AN EXPERT CONSULTANT SYSTEM IN RHEUMATOLOGY: AI/RHEUM

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A knowledge-based consultant system to assist physicians in the diagnosis of rheumatologic diseases is described. The system is designed to amplify the ability of non-rheumatologist user physicians in the rheumatology specialty area. In its current state the system, called AI/RHEUM, reasons from a knowledge base incorporating 26 diseases. Its diagnostic accuracy is 94% correct over 384 carefully studied clinical cases. AI/RHEUM offers the user assistance in the selection of additional laboratory or physical examination items which might help to narrow the differential diagnosis. The system also offers on-line detailed definitions and structured explanations of individual data items it requests, to assist users in improving the accuracy of observations they may not make routinely.

INTRODUCTION

Recent decision support systems, in which artificial intelligence techniques are used to amplify the knowledge base of the human decision maker, are now showing considerable potential in several areas of human endeavor [1]. Knowledge-based systems have found application in organic chemistry [2], mineral exploration [3], petroleum exploration [4], the configuration of computer systems [5], fault detection in computer systems [6], and in medicine.

Medical artificial intelligence systems have been developed for purposes such as the selection of antimicrobial therapy [7], diagnosis in internal medicine [8], ventilator management [9], the taking of a present illness [10], the diagnosis of problems in human hemostasis [11,12], and the diagnosis of rheumatologic diseases [13,14,15].

This paper is a progress report on the current state of a consultant system reasoning from a knowledge base which incorporates specialty knowledge of the expert rheumatologist. The system, called AI/RHEUM, offers an interaction patterned after a telephone consultation with an expert rheumatologist, to a user population of non-rheumatologist physicians. The AI/RHEUM knowledge base operates in the framework of the EXPERT consultant system developed by Kulikowski and Weiss at Rutgers University [16]. Portions of the rheumatology consultant system were developed to increase its potential as a training tool for medical students, fellows and house staff as well to improve the accuracy and reliability of observations specific to rheumatology by users not having specialty training in that field.

METHODS

The AI/RHEUM system reasons in a logical progression from specific clinical findings through intermediate hypotheses which represent pathophysiological states or useful aggregations of observations, to diagnostic conclusions. Its reasoning is embodied in production rules derived from formal criteria specified for each disease for which AI/RHEUM can formulate conclusions.

The model's original knowledge base encompassed 18 patient findings. The system now understands and can reason from a knowledge base incorporating 875 patient findings such as history and physical examination items, laboratory test results and radiographic observations.

Figure 1 presents as an example a portion of the patient data checklist on which this information is recorded. Taxonomic relationships among checklist items are denoted by indentations, indicating at a glance which responses may be skipped when the preceding question of the next higher level has been answered in the negative (e.g., item 20.24, "Synovitis" when answered in the negative allows the user to skip items 20.25 through 20.29).

____ 20.20 Synovial biopsy abnormal
____ 20.21 acid fast bacilli on stain
____ 20.22 granulomata
____ 20.23 rheumatoid changes
____ 20.24 Synovitis
____ 20.25 tenosynovitis
____ 20.26 foreign body
____ 20.27 traumatic
____ 20.28 toxic
____ 20.29 pigmented villonodular

Figure 1. Portion of Patient Data Checklist.

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Some of the findings represented on the patient data checklist are seldom encountered in a non-rheumatologic practice. Other findings may be interpreted by rheumatologists in ways unfamiliar to physicians trained in other specialties. For patient findings of this type, the AI/RHEUM system has available on line a series of expanded definitions. Each expanded definition offers four categories of explanation: WHAT (is this observation), WHY (is it being requested), HOW (is it performed), and REFS (literature citations which were the source of the definition).

An example of such an expanded definition is presented in Figure 2, for the checklist finding "Mononeuritis multiplex". During the findings input portion of the interaction, the user need only type "DEFINE" in response to a question to trigger the expanded definition option. The system offers him or her a choice of the WHAT, WHY, HOW, REFS, or ALL sections of the definition, and presents those portions requested.

WHAT: Mononeuritis multiplex is the simultaneous inflammation or degeneration of two or more peripheral nerves which are remote from one another.

WHY: Mononeuritis multiplex can occur in vasculitis if the nutrient arteries of peripheral nerve trunks are involved by the disease.

HOW: The patient with mononeuritis multiplex may present with motor or sensory changes which occur in an irregular and asymmetrical distribution on his body. These changes may be areas of paresthesia or anesthesia, loss of deep tendon reflexes, weakness or paralysis of muscle group. For example, a typical patient might present with paresthesia of the radial aspect of his left hand representing involvement of the left median nerve and weakness of his right foot and ankle representing right tibial nerve involvement.

REFS:
1. Lovshin, LL and Kernohan, JW: "Peripheral neuritis in periarteritis nodosa: a clinicopathologic study". Proc Staff Meeting Mayo Clinic 24:48, 1949.
2. Frohnert, PP and Sheps, SG: "Long-term follow-up of periarteritis nodosa". Am J Med 43:8, 1967.

Figure 2. Expanded Definition for Mononeuritis Multiplex.

Combinations or aggregations of findings representing higher-level concepts such as "severe renal involvement" or "mild myositis" are used in the reasoning process as intermediate hypotheses. These intermediate hypotheses frequently represent pathophysiological states, allowing physicians to specify their knowledge in useful medical terms rather than in unwieldy groups of findings. Concepts at higher levels may be formed when necessary by nesting or combining intermediate hypotheses. The current model includes 464 such hypotheses.

Since intermediate hypotheses are combinations of lower-level findings, they also must be carefully defined. Figure 3 presents an example of such a definition, for the intermediate hypothesis "hepatic dysfunction".

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Hepatic dysfunction:
  Abnormal liver enzymes, including
  at least two of the following three --
    alkaline phosphatase > 2X
      high normal threshold
    SGOT > 2X high normal threshold
    SGPT > 2X high normal threshold
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Figure 3. An Intermediate Hypothesis, Defined.

The current output of the AI/RHEUM reasoning process is a set of disease hypotheses in a differential diagnosis. Components of the differential diagnosis are further characterized as definite, probable, or possible. A summary of the reasoning which generated each component in the differential diagnosis is presented in terms of the findings which support the diagnosis and of the findings presently unknown which if known and positive would tend to strengthen the diagnosis. An example of the AI/RHEUM output for one of the cases tested is presented in Figure 4.

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Diagnoses are considered in the categories
  Definite, Probable, and Possible

Based on the information provided,
  the differential diagnosis is
    systemic lupus erythematosus (SLE) -- probable
    rheumatoid arthritis (RA)          -- possible

Diagnosis of SLE is supported by
  the patient findings:
    malar rash
    fever
    arthritis <=6 wks
    hypocomplementemia
    false positive VDRL or RPR
    fluorescent anti-nuclear antibody +
    lupus band test +
    circulating anticoagulant

Unknown findings which would help support
  the diagnosis of SLE:
    nephritis

Diagnosis of RA is supported by
  the patient findings:
    arthritis <=6 wks
    RA factor +, <1:320
    synovial fluid inflammatory
    ESR Westergren >30 mm/hr
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Figure 4. Example of AI/RHEUM Output.

The conclusions of the AI/RHEUM system thus include a statement of differential diagnosis, a list of the patient findings which support each component of the differential diagnosis, and a list of the patient findings for each component of the differential which were entered as unknown in the course of the initial interaction. The list of findings currently unknown is presented in a ranked ordering along a spectrum from findings inexpensive, easy and safe for the patient (e.g., body temperature) to findings expensive, difficult or potentially hazardous (e.g., renal biopsy). This ordered list constitutes a graded series of suggested next tests, the results of which would help the consultant system to narrow its differential diagnosis.

During the period of its development, the model has progressed from a relatively open-ended collection of rules pertaining to seven connective tissue diseases, to a carefully structured formulation of specific criteria for 26 rheumatologic diseases in six categories. These diseases are listed in Figure 5.

Connective Tissue Diseases
- Mixed connective tissue disease
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Progressive systemic sclerosis
- Polymyositis
- Sjogren's disease

Spondyloarthropathies
- Reiter's syndrome
- Ankylosing spondylitis
- Psoriatic arthritis
- Enteropathic arthritis

Crystal-induced Arthritides
- Gout
- Calcium pyrophosphate disease (pseudo-gout)

Infection-induced Arthritides
- Bacterial arthritis
- Gonococcal arthritis
- Tuberculous arthritis

Juvenile Rheumatoid Arthritis
- JRA, pauci-articular onset
- JRA, poly-articular onset
- JRA, systemic onset

Other Rheumatologic Disorders
- Primary Raynaud's syndrome
- Rheumatic fever
- Degenerative joint disease
- Polymyalgia rheumatica
- Fibrositis
- Carpal tunnel syndrome
- Polyarteritis nodosa
- Giant cell arteritis

Figure 5. Diseases Known to AI/RHEUM.

The formal criteria for each disease known to the system include major and minor findings, required findings ("must have" items), and exclusions ("must not have" items). Any of these elements in the criteria may be individual patient findings or may be intermediate hypotheses, aggregations or derivations of findings. The disease criteria are the consensus of discussions among clinicians from the Division of Immunology/Rheumatology at the University of Missouri - Columbia School of Medicine after recourse to the published literature in the field, with periodic review by an external panel of nationally known rheumatologists. An example of the formal disease criteria used by AI/RHEUM is found in Figure 6, for ankylosing spondylitis.

The disease criteria for ankylosing spondylitis have five major findings, eight minor findings, no required items, and eight exclusions. Some of these items are themselves intermediate hypotheses (e.g., major #3: "Limitation of lumbar motion, two or more planes", derived from three individual checklist findings). Note that in the column labeled "Definite", there are two sub-categories or combinations of findings (A and B). Either of these combinations would allow the characterization of a particular case as "Definite ankylosing spondylitis". Similarly, there are three combinations of findings by which a case can be classified "Probable ankylosing spondylitis" and two combinations by which a case can be diagnosed as "Possible ankylosing spondylitis".

Within a specific sub-category (e.g., "Probable ankylosing spondylitis, sub-category B"), there are multiple ways in which, to continue with that example, three or more of the five major findings and two or more of the eight minor findings can present. Requirements for the characterization of a case as ankylosing spondylitis become progressively less stringent in the transition from "Definite" to the "Probable" and "Possible" columns.

During the years in which the AI/RHEUM system has been under development, a number of physicians, information scientists, post-doctoral fellows and external review committees have found this means of specifying disease criteria unambiguous, readily understandable and medically sound. This form of knowledge representation in disease criteria has the additional benefit that it lends itself to an algorithmic interpretation in logical rules of the medical knowledge so densely compacted. The current model contains 1,014 production rules derived from the 26 sets of disease criteria which constitute its knowledge base.

	Major Findings	Minor Findings
	1. Low back pain >3 months	1. HLA B27
	2. Sacroiliitis, bilateral	2. Uveitis
	3. Limitation of lumbar motion, two or more planes	3. Arthritis: hip, knee or shoulder
	4. Limitation of chest expansion, <=2.5 cm	4. Pulmonary upper lobe fibrosis
	5. Syndesmophytes: bilateral, symmetric, marginal	5. Cardiac conduction system abnormalities
		6. Aortitis, or aortic insufficiency
		7. Enthesopathy
		8. Nail pitting, negative

	Definite	Probable	Possible
CLIN	A. Majors #1, #2 + 2 other majors + B. Majors #1, #2 + 1 other major + 2 minors +, from #1, #4, #5, #6	A. Majors #1, #2 + 1 other major + B. 3 majors + 2 minors + C. 2 majors +, incl #1 or #2 3 minors	A. 2 majors + B. Major #1 + 3 minors +
REQD	No requirements	No requirements	No requirements
EXCL	ANA +, >=1:320 DNA + (crith.), >1:100 ENA +, >=1:1000 Hypocomplementemia Psoriasis, skin or nails Keratodermia blennorrhagicum Circinate balanitis Mucosal ulcerations	No exclusions	No exclusions

Figure 6. Disease Criteria for Ankylosing Spondylitis.

RESULTS

The AI/RHEUM consultant model has been validated by retrospective testing with a total of 384 carefully studied clinical cases. The "ground truth" for correct diagnoses is a consensus opinion of at least two of three rheumatologists reviewing the patient chart. The results of this validation against real cases are summarized in Figure 7.

Connective Tissue Diseases
235/254 cases correct (93%)
Spondyloarthropathies
34/34 cases correct (100%)
Crystal-induced Arthritides
19/19 cases correct (100%)
Infection-induced Arthritides
29/30 cases correct (97%)
Juvenile Rheumatoid Arthritis
17/17 cases correct (100%)
Other Rheumatologic Disorders
26/30 cases correct (87%)

Overall
All cases -- 360/384 cases correct (94%).

Figure 7. Diagnostic Accuracy of AI/RHEUM.

CONCLUSIONS

A knowledge-based consultant system has been built which demonstrates the feasibility of providing diagnostic assistance in rheumatology. Retrospective analysis of 384 rheumatologic patients receiving care in an arthritis referral center has resulted in a diagnostic accuracy of 94%. Recognizing that assistance in diagnosis is a necessary but not a sufficient aid to the non-rheumatologist physician treating patients presenting with rheumatologic problems, we are adding assistance in patient management as the next area of development for AI/RHEUM.

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