Plenary Lecture

Bringing HELP to the clinical laboratory – use of an expert system to provide automatic interpretation of laboratory data.

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Introduction

In this paper we shall describe a routinely used and effective computer-based system for assisting the clinician in the role of decision-maker. We will first briefly discuss the philosophical issues associated with automated decision-making systems, then describe in detail how the system functions. In conclusion, we will discuss the areas in which we currently use data from the clinical laboratory for decision-making purposes and describe our evaluations of the automated decision-making aspects of the system.

Philosophical issues in automated decision-assistance

The volume and variety of clinical laboratory tests has substantially expanded during the last decades. This increased utilization has caused two types of problems for clinical pathologists: (1) they must assume increased management and production responsibilities, and (2) they must play a more active role in assisting their clinical colleagues to appropriately use, and interpret, the results of laboratory tests.

To manage the increased volume of tests performed in the laboratory, to provide more rapid results-reporting, and to ensure adequate records for the financial aspects of providing health care, most modern laboratories have turned to computer-based laboratory information systems. In such systems, many of the high-volume analysers have been directly interfaced to the information system. Although these systems have measurably improved the management and production of clinical laboratories, the main impact of these systems on improved patient care to date has been to improve the rapidity with which test results for the correct patient can be reported and to improve methods of quality control.

It is the goal of a new generation of computer programs to go beyond the management functions which are currently provided by laboratory information systems. These new systems can transfer the expertise (knowledge about laboratory tests) of trained clinical pathologists, as well as test results, to the physicians who are directly involved in patient care. In other words, computer programs have been developed and are continually emerging which can substantially assist the practising physician to interpret the meaning of laboratory test results for individual patients, e.g. convert numbers to diagnostic or therapeutic information. Over the years, algorithms and mathematical models[1,2] have been developed to interpret laboratory results, and thereby increase the efficacy and clinical impact of laboratory tests. By using traditional programing techniques these algorithms have been, or could be made, available in currently available commercial laboratory information systems.

In contrast to these traditional 'hard-coded' programs in which the algorithmic logic or expertise is embedded directly in the computer instruction codes, another approach to providing expert consultation has emerged during the 70's and 80's. In this latter approach the interpretive and clinical expertise (knowledge) is stored separately from the computer program that uses this knowledge to interpret clinical data (facts) about a patient. When the clinical expertise is stored in this separate representation it is referred to as the 'knowledge base' of a system.

There are several advantages to this knowledge-based approach. A single control program (sometimes called the 'inference engine') can function across broad areas of medical applications if the appropriate expert rules for multiple

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subspecialties are contained in the knowledge base. The clinical expertise and interpretative rules in the knowledge base can be reviewed, modified and expanded independently by clinicians who are not required to have programming capabilities. Any biases, judgements or logical errors remain exposed for scrutiny and discussion by the clinical, rather than the programming community. The independent representation of medical knowledge may also contribute solutions to the, as of yet, unanswered dilemmas regarding the responsibility and liability associated with the use of decision-making systems. This approach also allows the breadth and power of the system to be improved by adding to and modifying the knowledge base in a modular fashion.

'There is nothing magic' about knowledge-based systems. In a hard coded program the programmer must have explicitly foreseen every branching point in an algorithm. Such deterministic protocols or algorithms can have a positive impact on healthcare. However, traditional programs are most appropriate in non-complicated, straightforward situations where the logic is well defined. If there are complicated situations, the separate knowledge-base approach lets appropriate rules be applied to situations which the knowledge-base authors did not explicitly foresee or solve in advance. In order to accomplish this goal the computer must explicitly investigate all pertinent pathways. The trade-offs between the methods often involve issues of efficiency. It has generally been recognised that the power which leads to superior performance of a computer system comes from the richness and content of the expert knowledge contained in the program rather than the language or style in which it is programmed.

In order to implement in a practical manner a knowledge-based system for clinical decision-making we accomplished three tasks: (1) the decision-making system is embedded within a comprehensive clinical information system, (2) the knowledge base, though separate from the decision-making program, is constructed in a very modular, procedural representation, and (3) the appropriate decision logic is activated whenever data (facts) referenced in the decision criteria are stored in the clinical information system. This mode of activating the expert logic is known as a 'data driven' activation strategy. Based upon this philosophy, the user receives consultation in the form of likely diagnoses, interpretation of laboratory tests, alerts, or contraindication warnings about asking for assistance. The problems associated with an incomplete knowledge base are only partially solved with this approach; the program gives advice when it is able to speak authoritatively, but remains silent when it does not have any knowledge or facts about the problem.

Functional implementation of the HELP system

For the last decade we have been routinely performing automated medical decision-making in a clinical setting. The hospital-based decision-making system is known as HELP (Health Evaluation through Logical Processing)[3] and a key feature of the system is the integration of administrative data-processing functions as well as collection of clinical data from many sources to form a comprehensive clinical database. The resulting system thus has test-ordering, results-reporting and charge-capture capabilities as well as automated interpretation of clinical-data, alert-generation and diagnostic functions.

There are three major advantages for an approach in which the decision-making system is integrated with an on-line clinical database. As we have discussed, one of the most important is the fact that the decision-making capabilities can be automatically evoked whenever new data are added to the patient record.

A second advantage is that the entire computerised medical record (not just information from the clinical laboratory) can be used to provide clinical facts that are referenced in the decision logic. Thus, a patient with a negative sputum culture might still be identified as having a hospital-acquired pneumonia because of radiology findings or information provided by respiratory-therapy technicians.

The third advantage is that such a comprehensive collection of clinical data becomes the primary source which is used to review patient information. Administrative and management personnel rely on the system to capture charges and costs. Recognition of the central importance of this clinical database ensures that all involved personnel have vested interests in keeping the patient data accurate and up to date.

In the sections which follow we shall describe the overall functional design of the HELP system, then discuss specific issues relative to the inference capabilities and the data-driven logic-activation mechanism.

As can be seen in Fig. 1, the system essentially consists of three major components: a comprehensive clinical patient database, a separate knowledge base that contains expert logic, and an interpreter that controls the evaluation of the expert knowledge.

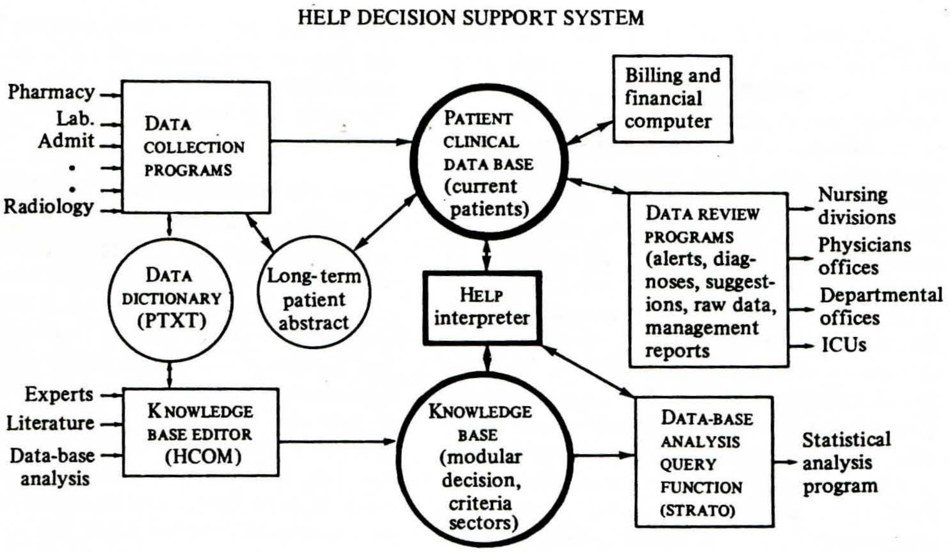

FIG. 1

Those elements in the upper half of Fig. 1 (data-collection programs, the long-term-patient file, the current-clinical-patient file, the reporting functions and the link to the financial system) are standard components that may be found in some currently available hospital information systems. The central clinical database integrates data from, and communicates with, computer systems in ancillary departments in order to allow test ordering and results review throughout the hospital. In our 520-bed hospital we presently have 361 terminals and 86 printers attached to a central system which is composed of a cluster of eight computers.

The long-term file contains on-line data for all previously admitted patients and consists of abstracts of clinical and demographic information likely to be useful if a patient is readmitted. The clinical data base contains all data gathered during the current admission. After a patient is released from the hospital the patient's record is stored in archives which are available for statistical assessment.

In order to facilitate the use of the patient-specific information that is contained in the clinical database, it must be stored in some uniquely identifiable form. In our system, clinical data are stored in a coded format which is defined using a data dictionary. The data dictionary is necessary in order to allow those who write programs to acquire patient data, build the logic contained in the expert knowledge base, or construct report formats to accurately reference specific data which may be stored in the patient database. We have chosen a coded format for the stored data in order to facilitate the rapid retrieval of data which are referenced in the decision-making logic and to allow the use of hierarchical relationships among medical terms. Other developers of knowledge-based systems have used uniquely defined symbols. As long as the user is insulated from the necessity of actually seeing the codes, the distinction between codes and symbols is somewhat artificial. In our case the codes are retranslated to display the medical terminology to those who review the data.

Another feature of the dictionary is the ability to define charges, fees and costs associated with an element (entity) in the dictionary. This feature allows creation of an entry in a transaction log whenever a laboratory test is ordered for a specific patient. The automated results reporting process confirms that the test has actually been done and the financial aspects of the transaction are transferred to the separate accounting computer. In this way, the clinical information system performs a 'charge capture' function and has improved the accuracy of the hospital's accounting procedures.

The HELP system also has general tools for creating report formats. In the intensive-care units of LDS Hospital the clinical-laboratory results, medications, input/output balances, etc., are listed in an integrated report which is organized around a systems-review/morbidity-index approach. In this report the laboratory data for blood gases and electrolytes are found in a different section from the creatinine and BUN

TABLE 1. A HELP frame which contains the decision logic for identifying certain classes of patients which may have a hospital acquired infection.

Title: Hospital Acquired Pneumonia (16.16.10).
Author: Peter Haug
Message: 'Patient may have Hospital Acquired Pneumonia.'
Declare Variables: admission_time **as** ADMIT TIME.

purulent_sputum **as** gram_stain_wbc's **or** resp_tx_sputum where gram_stain_wbc's **is** SOURCE: SPUTUM and (GRAM STAIN: MODERATE NUMBER OF WBC'S **or** GRAM STAIN: NUMEROUS WBC'S) and resp_tx_sputum **is** RESIRATORY THERAPY NOTES: PATIENT PRODUCING PURULENT SPUTUM

late_purulent_sputum **as** purulent_sputum **from** admission_time+3 days **until NOW,**

neutropenia **as** white_count **LE** 2.0 **where** white_count **is** CBC: WHITE BLOOD CELL COUNT,

surgery **as** OPERATIVE RECORD.

positive_chest_xray **as** CHEST XRAY FINDINGS: PULMONARY INFILTRATE/CONSOLIDATION

late_positive_chest_xray **as** positive_chest_xray **from** admission_time+3 days until **NOW,**

positive_sputum_culture **as** SOURCE: SPUTUM and BACTERIA PRESENT.

late_positive_sputum_culture **as** positive_sputum_culture **from** admission_time+3 days **until NOW,**

previous_admission **as** LAST ADMISSION **from** 30 days ago,

early_negative_chest_xray **as** early_chest_xray **and not** early_positive_chest_xray **where** early_chest_xray **is** CHEST XRAY FINDINGS **from** admission_time **until time of** positive_chest_xray **and** early_positive_chest_xray **is** CHEST XRAY FINDINGS: PULMONARY INFILTRATE/CONSOLIDATION **from** admission_time **until time of** positive_chest_xray.

Logic: If previous_admission **and** (purulent_sputum **or** neutropenia) **and** (positive_sputum_culture **or** positive_chest_xray) **then conclude,**

Else If (early_negative_chest_xray) and (neutropenia **or** late_purulent_sputum) **and** (late_positive_sputum_culture **or** late_positive_chest_xray) **then conclude,**

Else if surgery **and** positive_chest_xray **and (time of** positive_chest_xray – **time of** surgery **GE** 3 days **and time of** positive_chest_xray – **time of** surgery **LE** 10 days) **then conclude.**

Evoke: If purulent_sputum **or** positive_chest_xray **or** positive_sputum_culture

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measurements of renal status. In other settings the physician chooses the 'Lab Data' option on a computer terminal, sees a list of all tests performed on the patient of interest, and after selecting a test sees the time-ordered sequence of results for that test.

The elements in the lower half of Fig. 1 represent the additional features necessary for a decision-support system (knowledge-base editor, knowledge base and the HELP interpreter). The expertise contained in the knowledge base can be obtained from opinions of experts, the medical literature, or statistical experience represented in the patient database. The knowledge is stored as compiled 'HELP frames' which contain the logic necessary to make a specific decision. Because the knowledge representation in the HELP system is procedural (the frames themselves contain the logic which determines how they are to be evaluated), the medical-knowledge base supports a variety of decision-making models (IF... THEN... rules, patient-specific likelihood scores for ranking possible diagnoses, query for 'important' missing data, etc.).

The logic contained in the frame depicted in Table 1 contains criteria used to recognise patients who may have a nosocomial pneumonia. The bold face terms in the frame are syntactical and structured commands within the continually evolving HELP language. The top three headings of the frame give the title by which this frame is known in the knowledge base, the author, and the message that will be displayed if the logical criteria contained within the frame are satisfied. In order to qualify properly, the terminology which is used in the logical rules, the terms (variables/symbols) used in the rules are *declared.* These declarations refer back to terms (denoted by capitalised words) which are defined in the data dictionary. A powerful part of these declarations is the use of chronological constraints as well as qualification regarding the value for a variable.

The use of these defined terms in the logic section of the frame will cause the computer to search for existing data, trigger the evaluation of additional HELP logic modules, or ask for missing but desirable data. The procedural logic is written in a slightly structured, but understandable, language. The *logical criteria* in this case are a series of IF... THEN... rules.

The data-driving triggers are listed under the *evoke* heading. Whenever the laboratory reports a purulent sputum or a radiologist reports a chest radiograph with evidence of infiltrates or consolidation, the frame is evaluated. When new results are stored in the patient record or a specific block of frames (rules) in the knowledge base is otherwise activated, the compiled logic in the appropriate HELP frames is evaluated by performing the necessary queries to the patient database to see whether the data specified in the logic exist for the patient in question.

When the necessary criteria for a decision are satisfied, a new data string which reflects this result is stored in the patient record. This approach is sometimes called the blackboard method; when a new decision is written to the clinical database (blackboard) it may data-drive (evoke) other decisions which depend on this new conclusion as well as specified reporting mechanisms.

Interface to the clinical laboratory system

Whenever a patient is admitted to the hospital, moved to a new room, or discharged from the hospital, the central computer system notifies the laboratory computer system of these changes. The laboratory system maintains its own database of test results for internal integrity, quality control and operational functions, but results are reported by transferring the data to the central information system and storing the data in the comprehensive clinical database. When a laboratory test result is sent by the laboratory machine to the central computer it is temporarily held in a holding file (called a spooler). A translation program then takes the test results, one at a time, and translates them from the laboratory file format into the hierarchical codes used in the central database. Transferring a laboratory result to this central computer activates the charge capture mechanism in the central machine and triggers the appropriate expert logic. The blocks of this expert logic that are activated depend upon the type of test result which has been transferred. Thus, the communication between the systems is two-way: the laboratory system receives information from, and returns its results to, the central hospital system.

Experience with the decision-making aspects of the system

We currently make decisions in the many areas of medicine. The following list is not meant to be exhaustive, but rather to illustrate the variety of tasks which are addressed by the system:

Diagnosis: Pulmonary disease, anaemias, obstetrics, multi-organ-failure index, hospital-acquired infection ....

Patient management: Antibiotic usage, diet, obstetrics, ...

Data acquisition: Intelligent history, radiology findings, ...

Contraindications/alerts: Pharmacy, radiology, clinical laboratory, blood gas, ...

Test-result interpretations: Blood gas, haemodynamics, clinical laboratory, ECG, pulmonary function, electron microscopy, ...

Protocol management: Cardiac arrythmias, ...

Rather than dwell upon all of the specific types of individual decisions that the system is capable of making, we shall describe several of those applications in which laboratory data are used in combination with other sources of clinical data. These types of decisions cannot be easily generated in a stand-alone laboratory information system because they rely on the comprehensive nature of the clinical database.

Whenever a radiologic examination (Intravenous pyelorogram, vascular angiogram, etc.) is ordered in which substantial amounts of contrast media are to be injected, decision logic is triggered to ascertain the renal status of the patient. If the patient has abnormally elevated creatinine or BUN levels or other evidence of renal impairment, or if there is no evidence that the renal status has been assessed, the radiology personnel are alerted that the examination is potentially hazardous unless proper patient preparation and precautions are taken.

Data-driven decision logic is also used as the basis for our hospital's infectious-disease monitoring program.[4] Criteria have been stored in the knowledge base, which can be used to identify patients (1) with hospital-accquired infections, (2) not receiving antibiotics to which their pathogens are susceptible, (3) who could be receiving less-expensive antibiotics, (4) who receive prophylactic antibiotics longer than appropriate, (5) with infections at normally sterile sites, (6) with reportable diseases, and/or (7) with an antibiotic-resistant micro-organism. A report containing these alerts is automatically generated every day in the infectious-disease department.

Surveillance personnel using computer screening for two months identified more hospital-acquired infections than those who used traditional surveillance methods, while requiring only 35% of the personnel time.[5] During the same two-month period the computer-screening identified 37 patients (in a 520-bed hospital) not receiving appropriate antibiotics and 31 patients who could have received a less-expensive, yet equally efficacious, antibiotic. A one-month study demonstrated that the computer can automatically identify patients without evidence of infection who are receiving prophylactic antibiotics for an excessive period of time.

The infectious-disease knowledge base is also used to generate a respiratory-therapy-infection monitoring system. This program uses the knowledge base to identify patients who have conditions to which a respiratory therapist should be made aware and also for tracking pneumonias and bacteraemias which may have potentially been induced by the respiratory therapy. A daily report identifies patients with positive or pending tuberculosis, mumps, rubella or hepatitis tests, and/or patients with hospital-acquired pneumonias or bacteraemias who have also received respiratory therapy. The computer reporting programs also identify which of these patients have a common pathogen and determines whether the same respiratory therapist (technician) worked with two or more of the patients with common organisms during a specific time period.

One of the best-received and appreciated applications is the generation of pharmacy–laboratory alerts.[6] This application again illustrates the strengths of an integrated system with decision-making capability. When drugs are prescribed, the pharmacist enters these prescriptions into the computer. This entry activates decision logic which is based upon a combination of current medications as well as laboratory results. If the prescription is for a diuretic, a group of HELP frames which reference the use of diuretics in their logic are evaluated. One of these frames ascertains whether the prescribed drug is a potassium-sparing diuretic and whether the patient's present serum potassium level is within normal limits. If both of these criteria are not met, the computer suggests to the pharmacist that a potassium supplement may be advisable.

If a drug that can potentially impair kidney function (e.g. gentamicin) is prescribed when the serum creatinine or BUN levels are already high, the pharmacist is alerted that a different drug may be preferred. If a laboratory test to evaluate kidney function is not requested within 48 hours after the drug is prescribed, the pharmacist is also alerted.

After the pharmacist verifies that the suggested contraindication is valid, the prescribing physician is notified. For approximately 95% of the computer-generated alerts the physician changes the prescription. In our hospital population we find that 4% of the drugs and 2% of the patients receive pharmacy-related alerts. A large fraction of these alerts involve pharmacy–laboratory interactions. A study which estimated the costs associated with stay-extending contraindications showed that the entire pharmacy surveillance expert system was cost-effective by a 4 to 1 margin.[3] A second study showed that those patients with abnormal laboratory values came back into the normal range significantly faster if the physician or nurse was notified by the HELP system. Based upon these formal evaluations, as well as the broad acceptance of the system that has occurred as physicians have learned how to use the system, we feel confident that expert systems will play an expanding role in the proper utilization of laboratory results.

Summary

In domains where the types of data which are to be interpreted are relatively constrained (as in the case of specific laboratory test results), our modular data-driven approach can be very productive and well received by the clinical recipient of the data. The computer rarely surpasses the knowledge of an expert in the field of specialty; most of the alerts to experts result from lack of communication, imperfect memory, oversight or multiple decision-makers caring for the same patient.[7] In such cases, most of the alerts are immediately recognised as valid, so the need for elaborate explanations is not a high priority.

On the other hand, a non-specialist is alerted to the need for additional investigation, tests or collaborative support, by the fract that a reminder or diagnosis that s/he had not previously considered, appears. In other words, for the expert, a data-driven system provides unceasing oversight in high-volume low-yield situations where a small number of mistakes may uncommonly occur for reasons which are not related to the lack of knowledge of the provider. For the non-specialist the system suggests that the patient may have problems in a domain for which the physician needs additional support. In the present state of the art, we do not think that total reliance on the computer-contained knowledge is the ultimate source of this additional support; providing the awareness of the need may be the most important contribution. Once you know that you need help, it is usually obtainable.

In a discussion about how computer systems have failed, Friedman and Gustafson made the following observation. 'The great majority of computer applications to medicine, attempted to date, have been excessively modest in scope. Where in other fields the computer has been utilised to perform tasks previously incomprehensive to mankind, in healthcare delivery we have been satisfied to merely duplicate the physician. In mathematics, physics, banking, space exploration, etc., the computer is routinely called upon to perform tasks that all mankind, working 24 hours a day from creation, could not begin to duplicate, but in medicine our measure of success is diagnostic accuracy approaching a skilled clinician, ECG analysis which is substantially correct or historical data acquisition which saves the physician 5 minutes per patient. If our timidity were matched in other fields, it is very unlikely anyone could have justified the expense or the efforts necessary in these successful efforts. The disappointing impact of computer technology on medicine may have been caused by our inability ... to do more than emulate the efforts of an individual physician.'[8]

Data-driven knowledge-based systems do have the potential of doing something that no human being can logically do: scrutinise every piece of data that is collected for a patient and bring to bear the expertise of specialists regardless of the location of the patient or the time of day at which the data are collected. As the content of the knowledge base becomes richer and more comprehensive, such systems appear to be capable of tremendously improving the quality, and perhaps the economy, of medical care. In all cases, the ultimate decision-making responsibility does remain with the human clinician. Many have wondered about the legal aspects of disagreeing with a computer consultant or placing the blame if the computer gives poor advice that is heeded by a healthcare provider. In our experience the physician users generally feel that the risks that are avoided by the routine use of such a system substantially outweigh any potential legal disadvantages of such an approach.

Until now, most clinical laboratories could only deal with 'intramural' data, i.e. data which they produced themselves as a result of a request from a clinical ward or out-patient clinic. With the advent of hospital-wide computer systems or linked departmental computers, laboratories can now gain access to clinical information about the patients as well as reasons for ordering a test. When they are not required to function in a vacuum, pathologists (or the computers that contain portions of their expertise) are able to do a better job of combining clinical information and laboratory data to extend the diagnostic value of laboratory tests.

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