History of Computing in Medicine

Beginnings

- 1950's computers in bioengineering
- Early 1960's
  - Medline
  - Laboratory instrumentation computers (LINC)
  - MUMPS developed at MGH
  - GEMISCH (generalized medical information system for community health at Duke) (Stead MD)
- 1975 8080 processor – Altair 8800
- 1976 Apple Computers

Hackers: Steven Levy

Beginnings

- Initial application: automated patient questionnaire (Slack: ‘55) 1965
  - Patient centered computing
  - Cybermedicine
- Center for Clinical Computing
  - Dr. Slack maintained of Eliza that soliloquy, (with or without a computer) can be a valuable tool of mental health. He wrote: "Contrary to the common notion that soliloquy is a manifestation of mental illness, we believe that it is normal behavior---behavior that serves to help maintain emotional equilibrium."

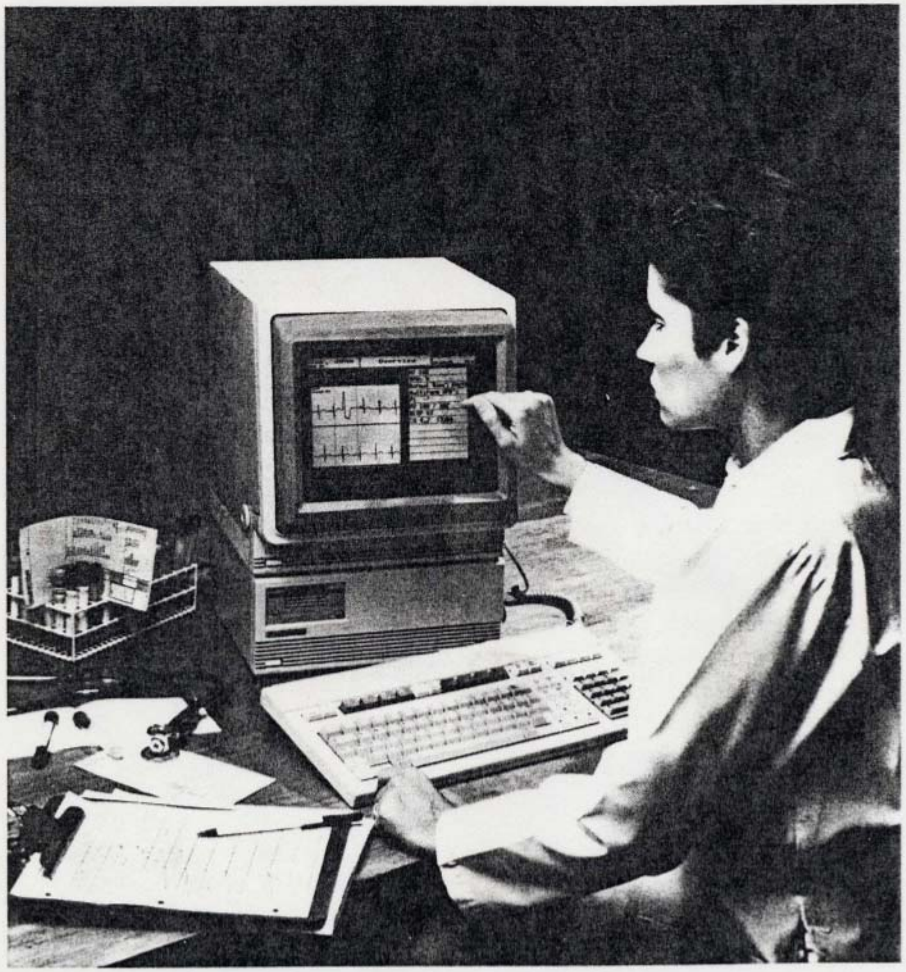


FIGURE 1.10. Departmental system. Hospital departments, such as the clinical laboratory, were able to implement their own custom-tailored systems when affordable minicomputers became available. Today, these departments often use microcomputers to support administrative and clinical functions. (Photograph courtesy Hewlett-Packard Company.)

Eliza

- Eliza (MIT 1960's) initially designed as a spoof vs. attempt to pass the Turing test
  - Eliza
  - Quack Eliza

MUMPS

- MGH utility multi-programming system (Octo Barnett 1966)
  - Thou shalt not declare variable types or file sizes.
  - Thou shalt not KILL, except for globals and variables.
  - Thou shalt not covet they neighbor's UCI (User Class Identification = computing area).
  - Remember string handling, for it shall make MUMPS special.

MUMPS

- Now known as M
  - A programming language with extensive tools for the support of database management systems. MUMPS was originally used for medical records and is now widely used where multiple users access the same databases simultaneously, e.g. banks, stock exchanges, travel agencies, hospitals.

MUMPS

- Language plus data structure
- Designed by MD's and engineers
  - Designed for medical environment
    - Low computing power – data entry >>> computing
    - Flexible string structure
    - Inverted tree structure (sparse)
    - Multi-user environment
    - Interpreted
      - More flexible, efficiency not necessary

MUMPS code

- f p=2,3:2 s q=1 x "f f=3:2 q:f*f>p!'q s q=p#f" w:q p,?$x\8+1*8
  - *prints a table of primes, including code to format it neatly into columns*

Beginnings

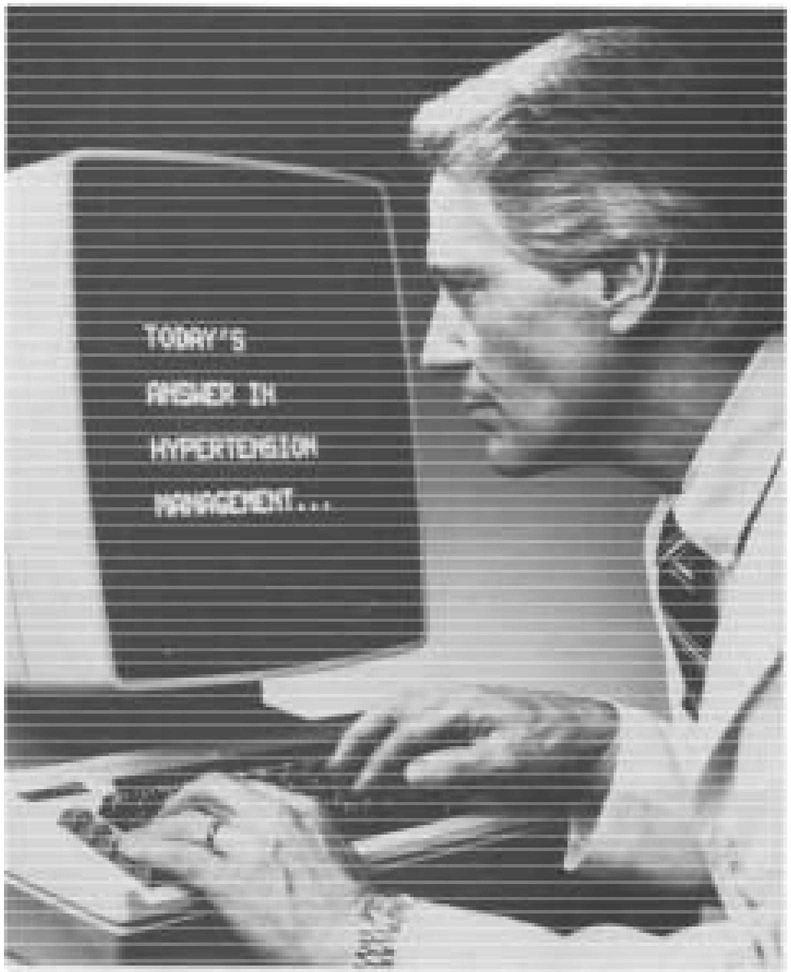
- 1977 – Medical Informatics defined
  - Discipline dealing with the problems associated with information, its acquisition, analysis and dissemination in the health care delivery process
- 1978 – DEC transitions from PDP to VAX
- 1980 – IBM PC (MS-DOS)
- 1982 – medical informatics definition expanded to include care, education and research

Beginnings

- 1983 – Shortliffe "medical informatics covers more than just applications of computers to medicine"
- 1986
  - Macintosh developed
  - AAMC "medical informatics combines medical science with several disciplines in the information and computer sciences…and provides methodologies by which these can contribute to better patient care"

Artificial Intelligence in Medicine

- Clancey, Shortliffe (1984)
  - Medical artificial intelligence is primarily concerned with the construction of AI programs that perform diagnosis and make therapy recommendations. Unlike medical applications based on other programming methods, such as purely statistical and probabilistic methods, medical AI programs are based on symbolic models of disease entities and their relationship to patient factors and clinical manifestations


TODAY'S
ANSWER IN
HYPERTENSION
MANAGEMENT...

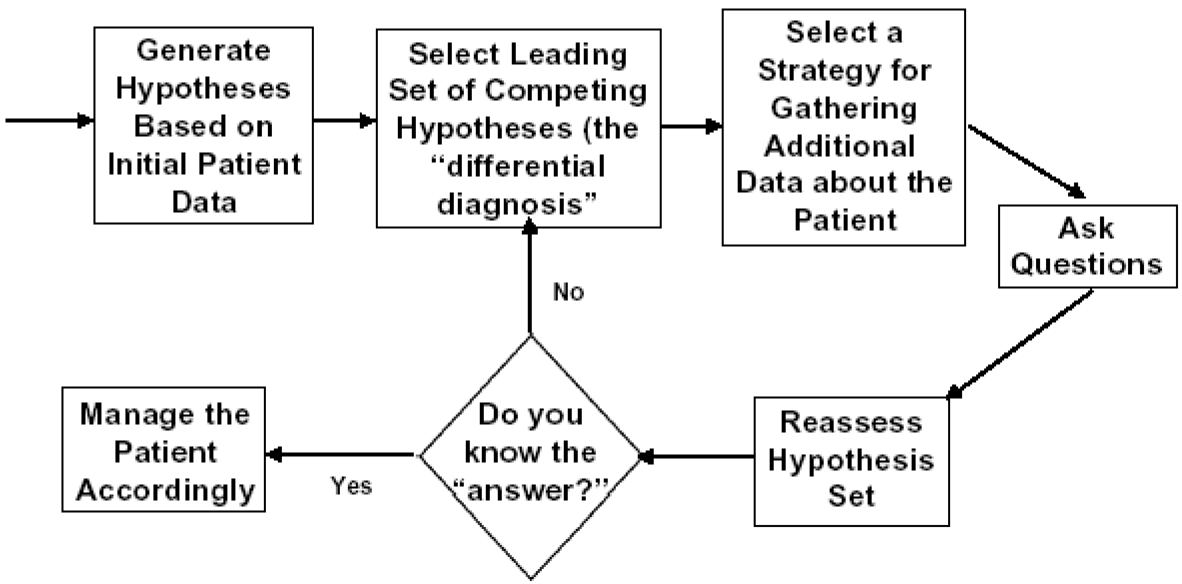
Early AIM

- Internist/QMR
  - Designed at University of Pittsburgh
- Mycin, Oncocin
  - Designed at Stanford by Shortliffe's group

AIM

- Internist
  - Designed to reproduce the behavior of a diagnostician

The Hypothetico-Deductive Approach



Internist-1 / QMR

Task: Diagnosis in internal medicine and neurology

- Scope: The entire field!
- Began in early 1970s as collaboration between Dr. Jack Myers (physician) and Prof. Harry Pople (computer scientist) at University of Pittsburgh
- Dr. Randy Miller (physician) worked on project throughout the 1970s and became project leader in 1980s
- Internist-1 was mainframe (Lisp) version of program, used to develop methods and extensive clinical knowledge base
- QMR is microcomputer version developed by Dr. Miller and collaborators during 1980s and now commercially available

Internist-1 → QMR

Jack D. Myers, MD

Jack D. Myers, MACP

Jack D. Myers, MACP, a pioneer in medical informatics, a member of the National Academy of Sciences and a former ACP President and Regent, died Jan. 31. He was 84.

Dr. Myers

After serving overseas in the Army medical reserves, Dr. Myers was chair of the department of medicine at the University of Pittsburgh. Dr. Myers was well known among the school's medical students and residents for his thorough teaching style and received ACP's Distinguished Teaching Award in 1981.

During the late 1970s, Dr. Myers began studying the field of artificial intelligence and computer-assisted medical education, and he became involved in building databases such as the Quick Medical Reference. He continued to contribute to the field of medical informatics almost until his death.

Dr. Myers served as an ACP Regent from 1971-75 and President from 1976-77. He also served on advisory councils for the National Institutes of Health. The National Academy of Sciences, Institute of Medicine, elected him to membership in 1976. ■

ACP Observer, June 1998

Disease Description in Internist-1

- DISEASE NAME
- DISEASE MANIFESTATIONS
  - Manifestation name
  - FW: Frequency weight (1, 2, 3, 4, 5)
  - ES: Evoking strength (0, 1, 2, 3, 4, 5)
- LINKS TO OTHER DISEASES
  - (each link has an ES and FW)
  - Types of disease-disease links:
    - » Disease1 causes Disease2
    - » Disease1 predisposes-to Disease2
    - » Disease1 precedes Disease2
    - » Disease1 coincident-with Disease2
    - » Disease1 systemic-manifestation-of Disease2
    - » Disease1 equivalent-to Disease2

Evoking Strengths

0 Nonspecific (i.e., manifestation occurs too commonly to be used to construct a differential diagnosis of individual diseases)

1 Diagnosis is rarely associated with listed manifestation

2 Diagnosis causes a substantial minority of instances of listed manifestation

3 Diagnosis is the most common but not the overwhelming condition associated with the listed manifestation

4 Diagnosis is the overwhelming consideration in the presence of listed manifestation

5 Listed manifestation is pathognomonic for the diagnosis

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Formulaic Use of Evoking Strengths

Evoking Strength	Weight of ES
0	1
1	4
2	10
3	20
4	40
5	80

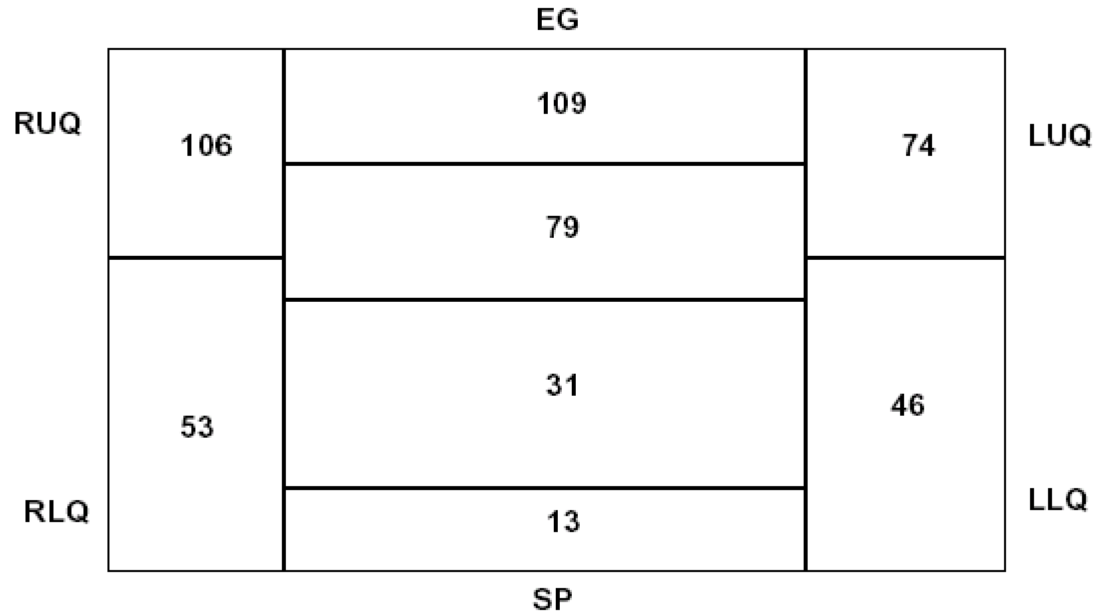
Internist-1 Disease Example

- **NAME** Primary Hyperparathyroidism
- **MANIFESTATIONS**
  - Serum phosphate decreased (ES3, FW3)
  - Constipation (ES0, FW2)
  - History of peptic ulcers (ES1, FW2)
    ..... (plus many others)
- **LINKS TO OTHER DISEASES**
  - <u>Causes</u> Nephrolithiasis (ES2, FW3)
  - <u>Predisposes-to</u> Pyelonephritis (ES1, FW2)
  - <u>Coincident-with</u> Pheochromocytoma (ES2, FW2)

DEI SUB NUMINE VIGET

Internist-1 Disease Counts For Abdominal Pain

Data as of 1982 — 502 disease in knowledge base



Hypothesis Invocation

(Data-Directed)

Positive Components:

A:

Evoking Strength	Score A
0	1
1	4
2	10
3	20
4	40
5	80

B: Bonus Score (for links to previously diagnosed diseases)

Score B = 20 x (frequency weight of the hypothesis as noted in the description of a disease already diagnosed)

Note: Range 0 to 100

Hypothesis Invocation

(Data-Directed)

Negative Components:

C: If a manifestation expected for an hypothesis is known to be absent:

Frequency Weight	Score C
1	-1
2	-4
3	-7
4	-15
5	-30

D: If a manifestation is present but not explained by the hypothesis:

Import	Score D
1	-2
2	-6
3	-10
4	-20
5	-40

Hypothesis Invocation

(Data-Directed)

For each disease evoked by <u>at least one</u> of the manifestations entered by the physician, a net score is calculated:

Net score = A + B + C + D

A + B: positive components

C + D: negative components

The disease with the highest net score becomes the pivotal disease for formulating a differential diagnosis.

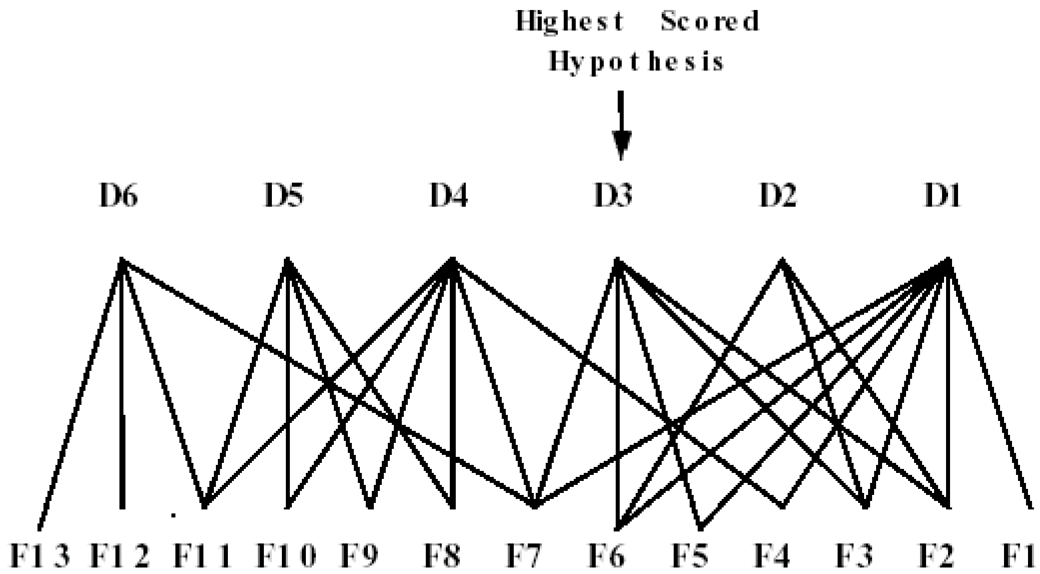
Determining the Differential Diagnosis

The Partitioning Algorithm

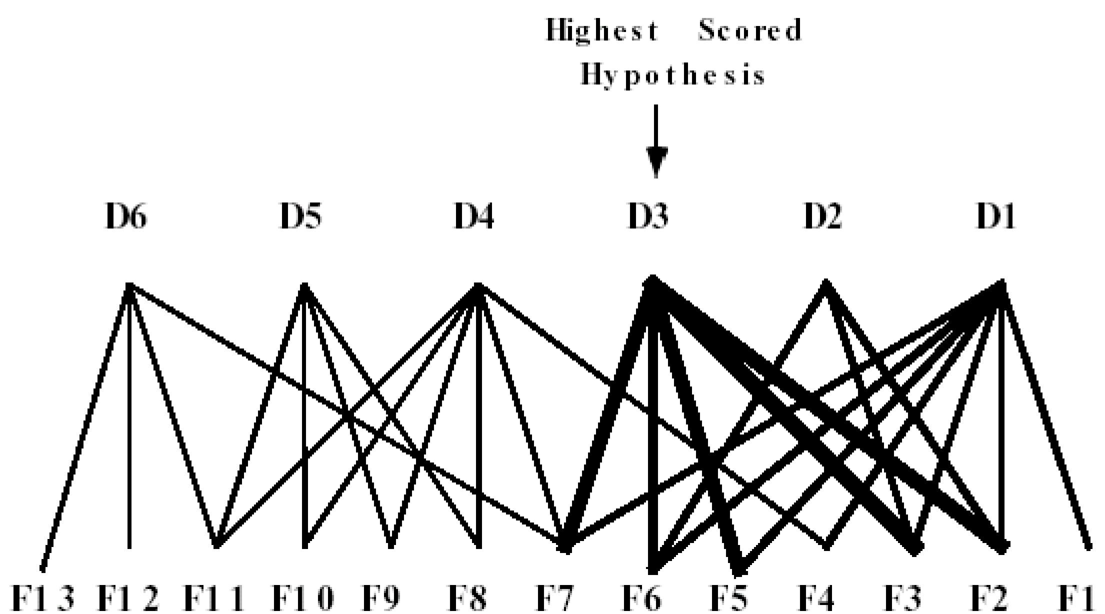
- The task is to determine all evoked hypotheses that are competitors to the topmost diagnosis (i.e., the hypothesis with the highest net score).
- Disease A and Disease B are competitors if, taken together, they explain no more observed manifestations than does one of them taken alone (ignoring frequency weight so long as it is greater than or equal to 1).
- Internist-1 then "considers" all manifestations explained by the current differential diagnosis (the "current problem area", or CPA) and sets aside for later ("disregards") all manifestations not yet explained.

Internist Partitioning Algorithm

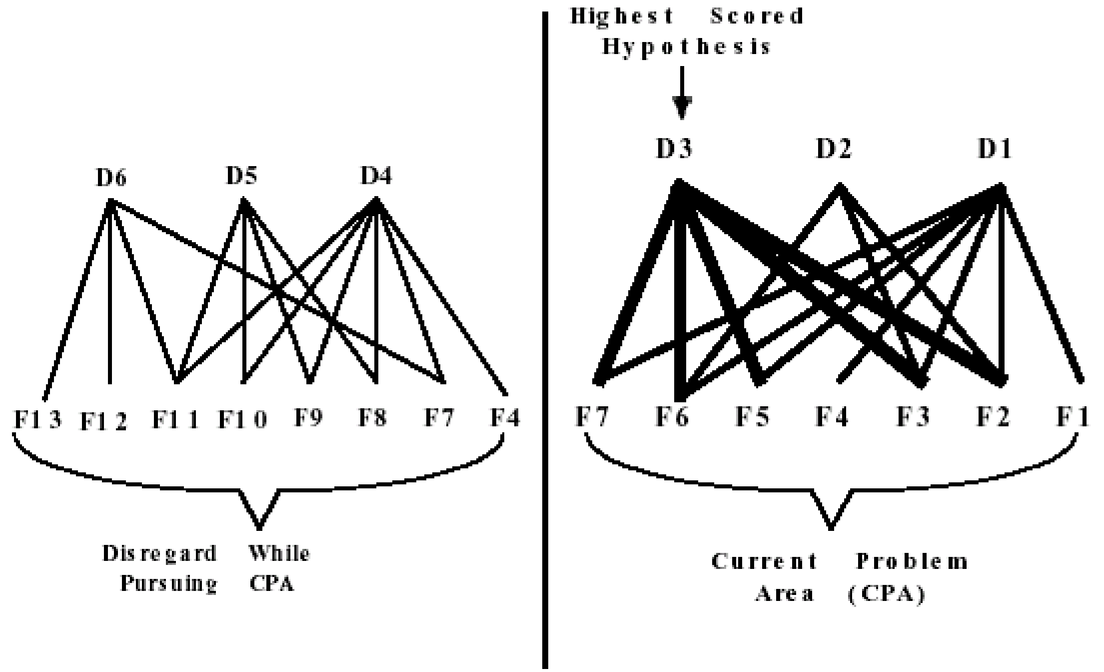
1



Internist Partitioning Algorithm



Internist Partitioning Algorithm



Pursual Mode

- Used when 45 < [top net score - second net score] < 90
- Select questions designed to establish diagnosis with top score
- Use findings with a high evoking strength for the first hypothesis

Rule-out Mode

- Used when at least five hypotheses exist in the range within 45 points of the top scoring hypothesis
- Ask questions designed to eliminate the competitors with the lowest net scores
- Use findings that have a high frequency weight for the lowest scoring competitors

Discriminate Mode

- Used when two to four hypotheses exist within the range of 45 points from the score of the first diagnosis
- Ask questions attempting to maximize the variance of the scores for the hypotheses in the top group

General Question-Generation Strategies

- Ask questions in small groups, recalculating disease scores after each batch of questions
- Ask questions ordered by ease with which the information can be obtained clinically (history first, then physical exam, then tests ordered by their degree of risk, discomfort, and expense)
- Process all answers in one batch, thereby creating a new differential diagnosis, possibly with a different pivot disease
- Repeat the partitioning and differential diagnosis using the partitioning algorithm and the question-selection strategies

Evaluation of Internist-1

(Miller et al., NEJM, 8/19/82)

- Used CPC's from 1969 issues of the New England Journal of Medicine
- Published CPC's included difficult, complex cases, often with multiple diagnoses
- Diagnoses assigned by ward team and by expert discussant were known for each case
- "Gold standard" was generally the tissue diagnosis determined by pathologists from biopsy or autopsy
- Only cases in which the final diagnoses were in the Internist-1 knowledge base were used (19 of 42 cases [45%] in which there were an average of 3 major diagnoses per case

Results for the 19 Cases

	Internist-1	Clinicians	Discussant
Total possible diagnoses	43	43	43
Definitive, correct	17	23	29
Tentative, correct	8	5	6
Failed to make correct diagnosis	18	15	8
Definitive, incorrect	5	8	11
Tentative, incorrect	6	5	2
Total no. of incorrect diagnoses	11	13	13
Total no. of errors in diagnosis	29	28	21

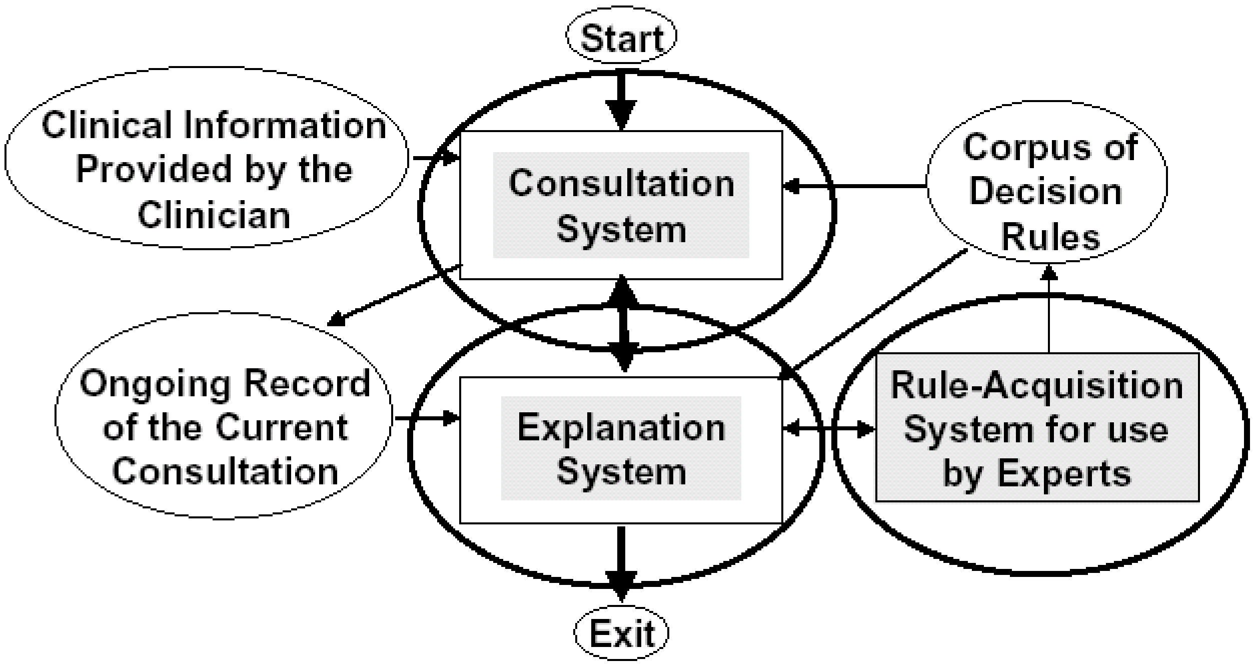
Internist-1 Evaluation

- Out of 18 diagnoses missed by the program, 11 were missed by one of the other groups
- Program was right in 7 cases where at least one of the other groups was wrong
- In 80% of the cases where Internist-1 was wrong, one of the other groups was wrong too
- Overall mistakes: Internist-1 29, clinicians 28, experts 21
- Note: CPC's are not representative of routine clinical cases seen in normal hospital or outpatient clinic environment

Internist/QMR Problems

- No anatomical reasoning
- No temporal reasoning
- Concluding a diagnosis causes deletion of explained findings — cannot be used again to support another diagnosis
- No treatment of compensating symptoms or synergistic diseases
- No true use of causality or pathophysiologic model
- Assumes conditional independence of findings
- No clear probabilistic model

MYCIN: An Overview



Nature of Clinical Consultation

Sample MYCIN Rule

PREMISE: ($AND (SAME CNTXT GRAM GRAMPOS)
(SAME CNTXT MORPH COCCUS)
(SAME CNTXT CONFORM CLUMPS))
ACTION: (CONCLUDE CNTXT TALLY STAPHYLOCOCCUS TALLY 700)

or (translated into English):

IF: 1) The gramstain of the organism is grampos
2) The morphology of the organism is coccus
3) The conformation of the organism is clumps
THEN: There is suggestive evidence (.7) that the identity of the organism is staphylococcus

Sample MYCIN Case -1

30) Is Case 168 a compromised host (e.g., alcoholic, sickle-cell-disease, immunosuppressed)?

** NO

31) For how many days has Case 168 had abnormal neurologic signs?

** 1

32) For how many days has Case 168 had neurological symptoms?

** 9

Has Case 168 had recent evidence of tender or enlarged salivary glands?

** WHY

Sample MYCIN Case -2

[i.e., WHY is it important to determine whether Case 168 has shown symptoms of mumps?]

[2.0] This will aid in determining the type of infection.

It has already been determined that:

[2.1] the infection which requires therapy is meningitis

Therefore if:

[2.2] Case 168 has shown symptoms of mumps

Then:

there is weakly suggestive evidence (.4) that the type of infection is viral

Author: Yu

Literature: C. Wilfert, NEJM 280:855 (1969)

Sample MYCIN Case -3

My therapy recommendation will be designed to treat for organisms that either are very likely or, although less likely, would have a significant effect on therapy selection if they were present. It is important to cover for the following probable infection(s) and associated organism(s):

INFECTION-1 is MENINGITIS

+ <Item-1> MYCOBACTERIUM-TB [from clinical evidence only]

.... COCCIDIOIDES [from clinical evidence only]

.... CRYPTOCOCCUS [from clinical evidence only]

.... VIRUS [from clinical evidence only] - Give Supportive Therapy

[My recommendation will cover for all of the most likely items (indicated by a + above). Less likely items will be covered unless this would require an excessive number of drugs.]

Sample MYCIN Case -4

My preferred therapy recommendation is as follows:

Give the following in combination:

1) ETHAMBUTAL

Dose: 1.28g (13 100mg tablets) q24h PO for 60 days [calculated on basis of 25 mg/kg] then 770 mg (7.5 100mg tablets) q24h PO [calculated on basis of 15 mg/kg]

Comments: Periodic vision screening test are recommended for optic neuritis

2) INH

Dose: 513mg (5 100mg tablets) q24h PO [calculated on basis of 10 mg/kg]

3) RIFAMPIN

Dose: 600 mg q24h PO

Comments: Administer dose on an empty stomach

Sample MYCIN Case -5

** HOW DID YOU DECIDE TO TREAT FOR MYCOBACTERIUM-TB IN THIS CASE?

ITEM-1 is Mycobacterium-tb associated with meningitis. I decided to treat ITEM-1 on the basis of clinical evidence alone.

The following rules concluded about:

the likelihood that Mycobacterium-tb is one of the organisms (other than those seen on cultures or smears) that might be causing the infection

523 579

Which of these rules do you wish to see?

** 579

Sample MYCIN Case -6

RULE 579

If:
1) The infection that requires therapy is meningitis,
2) The patient's chest x-ray is abnormal, and
3) Active-tb is one of the diseases that the patient's chest x-ray suggests

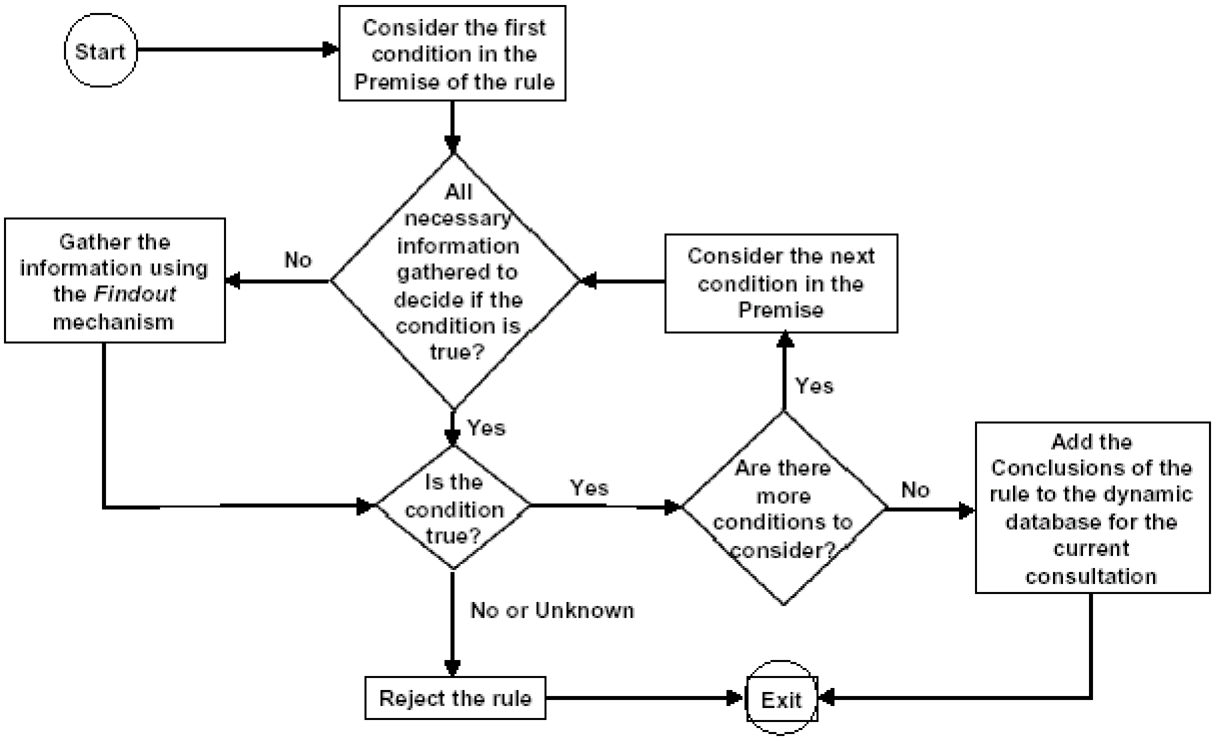
Then: There is strongly suggestive evidence (.8) that Mycobacterium-tb is one of the organisms (other than those seen on cultures or smears) that might be causing the infection

Author: Yu

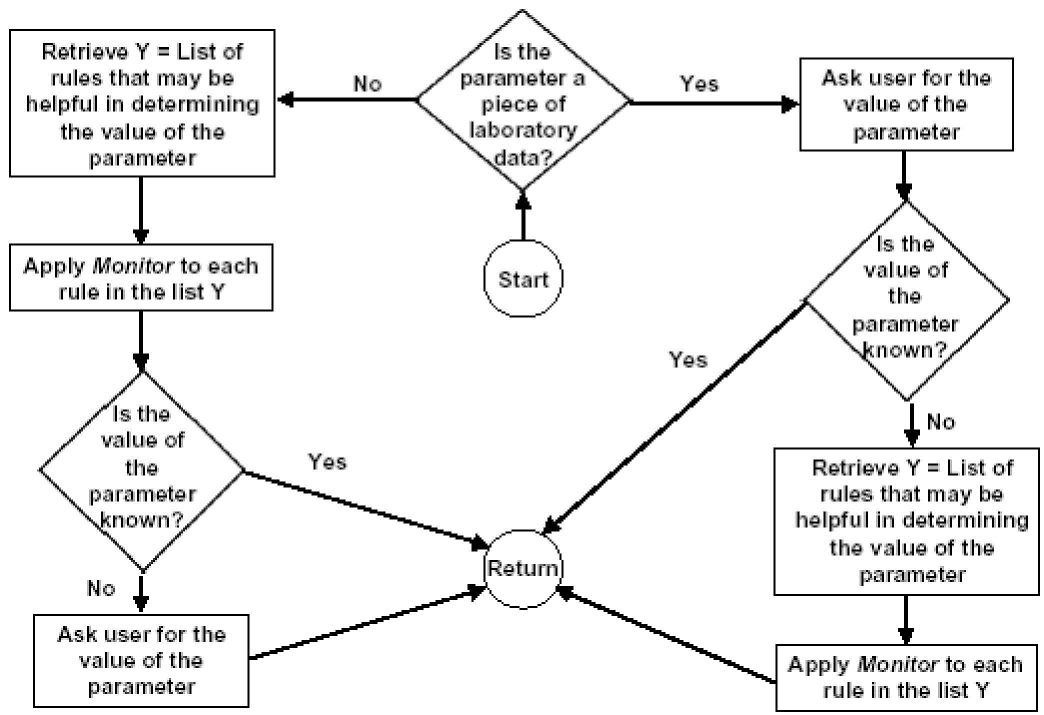
Reasoning Methods in AI Systems

- Goal-Directed Reasoning (Backward Chaining)
  - e.g., MYCIN
- Data-Driven Reasoning (Forward Chaining)
  - e.g., Ventilator Manager (VM)
- Hypothesis-Directed Reasoning
  - e.g., Internist-1
- Opportunistic Reasoning
  - e.g., the "blackboard" architecture

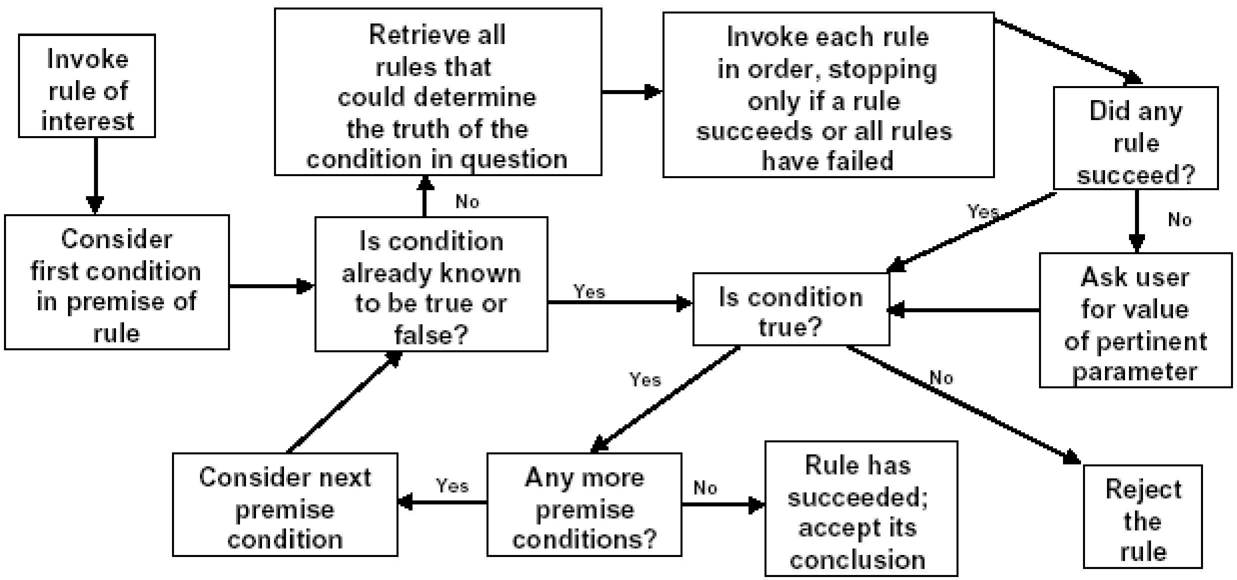
MYCIN's *MONITOR* Mechanism



MYCIN's *Findout* Mechanism



Generic Algorithm for Goal-Directed Rule Invocation



N.B. This algorithm is depth-first and assumes that users may know the value of a parameter if the rules are unsuccessful in concluding it. Rule Premises are assumed to be conjunctions of conditions.

MYCIN's Goal Rule

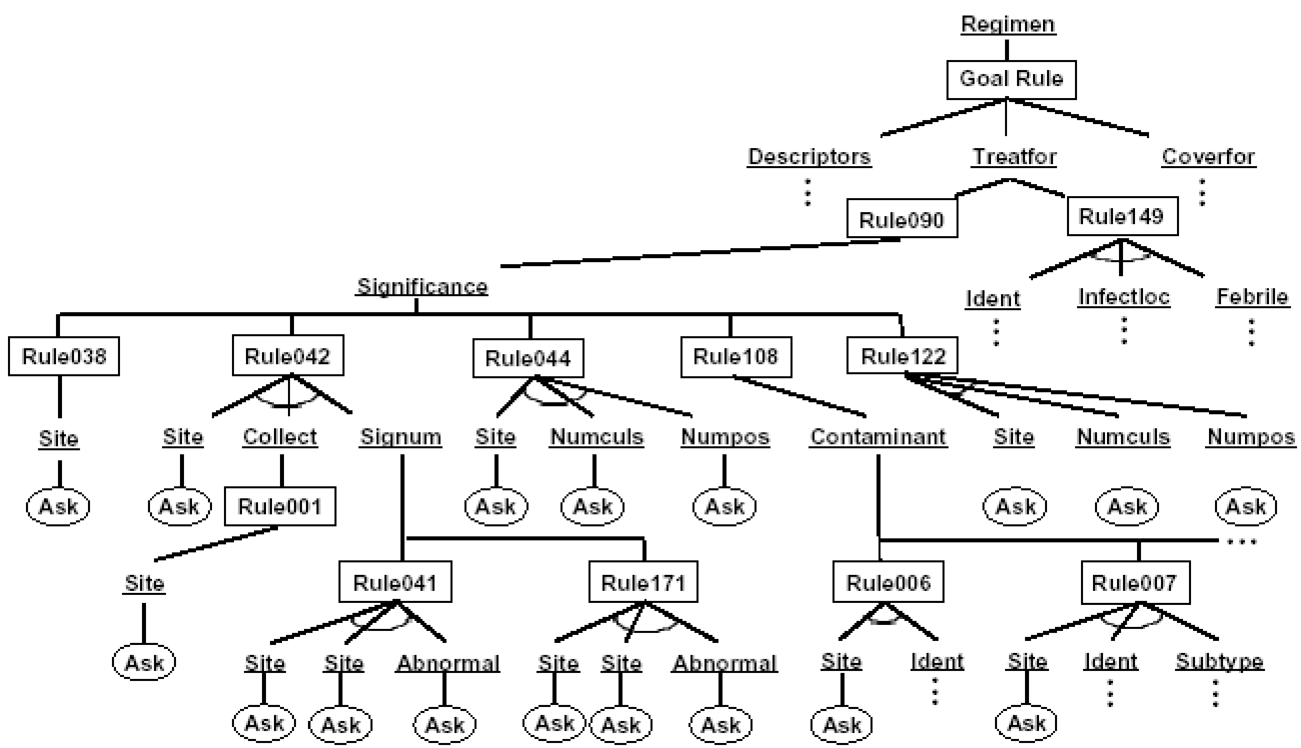
IF:

1) Information has been gathered about organisms isolated from this patient, organisms noted on smears taken from this patient, negative cultures of this patient, suspected infections without microbiological evidence, current drugs of this patient, and prior drugs of this patient,
2) An attempt has been made to deduce the organisms which require therapy, and
3) You have given consideration to organisms (other than those noted in cultures and smears) that might be present

THEN:

Determine the best therapy recommendation from among the drugs likely to be effective against the significant organisms, or indicate that no therapy is required at this time

Sample MYCIN Reasoning Network



Maturation of medical computing

Data	The individual items made available to the analyst. Examples would be a patient's sex, age, weight or blood pressure value.
Information	A set of data with some interpretation or value added. For example, we say we infer that a difference exists if an 80-kg person has a height of 150 cm or 195 cm.
Knowledge	A set of rules, formulas, or heuristics used to create information from data and information.

APPLICATION	1950s	1960s	1970s	1980s
Data	Research	Prototype	Mature	Refined
Information	Concepts	Research	Prototype	Mature
Knowledge	Concepts	Concepts	Research	Prototype

History 1985-1995

- Emergence of HIS
  - Financial information ahead of clinical information
- Introduction of PC's into offices (initially for clerical use)
- PC's on units for data output
  - Statlan (DOS based – non Y2Kcompliant)
- Clinical information systems (CIS)

History 1995-present

- Internet medicine
- Wiring of health systems
- PC’s in MD’s offices
- PC’s for order entry, web access etc.
- Acquisition of large data bases

Now

- AI in medicine (nascent)
- Computers in the business of medicine
  - Electronic billing (maturing)
- Information flow
  - Lab, radiology (maturing)
  - Medical Record (nascent)
- Patient care
  - Intelligent monitoring (nascent)

Now

- Consumer awareness
  - Information availability (growing rapidly)
  - Quackery!!! (growing rapidlier)
- Efficiency gains
  - Decreased personnel (nascent)
  - Best/least costly practices (nascent)
  - Information flow (nascent)

Current resources

- AMIA curriculum 2001
- Health information resources on the web
- IT Medical Literature
- Newsgroups/chat rooms/support
- Health news

Future

- Compare American (vs. Japanese) industry in the late 1980's
- Barriers