The Computer as a Diagnostic Consultant, with Emphasis on Use of Laboratory Data

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In this preliminary study concerning the applicability of expert computer systems, such as INTERNIST-I, to providing advice to clinical pathologists regarding patients' diagnoses and the pertinence of performing further laboratory tests, 32 complex cases, drawn from Case Records of the Massachusetts General Hospital, were analyzed diagnostically by computer, on the basis of clinical laboratory data only. Half (16 cases) were diagnosed correctly, but in 15 of the rest no diagnostic conclusion could be reached. However, no diagnostic errors were made. The study provides preliminary evidence that expert computer systems can be useful to clinical pathologists and clinical internists in guiding the laboratory workup of patients toward correct diagnosis.

Additional Keyphrases: data handling · artificial intelligence

In the past decade or so, numerous programs have been written to allow the computer to serve as a diagnostic consultant. The more elaborate of these have utilized the techniques of "artificial intelligence," in which the computer uses heuristic rules and attempts to emulate the human diagnostic process. One such program, INTERNIST-I, provides diagnostic advice in the broad field of internal medicine (1). The expert knowledge base, which is an essential component of this program, now includes about 575 diseases and more than 4000 individual manifestations of disease (demographics, historical items, symptoms, physical signs, and laboratory data of all sorts, including microbiological data and biopsies). Details of the organization of INTERNIST-I have been reported elsewhere (1). In brief, the knowledge base is constructed by "profiling" a disease entity from the broad field of internal medicine. All of the clinical manifestations of the disease are listed in the order stated above. Two numbers are assigned to each manifestation, from 1 to 5, with 5 being maximum. The first number ("evoking strength") answers the question, "On the basis of this finding alone, how strongly does the diagnostician consider this disease as compared with all others in internal medicine?" The second number ("frequency") states, that given the disease, this manifestation occurs with a certain frequency (1 = rare or minimal, 2 = a significant minority of cases, 3 = about half of the cases, 4 = a significant majority, and 5 = essentially all, i.e., a necessary component of the disease). Each manifestation is assigned a third number ("importance") indicating to the computer program how necessary it is to explain the manifestation in whatever diagnosis is arrived at.

The inference engine of INTERNIST-I considers each disease with which any positive manifestation is compatible on the basis of the evoking strength numbers. Thus no potential diagnosis is overlooked. Naturally, positive manifestations will cluster under the most probable diagnoses. Mathematical values for each of the three numbers allows a ranking of the diagnoses evoked. The list is then partitioned on the basis of similarity of support by using the best-supported diagnosis at this point as the anchor. If this leading contender has adequate support for diagnosis, it is concluded. If not, the system enters an interrogative mode to indicate what additional observations or measurements are important in the solution of the diagnostic problem. The system is also programmed with all the known interconnections among diseases ("links"). When one diagnosis is established, the program awards bonuses to linked diagnoses so that, evidence permitting, a set of interrelated diagnoses will be made.

INTERNIST-I until recently operated only on mainframe computers, e.g., DEC 2060, but it has now been adapted to the IBM PC-AT.

INTERNIST-I operates quite successfully on difficult clinical problems in internal medicine, such as clinical pathological conference cases. It is not yet available for general clinical use, because some 200 diseases remain to be profiled and entered into the program.

Program Operation

In operation, the user enters the positive and the negative observations regarding the patient, in as uninterpreted a fashion as possible. In the case illustrated (Figure 1) the computer finds many of the positive manifestations supporting the diagnosis of Wegener's granulomatosis (CONSIDERING list). The DISREGARDING list cites the items of information that are not explained by Wegener's granulomatosis. These are set aside temporarily. The PURSUING mode of diagnosis is used when the computer has strong evidence for a given diagnosis and will attempt to acquire further clinching evidence, in this case one of three biopsies. [None of these were performed with this patient; in fact, there was heated discussion among the clinicians as to whether lung biopsy or renal biopsy had priority, but the renal biopsy was given preference.] By the statement, CONCLUDE "Wegener's granulomatosis," the computer is informing the user that, in its analysis, biopsy proof is really not required even though it was recommended.

The program now looks up all interconnections of Wegener's granulomatosis with all other diseases in the knowledge base so as to make, information permitting, a set of diagnoses of interrelated diseases rather than independent ones. On reviewing the DISREGARDING list, intergran-I finds considerable evidence for renal disease. Rapidly progressive glomerulonephritis occurs in about one-half of the patients with Wegener's granulomatosis and thus is a strong candidate. Acute pyelonephritis is a competitor because it is so common and because leukocytes and leukocyte
Fig. 1. INTEREST-I diagnostic case analysis in the usual full mode

INIT: initiation of list of positive findings; NEG: negative findings; HX: history; OMIT: information requested is unknown or a procedure was not performed; GTR, greater than; N/A, a specific single item of information is not available. (S), (ES), and (IES) indicate that the word may be either singular or plural (this practice reduces greatly the number of words the computer must be able to recognize). AFFIRM is the command to return the program to a positive mode.

CAGE
CASE NAME: USP975456584
TYPE: JOURNAL
DIAGNOSIS: (TERMINATE BY "GO")
+MEDECINERS BRANIKOLAXIS
+ID
+INIT
+SEX MALE
+AGE 14 TO 25
+RESPIRATORY INFECTION UPPER RECENT HX
+FEVER
+FHMITIS ACUTE
+HEMATOCRIT BLOOD LESS THAN 35
+DYSPEA AT REST
+DYSPEPSIA GROSS
+FACE HEABO
+TACHYCARDIA
+TACHYPNEA
+CONJUNCTIVA AND/OR MOUTH PALOR
+MOUTH MUCOSA PETECHienne
+SKIN RASH VEICULAR
+CHEST MOVEMENT RESPIRATORY DECREASED BILATERAL
+BREATH SOUND (S) DECREASED GENERALIZED
+HEART MURMUR SYSTOLIC APEICAL
+URINE SPECIFIC GRAVITY STAB 1.080
+PROTEINURIA
+URINE SEDIMENT CBC
+URINE SEDIMENT RBC
+URINE SEDIMENT COARSE GRANULAR CAST (B)
+URINE SEDIMENT ERC CAST (B)
+URINE SEDIMENT RENAL TUBULAR CELL CAST (B)
+HBC 14,000 TO 30,000
+HBC ERDISPHIL (B) 5TR THAN 600
+HBC RICULOCYTE (B) 5TR THAN 5 PERCENT
+BLURBUN SERUM CONJUGATED INCREASED
+LDH SERUM 5TR THAN 150
+CHEST XRAY UPPER LUNG FIELD (B) DENSITY (IES)
+CHEST XRAY LOWER LUNG FIELD (B) DENSITY (IES)
+CHEST XRAY PLEURAL EFFUSION (B) SMALL
+OXYGEN TENSION BLOOD ARTERIAL LESS THAN 80
+CARBON DIOXIDE TENSION BLOOD ARTERIAL DECREASED
+SPUTUM PURULENT
+ABDOMEN PAIN GENERALIZED
+STUPO LETHARY OR SOMNOLENCE
+BLEEDING TIME INCREASED
+CALCIUM SERUM DECREASED
+PICES BLOOD
+MORE DISCHARGE MUCOPURULENT
+SNEEZING
+HOMOSEXUALITY MALE
+SORONOCIA RECENT HX
+HEADACHE SEVERE
+DIABORE ACUTE
+OOSBUIA HX
+COUGH CHRONIC Productive HX
+SYPHIA HX
+SYPHIA BLOOD (B)
+RAYNAUDS PHENOMENON
+HABITURIA HX
+BLEEDING EXCESSIVE AFTER MINOR TRAUMA HX
+CIGARETTE SMOKEH HX
+DRUG Abuse HX
+PRESSURE ARTERIAL SYSTOLIC 95 TO 125
+PRESSURE ARTERIAL SYSTOLIC 95 TO 125
+LUMP NODE (S) ENLARGED
+SINUS (IEB) TENDERNESS
+RENCH DIFUSE
+HETAPLOEMIAL PRESENT
+SPLENOMEDIAL PRESENT
+JOINT (B) EFFUSION
+JOINT (B) RANGE OF MOTION DECREASED
+PLATELETS LESS THAN 50,000
+PROTEOMIN TIME INCREASED
+ACTIVATED PARTIAL THROMBOPHILIN TIME INCREASED
+UREA NITROGEN SERUM 30 TO 59
+CREATINE SERUM INCREASED NOT OVER 114 MG PER DL
+GLUCOSE PLASMA FASTING 130 TO 300
+CREATINE KINASE SERUM INCREASED
+CHEST XRAY CAVITY (IES)
+PH BLOOD ARTERIAL 5TR THAN 7.5
+BOWEL SOUND (S) DECREASED
+ALBUMIN SERUM LESS THAN 3 GRAM (S) PER DL
+CHEST XRAY LUNG ADENOPATHY BILATERAL
+CHEST XRAY LUNG ADENOPATHY UNILATERAL
+SINUS XRAY OCUPANCY (IES)
+ANTIBODY MEROPEEL TITER 112 OR 5TR
+ANTIBODY GLomerULAR BASMENT MEMBRANE BY SERUM RIA
+SPUTUM BACTERIA ACID FAST/BACTERIA
+TUROBACULIN SKIN TEST POSITIVE
+SKIN TEST BATTERY NON REACTIVE
+AAA POSITIVE
+COOMBS TEST DIRECT POSITIVE
+COOMBS TEST INDIRECT POSITIVE
+COLD AGGLUTININ (B) PLASMA INCREASED
+HEPATITIS B SURFACE ANTIGEN
+ANTIBODY HEPATITIS B SURFACf ANTIGEN
+BO
+INIT
+METERS LOCALIZED
+DR
+RUN

Internist-1 consultation SUMEX-AIM Version
2-28-85 07:06:38
THE INTERNIST-1/CADUCEUS KNOWLEDGE BASE STRUCTURE AND CONTENT
ARE COPYRIGHT (c) 1985 BY JACO. S. PAYERS, M.D. AND THE BOARD OF
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collecting lists
SKAP. SOURCE FROM cells
RUNNING AT 7500S, LOAD 2.0

DISREGARDING: BREATH SOUND (S) DECREASED GENERALIZED, MOUTH MUCOSA PETE
CHINE, SKIN RASH VEICULAR, STUPO LETHARY OR SOMPLOENCE, BLURBUN SER
UM CONJUGATED INCREASED, CALCIUM SERUM DECREASED, URINE SEDIMENT COARSE
GRANULAR CAST (S), URINE SEDIMENT RENAL TUBULAR CELL CAST (S), URINE SEDIMENT
HBC, URINE SEDIMENT ERC CAST (B), HBC RICULOCYTE (B) 5TR THAN 5 PERCENT

CONSIDERING: AGE 14 TO 25, SEX MALE, ABDOMEN PAIN GENERALIZED, DYSPEA
AT REST, CONJUNCTIVA AND/OR MOUTH PALOR, FACES BLOOD (FOWER, HEMO
PYTIS GROSS, MORE DISCHARGE MUCOPURULENT, MLisa LOCALIZED, SPUTUM PURUL
ENT, COUGH CHRONIC, HABITURIA, CHEST XRAY LUNG UPPER FIELD (S) DENSITY (IE
S), CHEST XRAY PLEURAL EFFUSION (S) SMALL, CHEST XRAY LUNG UPPER FIELD (S)
DENSITY (IES), HEMATOCRIT BLOOD LESS THAN 35, PROTEINURIA, URINE SEDIM
ENT HBC 14,000 TO 30,000, HBC ERDISPHIL (B) 5TR THAN 600, CARBON DI
OXIDE TENSION BLOOD ARTERIAL DECREASED, OXYGEN TENSION BLOOD ARTERIAL LO
SS THAN 80

PURSUING: MEDECINERS BRANIKOLAXIS

Please Enter Findings of BONE MarROW BIOPSY
+INIT

(continued on next page)
casts were observed in the urinary sediment. Several non-conclusive questions are asked of the user; as a result, focal glomerulonephritis replaces acute pyelonephritis on the DISCRIMINATE list. The experienced user can tell that both acute pyelonephritis and focal glomerulonephritis are, in the first place, weak competitors of rapidly progressive glomerulonephritis. After two more questions, the program decides that a renal biopsy is the way to settle the diagnostic issue. After this is done, the user enters the positive and negative findings from the biopsy, thus allowing the system to CONCLUDE "rapidly progressive glomerulonephritis." If allowed to continue, the program would reexamine the DISREGARDING list to determine whether a third problem should be considered; actually, there is no important one in this case.

Retrospective Application

After observing a demonstration of the diagnostic capabilities of INTERNIST-I (as above), several clinical pathologists inquired as to whether laboratory data alone could be analyzed to guide further laboratory studies and thereby diagnosis. As a test of this suggestion, I selected 32 Case Records of the Massachusetts General Hospital (New England Journal of Medicine, reference citations available upon request) from cases recently analyzed by the full diagnostic format of INTERNIST-I. The only cases not selected were those in which there were only five or fewer positive laboratory findings of a quite nonspecific sort, such as a moderately decreased hemoglobin concentration or mild to moderate proteinuria. The 32 were then analyzed on the basis of laboratory data only. Gender and age of the patients were included so that the program would not consider gynecological diseases in males, etc. Microbiological studies and biopsy results were considered to be in the purview of laboratory data, but studies from special laboratories such as radiological results, electrocardiograms, pulmonary function tests, etc., were not.

Figure 2 shows an example of one of the 32 analyses. The diagnosis of malabsorption is not difficult, and the system knows that it occurs in a significant minority of instances of intestinal amyloidosis. That information plus the increase in serum and urinary light chains points to a diagnosis of
-CREATININE SERUM INCREASED NOT OVER 2.9 mg PER dL
-SCHILLING TEST B12 ABSORPTION DECREASED
-FECES GUAIAC TEST POSITIVE
-PROTEINURIA
-GLUCOSURIA
-PLATELETS LESS THAN 50 000
-PLATELETS 50 000 TO 150 000
-PROTHROMBIN TIME INCREASED
-UREA NITROGEN SERUM 30 TO 59
-GLUCOSE PLASMA FASTING 130 TO 300
-CALCIUM SERUM DECREASED
-CALCIUM SERUM INCREASED
-ALBUMIN SERUM LESS THAN 3 GRAM (S) PER dL
-VITAMIN B12 SERUM LESS THAN 200
-FOLATE SERUM LESS THAN 3 ng PER mL
-AFFIRM

*GO

DISREGARDING: IMMUNOELECTROPHORESIS SERUM LIGHT CHAIN (S) ONLY INCREASED, IMMUNOELECTROPHORESIS URINE LIGHT CHAIN (S) INCREASED

CONSIDERING: AGE GTR THAN 55, SEX MALE, CHOLESTEROL SERUM DECREASED, FECES FAT INCREASED MICROSCOPIC, XYLose ABSORPTION TEST ABNORMAL

PURSuing: MALABSORPTION

PLEASE ENTER FINDINGS OF FECES EXAM ROUTINE

*GO

FECES LIGHT SHINY BULKY?

N/A

CAROTENOIDs SERUM DECREASED?

N/A

PLEASE ENTER FINDINGS OF GLUCOSE TOLERANCE TEST

*OMIT

FECES FAT GTR THAN 7 GRAM (S) PER DAY?

N/A

CONCLUDE: MALABSORPTION

CONSIDERING: IMMUNOELECTROPHORESIS SERUM LIGHT CHAIN (S) ONLY INCREASED, IMMUNOELECTROPHORESIS URINE LIGHT CHAIN (S) INCREASED

PURSuing: GASTROINTESTINAL AMYLOIDOSIS

PLEASE ENTER FINDINGS OF INTESTINE BIOPSY

*GO

INTESTINE (SMALL) BIOPSY AMYLOID?

YES

PLEASE ENTER FINDINGS OF GASTROSCOPY

*GO

STOMACH ENDOSCOPY BIOPSY AMYLOID?

YES

CONSIDERING: IMMUNOELECTROPHORESIS SERUM LIGHT CHAIN (S) ONLY INCREASED, IMMUNOELECTROPHORESIS URINE LIGHT CHAIN (S) INCREASED, INTESTINE (SMALL) BIOPSY AMYLOID, STOMACH ENDOSCOPY BIOPSY AMYLOID

CONCLUDE: GASTROINTESTINAL AMYLOIDOSIS

DIAGNOSIS: GASTROINTESTINAL AMYLOIDOSIS, MALABSORPTION NIL

Gastrointestinal amyloidosis, which is substantiated by biopsies. INTERNIST-I is programmed to ask a series of questions before it recalculates after a single positive answer, thereby explaining the recommendation of two biopsies when only one is required.

Using laboratory data alone, the correct diagnosis was made by the computer in 16 of the 32 cases. A 17th case was also correctly diagnosed but the program’s logic was faulty and it only stumbled upon the correct diagnosis. Upon reviewing the printout of the case, we discovered an error in the knowledge base. When that was corrected, analysis operated properly and the correct diagnosis of renal vasculitis was made. No diagnostic conclusion was reached in the other 15 cases, but there was no incorrect diagnostic commitment. Several of the undiagnosed cases were “mechanical” problems such as aortic dissection and constrictive pericarditis, for which clinical laboratory data alone cannot suffice.

Table 1 lists the cases correctly diagnosed and undiagnosed.

**Discussion**

This limited exercise indicates that expert computer systems, which must include an expert knowledge base, are capable of analyzing correctly clinical laboratory information unsupported by medical history or physical examination. In some cases, other laboratory information, such as radiological findings, are critical to diagnosis; in other cases, not. In some cases clinical laboratory data are adequate for

<table>
<thead>
<tr>
<th>Table 1. INTERNIST-I Disposition of 32 Cases to Be Diagnosed</th>
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<tbody>
<tr>
<td><strong>Correctly diagnosed</strong></td>
</tr>
<tr>
<td>Nephrotic syndrome, acute tubular necrosis</td>
</tr>
<tr>
<td>Plasma cell myeloma, acute tubular necrosis</td>
</tr>
<tr>
<td>Hemochromatosis</td>
</tr>
<tr>
<td>Tuberculous meningitis</td>
</tr>
<tr>
<td>Acute intermittent porphyria</td>
</tr>
<tr>
<td>Viral hepatitis</td>
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<tr>
<td>Pulmonary lymphoma</td>
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<tr>
<td>Malignant lymphoma (non-Hodgkin’s type)</td>
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<tr>
<td>Schizocytic hemolytic anemia</td>
</tr>
<tr>
<td>Hepatic Wilson’s disease</td>
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<tr>
<td>Lymphoma of small intestine</td>
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<tr>
<td>Secondary meningeal neoplasm</td>
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<tr>
<td>Gastrointestinal amyloidosis, malabsorption</td>
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<tr>
<td>Toxic shock syndrome</td>
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<tr>
<td>Plasma cell myeloma</td>
</tr>
<tr>
<td>Acute viral hepatitis</td>
</tr>
<tr>
<td>Renal vasculitis</td>
</tr>
</tbody>
</table>

| **No conclusive diagnosis** |
| Hashimoto’s thyroiditis |
| Aortic dissection |
| AIDS |
| Legionellosis |
| Pneumocystis pneumonia |
| Constrictive pericarditis |
| Diffuse vasculitis |
| Pheochromocytoma |
| Malignant lymphoma (non-Hodgkin’s type) |
| Pulmonary thromboembolism |
| Crohn’s disease of colon |
| Tularaemia |
| Ileococcal tuberculosis |
| AIDS |
| Pheochromocytoma |

| **Reason for no conclusion** |
| Inadequate information |
| Mechanical disease |
| Inadequate information |
| Inadequate information |
| Inadequate information |
| Inadequate information |
| Inadequate information |
| Inadequate information |
| Inadequate information |
| Inadequate information |
| Inadequate information |
| Inadequate information |

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the expert system to recommend an immediate diagnostic conclusion. In most cases, however, the immediate clinical laboratory data provoke a set of diagnostic hypotheses, whereupon the expert system suggests other laboratory tests that would be useful or essential in the solution of the diagnostic problem.

The small study reported here is both preliminary and retrospective, involving problem or unusual cases to test the diagnostic procedure and capability. The results are promising in about one-half of these difficult cases. Of course, a more telling test of the potential role of expert computer systems in the practice of clinical pathology would be a prospective study, analyzing clinical laboratory results on individual patients from the initial aggregation through several stages of accumulation of information, and, it is hoped, to a final diagnostic conclusion.

Reference