it into a larger context (Table 3) (12).

Individual Patients

The most rudimentary of information systems simply conveys requests for testing, transmits test results back to the physician, and bills the patient or insurance company. That level of activity is little more than simple bookkeeping. Ideally, a powerful information system would maintain all results generated on a patient forever and be able to relate laboratory results to other clinical information from radiology, pharmacy, and physician notes in a wholly integrated medical record. This birth-to-present record should also be portable so that it can be immediately available to any physicians who may treat a patient and at any location within a region or even at distant cities. Use of a longitudinal medical record lends itself to fine-tuning the interpretation of laboratory results, an example of which is personalized reference ranges for individual patients.

TABLE 3. Interpretation of Test Results

Individual patients
<ul style="list-style-type: none"> • Life-long record of results • Integrated medical record • Individualized reference ranges • Artificial intelligence, neural networks, fuzzy logic, simulation • Expert rules to recommend follow-up testing • Esoteric test use • Genetic testing • Inpatient monitoring
Population groups
<ul style="list-style-type: none"> • Screening populations for trends (nutrition, infections, etc.) • Epidemiology through linked information systems • Evaluation of new instrument capabilities
Management of test results
<ul style="list-style-type: none"> • Repository of clinical laboratory results • Mining large data bases for new knowledge • Establishing minimum of testing for efficient screening and monitoring • Professional responsibility and intellectual curiosity

Various forms of smart system capabilities may be implemented for analyzing a patient's laboratory record. These include artificial intelligence, neural networks, fuzzy logic, and complex simulation programs that model the body's physiology and can predict the effects of various treatments in an individual patient based on all that is in the patient's record. A smart system should aid the physician in complex situations by using expert rules to recommend additional tests to follow-up on preliminary findings. This assistance may be most useful when considering esoteric procedures with which the physician has little personal experience (e.g., coagulation, immunology, metabolic diseases, genetic testing, and other special studies).

Patient care is divided into episodes with markedly different intensity, all of which should be handled by the same smart information system. The majority of a lifespan is covered by wellness testing during which asymptomatic patients should be tested at regular intervals for disease that may arise at a later age. The goal is to minimize human suffering and financial costs by treating diseases before they do irreversible damage. Wellness testing is complex in the number of different tests offered for particular patients and at what ages and intervals; a smart system would track such testing and prompt physicians and patients to keep to schedule. The ultimate in wellness testing is genetic testing, an area that is currently being both explored and debated (13). Although technically feasible for many hereditary diseases, genetic testing is still relatively expensive and requires a great deal of technical and professional interpretive expertise. A powerful information system would be very helpful in assessing which persons will benefit the most from specific genetic tests by calculating a composite risk based on multiple factors.

Finally, the intensity of care and the density of laboratory

results is highest for inpatients, particularly when monitoring is done for intravenous fluid and drug therapy. The mathematical modeling of patient physiology plus graphical presentation will add a new tool to aid physicians in predicting individual patient response to therapy and for taking action when the predicted response does not occur.

Population Groups

Information systems have the ability to sort through results from entire populations of patients thereby searching for trends in the general health within a medical center. Algorithms can search for composite features such as nutrition using both chemistry results (e.g., albumin, prealbumin, other proteins) and hematology results (e.g., hemoglobin, cell counts, erythrocyte indices) which are commonly ordered. Patterns in community-acquired and nosocomial infections may also emerge from systematic review of results; antibiotic resistance should also be monitored. The role of medication in causing side-effects such as renal failure, hepatic failure, or peripheral cytopenias due to bone marrow failure may also be documented through coordinated review of therapies and laboratory results through an interface to a pharmacy computer. Side-effects from drugs may go unnoticed unless a conscious effort is made to detect them (14), a tedious and labor-intensive process that should be done by an information system. A further extension would be to link information systems throughout a geographic region so that epidemiology can be incorporated as an automated monitor for the general public health.

Population studies may also be useful to the clinical laboratory when evaluating a new instrument with enhanced capabilities. At present, significant new analytic capabilities are emerging on hematology analyzers for better cell counting precision (especially at low platelet counts), for performing a highly precise enumeration of immature granulocytes (much better than manual band count), for automated reticulocyte counts, and for lymphocyte surface markers. What is the clinical need for any of these enhancements when applied to all routine specimens? The answer lies in massive data sets of patient results once those new methods come into practice.

Management of Test Results

In the overall management of test results, clinical laboratories are the repositories for literally millions of pieces of data. Information systems should provide secure storage of those data so they are not intercepted by unauthorized persons while they do remain readily available to physicians. The wide use of the Internet for business, education, entertainment, and other aspects of our lives will also encourage physicians to communicate professionally using Web-browser technologies. Patient confidentiality may be at risk unless highly sophisticated security routines can be employed on the Internet for transmission of laboratory results.

Although numerical data such as measurements of chemi-

cal and hematologic analytes are readily stored in a form that can be searched, others such as qualitative or textual results from bacteriologic culture with specific organisms and antibiotic sensitivities are not. These data elements must be stored in a readily searchable data base. A typical search in this instance might look at numbers and types of organisms from positive blood cultures or the antibiotic sensitivities of all isolates of each bacterial species cultured in a twelve-month period. The structure of the data base and how the elements are formulated are crucial to the ability to search and use those data in a meaningful way.

Once data elements are coded in a searchable format, we can expect to mine large data bases to identify and to quantify relationships between analytes not previously suspected. This approach may uncover new knowledge; it will certainly define what are the efficiencies of tests in screening for and monitoring disease. Whatever redundancy exists in today's testing protocols may be better defined with an information system searching for improved diagnostic efficiencies.

What leads us as laboratorians to build and maintain clinical data repositories? There are at least two significant motivations. One is the professional responsibility to make the data base as good as it can be for the benefit of patients and society. Another is sheer intellectual curiosity about one's own profession and about the data generated in a laboratory. We should be intensely interested in how it can be used most effectively for medical care.

STABILIZATION OF LABORATORY ECONOMICS

By virtue of their leadership in technology and administration, laboratorians have recently been drawn into a whole series of actions concerning laboratory economics (Table 4). Just as laboratorians have the responsibility for internal operations, they also have the responsibility for the financial well being of their enterprise. In this regard, billing for services rendered has become a challenge because of all the information required to submit a bill. If the process is not done correctly, no payment is received, and the laboratory may ultimately have to go out of business if its revenues do not cover operating costs. Accordingly, all parties who supply goods

TABLE 4. Stabilization of Laboratory Economics

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- Responsibility for financial well being of enterprise
 - Completeness of billing for services rendered
 - Medicare reimbursements for outpatient care
 - Medical review policies
 - ICD-9
 - CPT
 - Billing errors now considered illegal
 - Hospital and laboratory compliance plans
 - Balanced Budget Amendment
 - Negotiated Rule Making Committee
 - Central issue: medical necessity and its documentation
 - Future policies and informatics resources
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and services to laboratories should also have an interest in billing accuracy and completeness.

The myriad requirements now imposed (and frequently changed) to bill for services is itself a substantial challenge for an information system to control; and much billing may be rejected or not done at all because of inadequate documentation. One solution is a comprehensive informatics approach to billing with the realization that changes in billing procedures imposed by insurance carriers must be accommodated rapidly to avoid denial of payments. The reality is that large billing systems today require substantial programming efforts to respond to changes in policy coverage. Thus insurance carriers have a strong incentive to continue making changes because they will most likely not be billed for some fraction of services during the lag phase when laboratories or their hospitals are making adjustments to their billing routines.

In the United States, billing procedures for outpatient services covered by Medicare and Medicaid have become a major focus of attention as the federal government has changed its requirements. Different local medical review policies have been in place for years for selected laboratory procedures to delineate which diagnoses are acceptable for reimbursement by Medicare intermediaries. The basic format consists of matching the code for diagnosis (commonly used as the International Classification of Diseases, 9th Revision or ICD-9) against the code for the test (Current Procedural Terminology or CPT). In the past, if the diagnosis did not support medical necessity for the test, payment was denied. More recently, the federal government has taken the position that billing for medically unnecessary tests (according to medical review policies) is illegal. Thus laboratories can no longer bill Medicare or Medicaid for tests that they have performed at a physician's request if the ICD-9 code does not support that CPT. If they do bill for ICD-9/CPT mismatches, they risk sanctions such as fines and criminal prosecution.

Virtually all laboratory tests of substantial volume will soon fall under national medical review policies that have been drafted by the Negotiated Rule Making Committee working under mandate from the Balanced Budget Act of 1997. That committee included representatives from laboratory and medical groups as well as from the Health Care Finance Administration. They were charged with establishing new coverage policies through consensus and with the advice of several advisory work groups.

At this time, the central issue for laboratories is to document the diagnosis for an outpatient encounter to support the CPT of a procedure. If the physician's diagnosis does not establish medical necessity, then the patient is to be asked to assume financial responsibility by signing an Advanced Beneficiary Notice that specifies which tests will not be covered by Medicare. This whole process is complicated and difficult to complete, and it requires substantial computer power and software to implement it successfully. Most laboratories are

still working on ways to comply with it and with other aspects of the new dictates for proper behavior.

What does the future hold for new policies and for the expectation that informatics can contribute to solutions? Whatever is proposed, speed of implementation will be paramount.

SUMMARY

This article provides a perspective on current issues in the clinical laboratory for which solutions will entail manipulation of information in new ways. The areas covered include assisting physicians in ordering tests, improving efficiencies within laboratories, interpretation of tests, and financial responsibilities. The common theme through all these points is that they can all benefit from powerful information systems. The potential market for such systems is very large because virtually all laboratories will need to deal with the same set of problems and to comply with expectations from physicians, insurance carriers, and governmental regulatory agencies.

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