

Decision Support via Expert Systems

6.872/HST950

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Components of an Expert System

- Knowledge
 - In various forms: associations, models, etc.
- Strategy
 - Baconian, exhaustive enumeration, on-line, etc.
- Implementation
 - Programs, pattern matching, rules, etc.

Flowchart

BI/Lincoln Labs Clinical Protocols 1978

U.T.I./ VAGINITIS PROTOCOL (12/75)

Unit#: _____ Date: _____

Name: _____

Birthdate: _____ Phone: _____

Provider: _____

Chief complaint(s) _____

yes no SUBJECTIVE

Vaginal discharge, unusual
Days duration _____

Vaginal/vulvar itch/irritation
Days duration _____

Pain/burning on urination
Inside urethra _____
Outside on a raw area _____
Days duration _____

Unusually frequent urination
Days duration _____

Rx for any of above in past 3 mo
Age ≥ 45 _____
Pregnant now _____
Diabetic _____

New pain side/back/belly/pelvis
Severe _____

Any blue boxes checked
Gyn procedure in past 2 mo _____
Meds inserted into vagina
in past few days _____

Any grey boxes checked
Incontinence (prior to UTI Sx) _____
Vomiting/too nauseated to eat _____
Fever by Hx in past 48 hrs _____
Chills, teeth chatter _____
Hx of hospitalization for UT prob. _____
Kidney X-ray (IVP) _____
Bladder/kidney stones _____
Cystoscopy/in-dwelling catheter _____
High blood pressure _____
Had a UTI before age 12 _____
Past UTI's ≥ 3 _____
Antibiotic taken in past 3 weeks _____

OBJECTIVE

Temperature ≥ 100 _____
 Systolic BP ≥ 160 or Diastolic ≥ 95
BP: _____

Any grey boxes checked
CVA tenderness _____

Do urinalysis and culture

Bact _____ WBC _____ RBC _____

$\geq 3+$ protein _____
 Any sugar _____
 Bact $\geq 2+$ or WBC $\geq 20?$ **Dx UTI** _____
 ≥ 10 RBC _____
 $\geq 2+$ protein _____

Any blue boxes checked _____
 Any red boxes checked? **Consult MD** _____
Do Pelvic (Pap & GC culture) _____
 Abnormalities-not discharge _____
 Cervix painful on movement _____
 Urethral/cervical discharge? _____
Do GC gram stain _____
 Abnormal vaginal discharge _____
 Looks like cottage cheese? **Dx monilia** _____
 Monilia prep positive? **Dx monilia** _____
 Trich prep positive? **Dx trichomonas** _____
 Any vag dx? **Dx non-specific vaginitis** _____

Any dx yet? _____
 Any greys? **Dx urethritis** _____

Any reds? **Consult MD** _____
 Will consult MD for other reasons _____

PLAN (also see back of protocol)

Dx of trichomonas? **Rx Flagyl** _____
 Dx of monilia? **Rx Mycostatin** _____
 Dx of non-specific vaginitis? _____
 Sulfa allergy? **Consult MD Rx Sultrin** _____

Dx of UTI/urethritis _____
 Dx of urethritis/vaginitis _____
 Dysuria so bad pt can hardly urinate _____
 Frequency interfering with work
or sleep? **Rx as below but tell pt
to wait for culture result before
beginning med.** _____

Sulfa allergy? **Rx Sulfisoxazole** _____
 Tetracycline allergy? **Rx Tetracycline** _____
 Penicillin/Ampicillin allergy? _____
 Consult MD Rx Ampicillin _____

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Codifying Human Knowledge

- Decomposition into “chunks” of knowledge, chaining of inferences
- Matching of case data to prototypical situations
- Using causal models (pathophysiology) to figure out cases

Mycin—Rule-based Systems

- **Task: Diagnosis and prescription for bacterial infections of the blood (and later meningitis)**
- **Method:**
 - **Collection of modular rules**
 - **Backward chaining**
 - **Certainty factors**

RULE037

IF the organism

1) stains grampos

**2) has coccus
shape**

3) grows in chains

THEN

**There is suggestive
evidence (.7) that the
identity of the
organism is
streptococcus.**

Mycin consult

-----PATIENT-1-----

- 1) Patient's name: **FRED SMITH**
- 2) Sex: **MALE**
- 3) Age: **55**
- 4) Have you been able to obtain positive cultures from a site at which Fred Smith has an infection? **YES**

-----INFECTION-1-----

- 5) What is the infection? **PRIMARY-BACTEREMIA**
- 6) Please give the date when signs of INFECTION-1 appeared. **5/5/75**
The most recent positive culture associated with the primary-bacteremia will be referred to as:

-----CULTURE-1-----

- 7) From what site was the specimen for CULTURE-1 taken? **BLOOD**
- 8) Please give the date when this culture was obtained. **5/9/75**
The first significant organism from this blood culture will be called:

-----ORGANISM-1-----

- 9) Enter the identity of ORGANISM-1. **UNKNOWN**
- 10) Is ORGANISM-1 a rod or coccus (etc.)? **ROD**
- 11) The gram stain of ORGANISM-1: **GRAMNEG**

...

Davis, *et al.*, *Artificial Intelligence* **8**: 15-45 (1977)

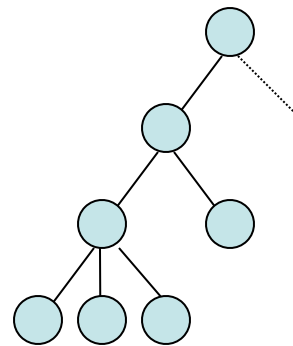
How Mycin Works

- To find out a fact
 - If there are rules that can conclude it, try them
 - Ask the user
- To “run” a rule
 - Try to find out if the facts in the premises are true
 - If they all are, then assert the conclusion(s), with a suitable certainty
- Backward chaining from goal to given facts

★ *Dynamically traces out behavior of (what might be) a flowchart*

★ *Information used everywhere appropriate*

★ *Single expression of any piece of knowledge*



Explore Mycin's Use of Knowledge

**** Did you use RULE 163 to find out anything about ORGANISM-1?**

RULE163 was tried in the context of ORGANISM-1, but it failed because it is not true that the patient has had a genito-urinary tract manipulative procedure (clause 3).

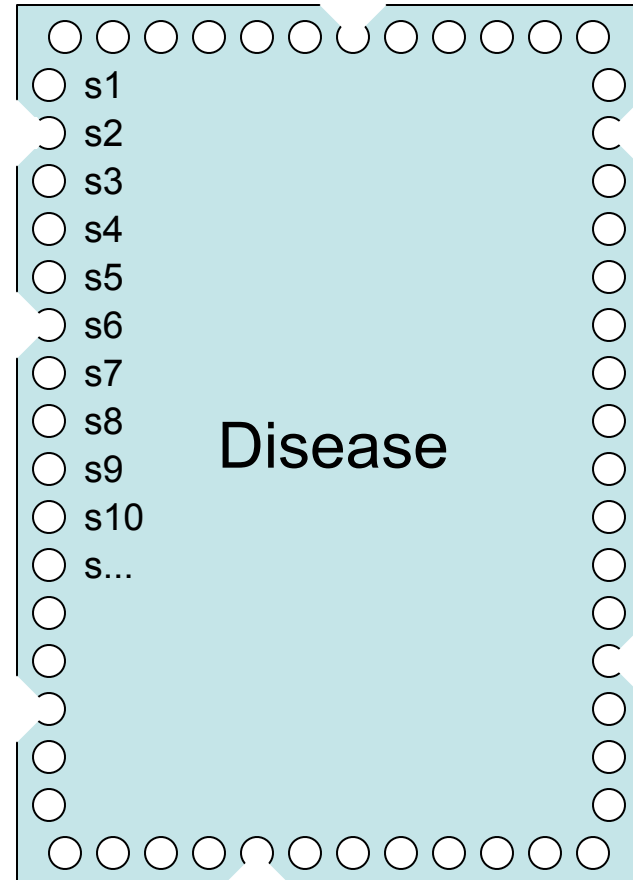
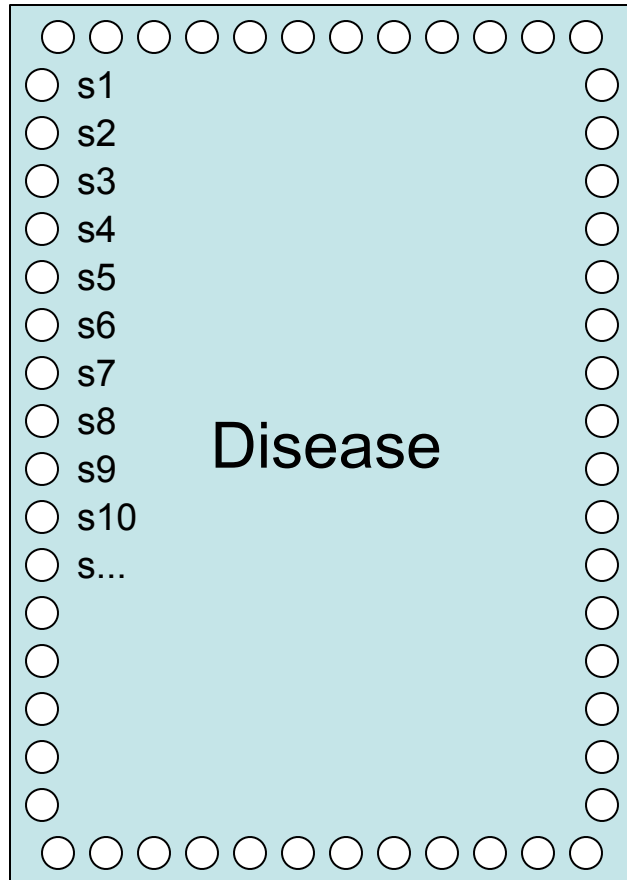
**** Why didn't you consider streptococcus as a possibility?**

The following rule could have been used to determine that the identity of ORGANISM-1 was streptococcus: RULE033

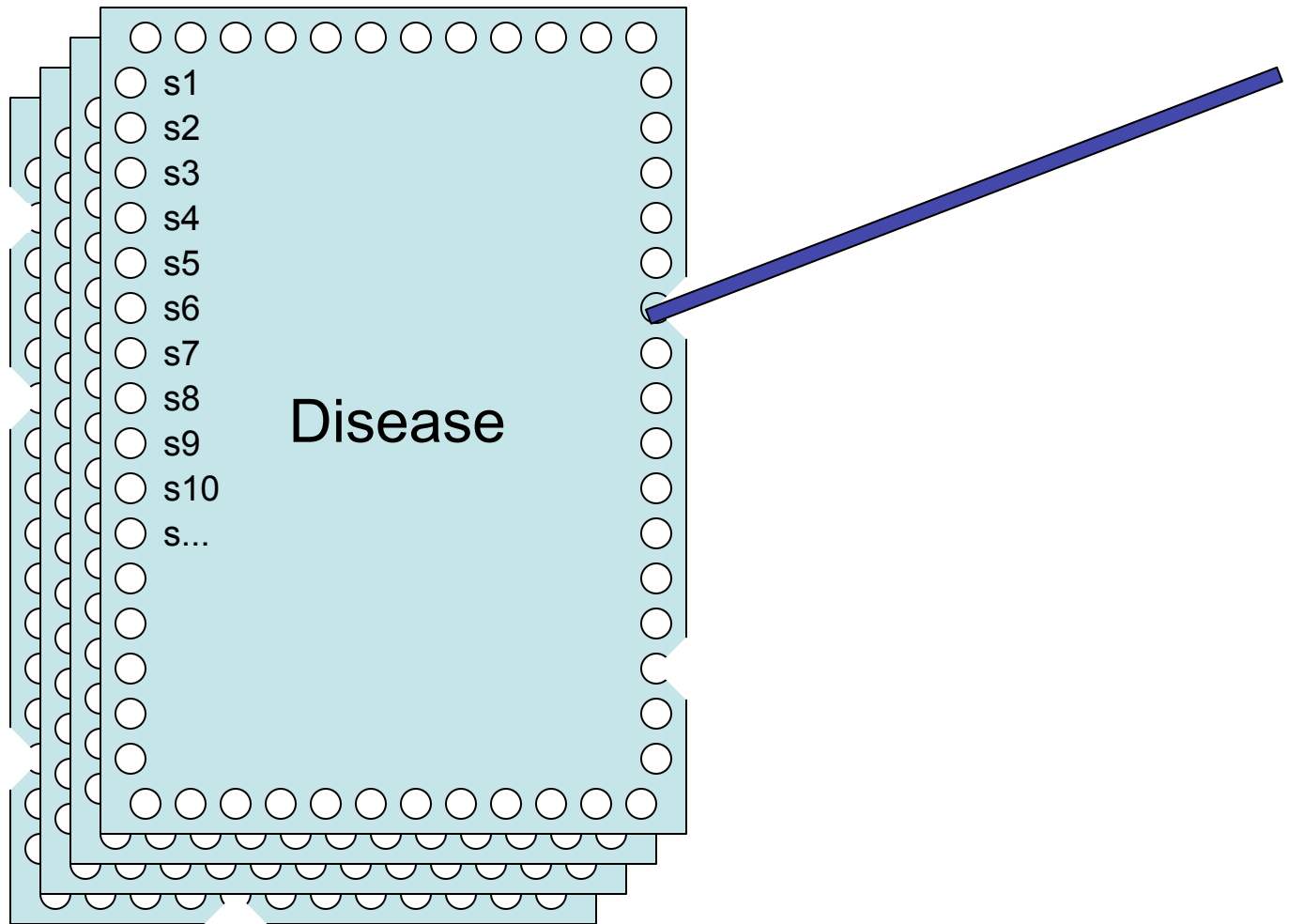
But clause 2 (“the morphology of the organism is coccus”) was already known to be false for ORGANISM-1, so the rule was never tried.

Davis, *et al.*, *Artificial Intelligence* 8: 15-45 (1977)

Even Simpler Representation



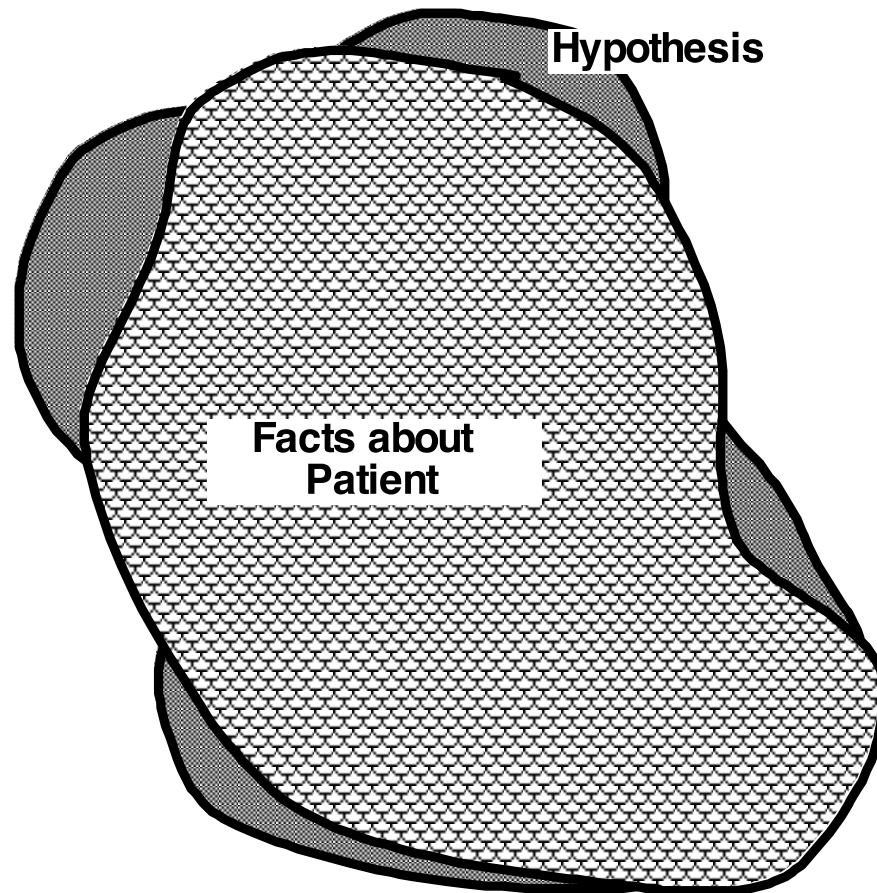
Diagnosis by Card Selection



Diagnosis by Edge-Punched Cards

- Dx is intersection of sets of diseases that *may cause* all the observed symptoms
- Difficulties:
 - Uncertainty
 - Multiple diseases
- ~ “Problem-Knowledge Coupler” of Weed

Taking the Present Illness—Diagnosis by Pattern Directed Matching



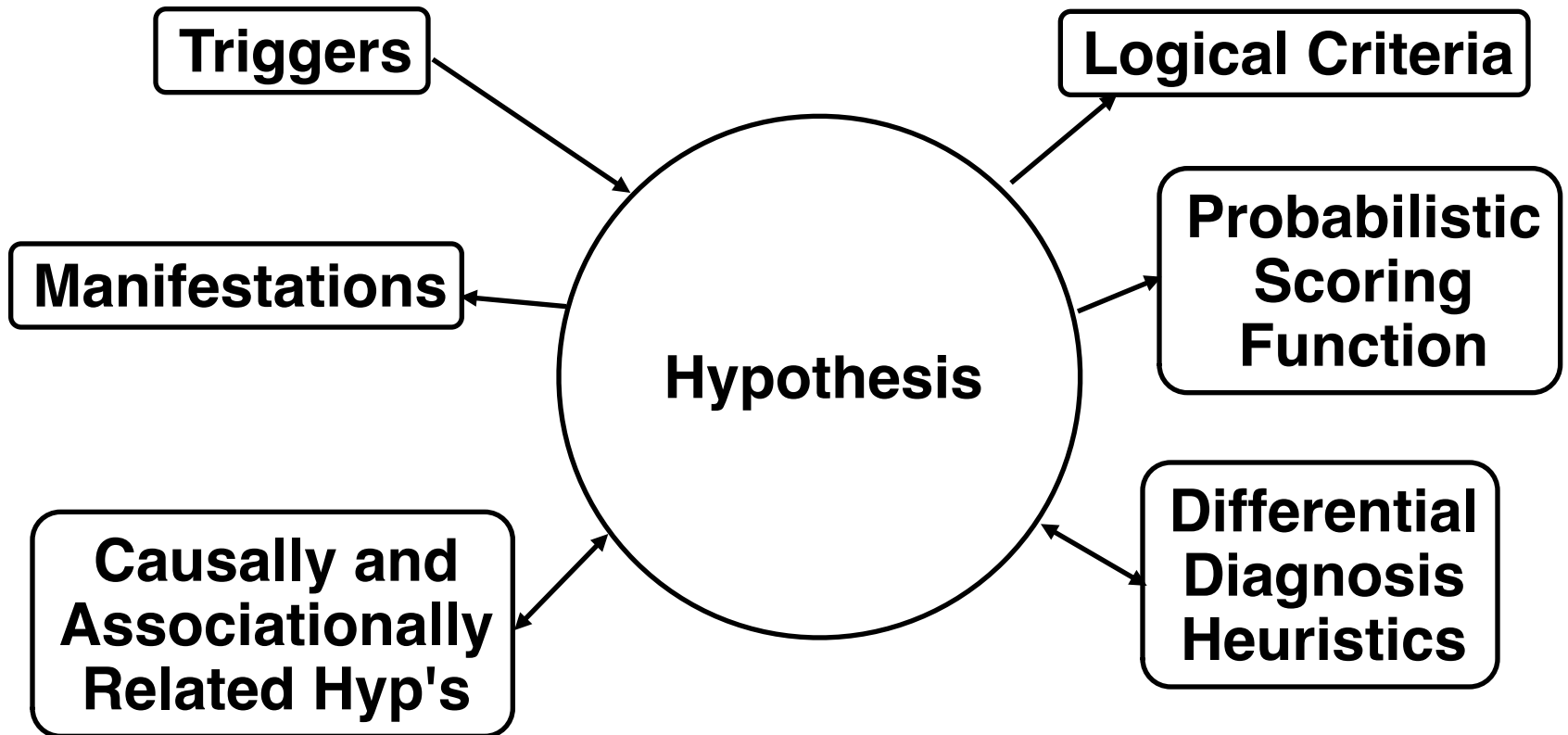
PIP's Theory of Diagnosis

- From initial complaints, *guess* suitable hypothesis.
- Use current active hypotheses to guide questioning
- Failure to satisfy expectations is the strongest clue to a better hypothesis; *differential diagnosis*
- Hypotheses are *activated, de-activated, confirmed or rejected* based on
 - (1) logical criteria
 - (2) probabilities based on:
 - findings local to hypothesis
 - causal relations to other hypotheses



The Scientific Method

Memory Structure in PIP



PIP's Model of Nephrotic Syndrome

NEPHROTIC SYNDROME, *a clinical state*

FINDINGS:

- 1* Low serum albumin concentration
2. Heavy proteinuria
- 3* >5 gm/day proteinuria
- 4* Massive symmetrical edema
- 5* Facial or peri-orbital symmetric edema
6. High serum cholesterol
7. Urine lipids present

IS-SUFFICIENT: Massive pedal edema & >5 gm/day proteinuria

MUST-NOT-HAVE: Proteinuria absent

SCORING . . .

MAY-BE-CAUSED-BY: AGN, CGN, nephrotoxic drugs, insect bite, idiopathic nephrotic syndrome, lupus, diabetes mellitus

MAY-BE-COMPLICATED-BY: hypovolemia, cellulitis

MAY-BE-CAUSE-OF: sodium retention

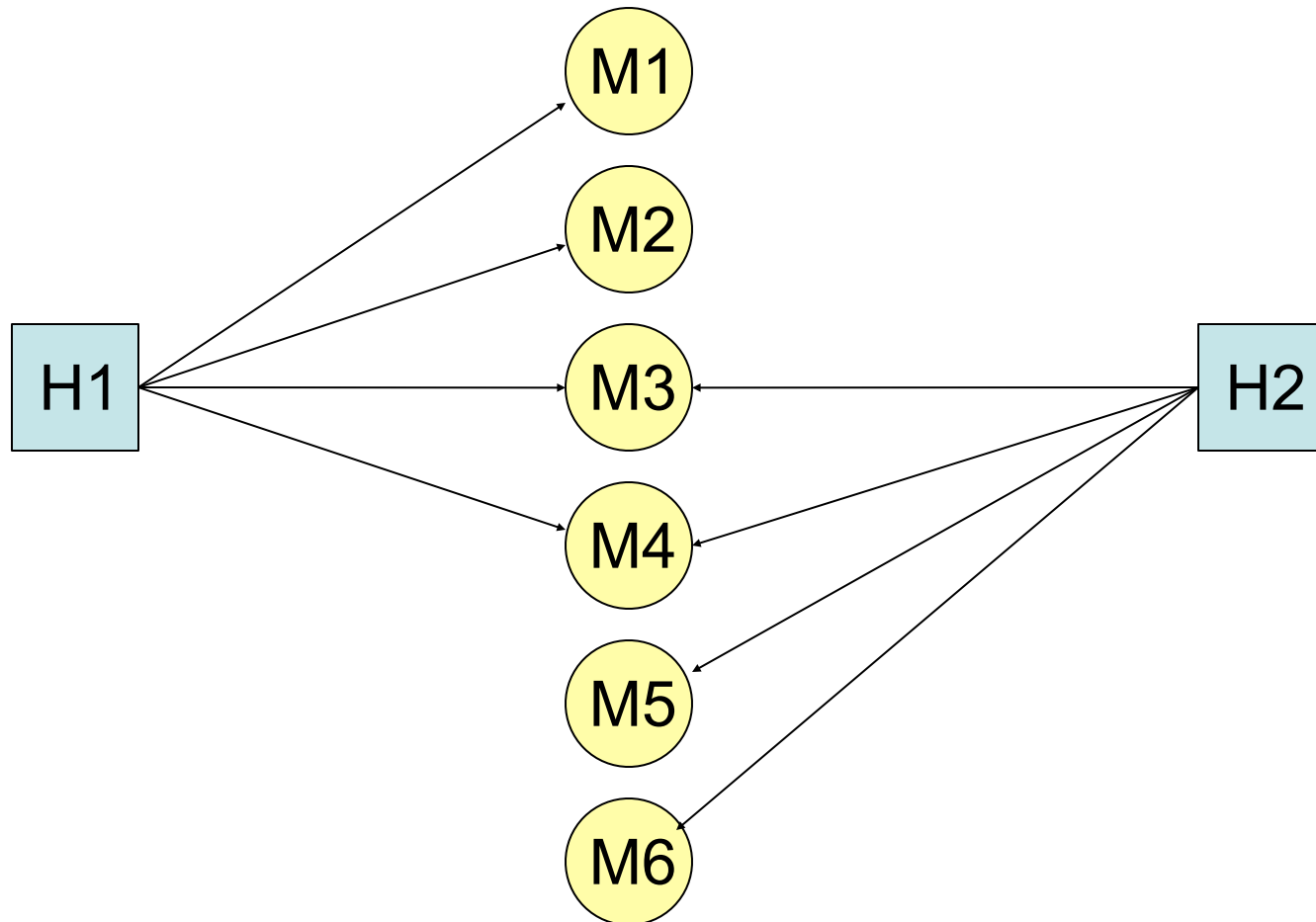
DIFFERENTIAL DIAGNOSIS:

neck veins elevated \Rightarrow constrictive pericarditis

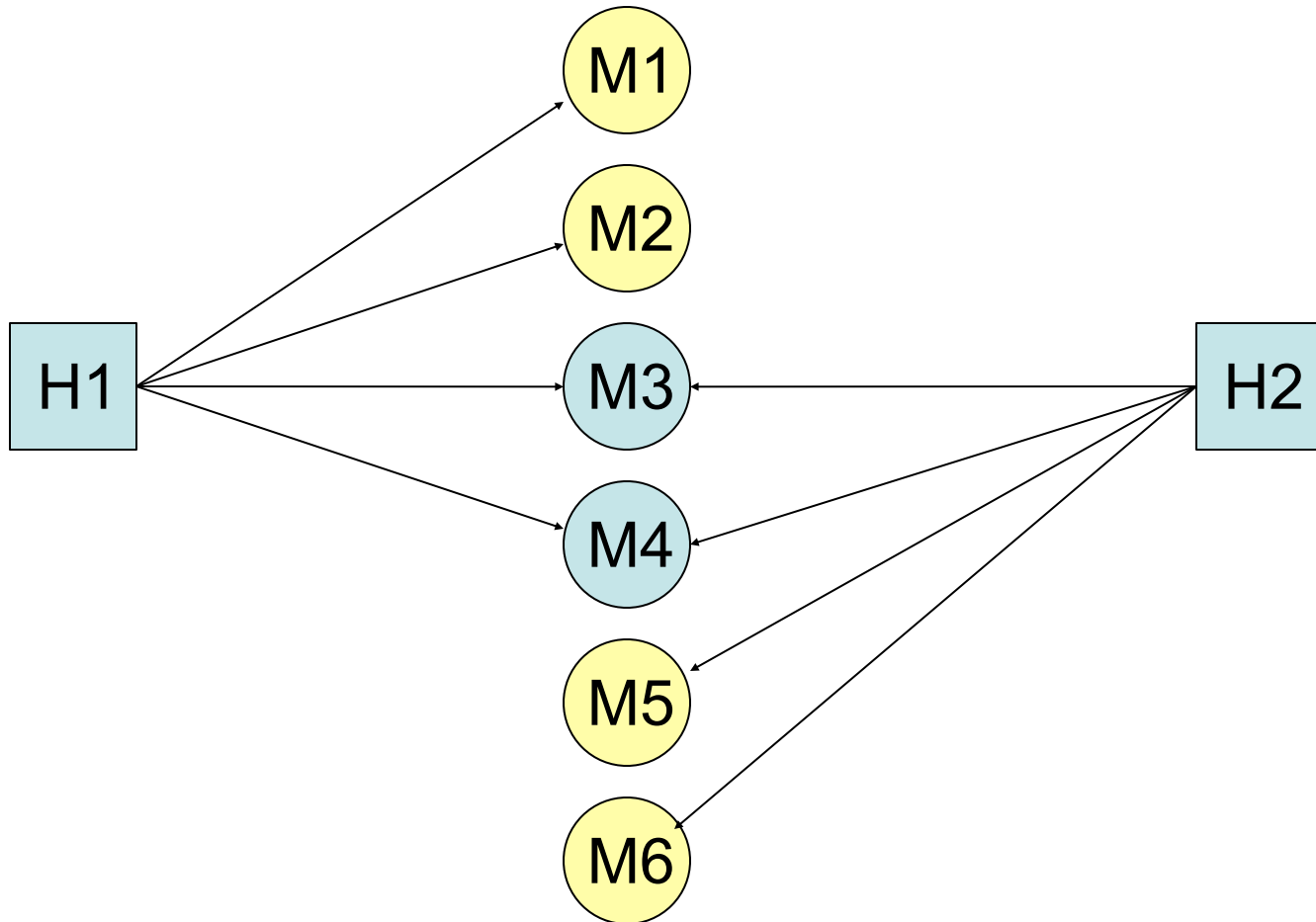
ascites present \Rightarrow cirrhosis

pulmonary emboli present \Rightarrow renal vein thrombosis

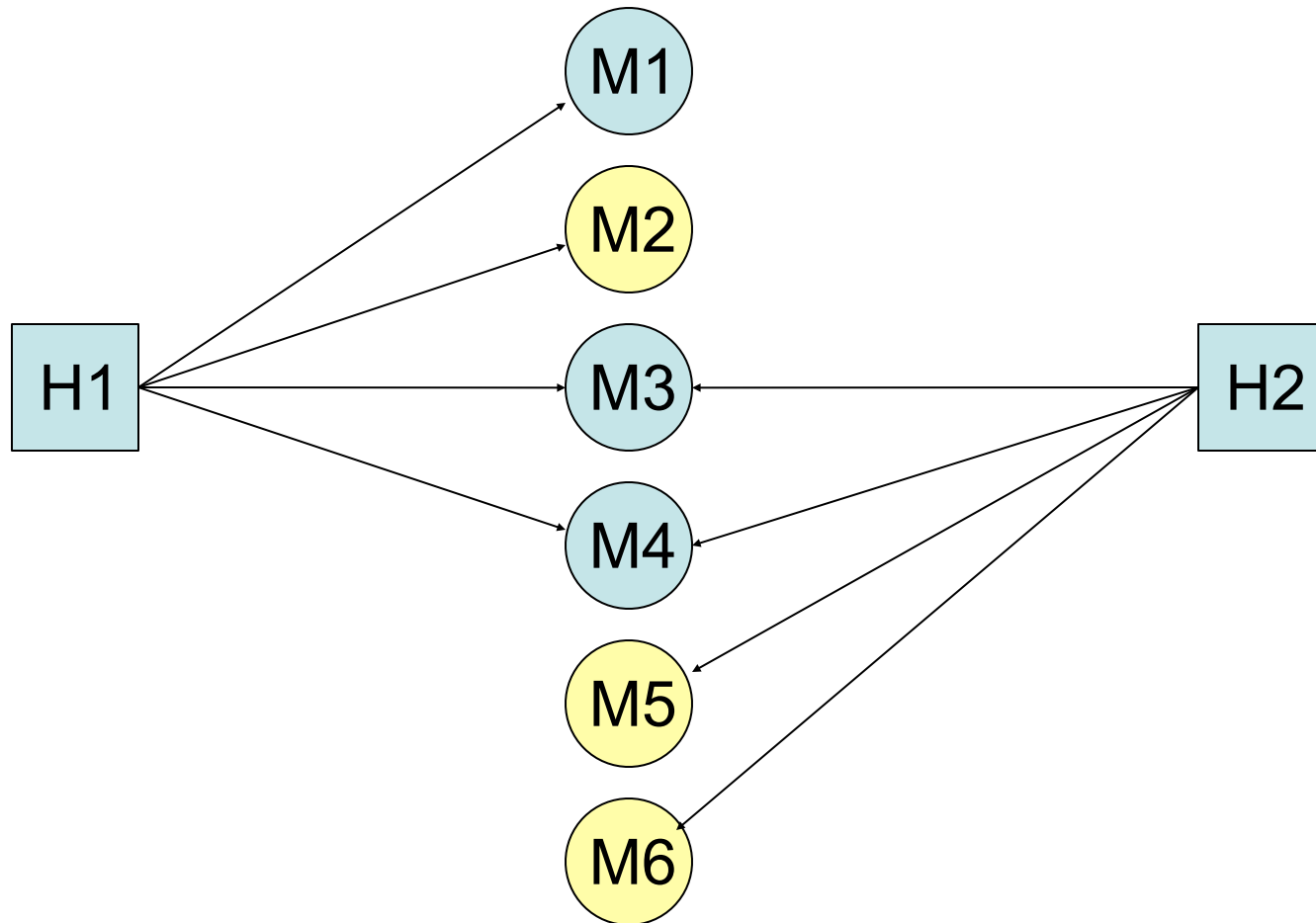
QMR Partitioning



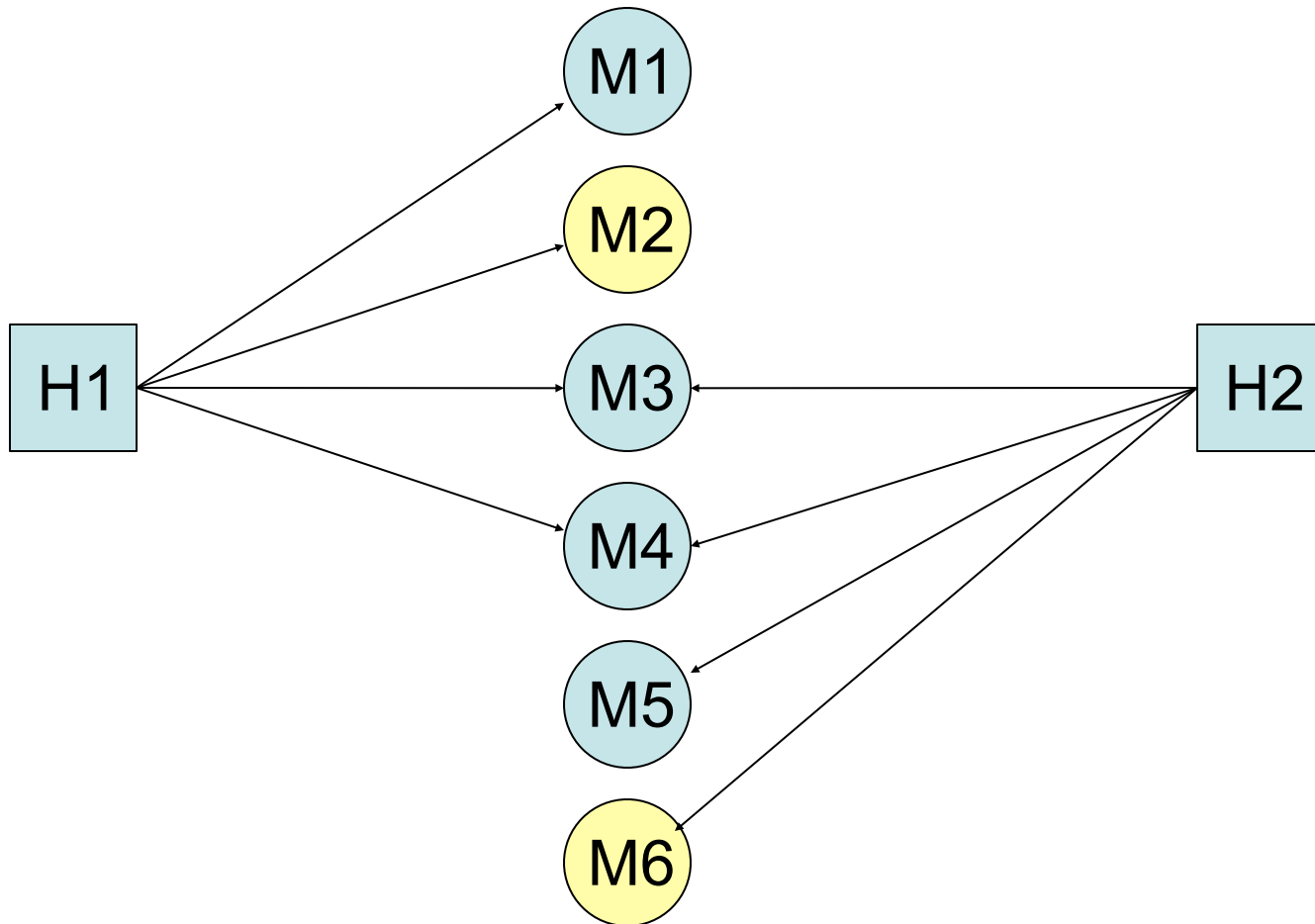
Competitors



Still Competitors



Probably Complementary



Multi-Hypothesis Diagnosis

- Set aside complementary hypotheses
- ... and manifestations predicted by them
- Solve diagnostic problem among competitors
- Eliminate confirmed hypotheses and manifestations explained by them
- Repeat as long as there are coherent problems among the remaining data

Internist/QMR

- Knowledge Base:
 - 956 hypotheses
 - 4090 manifestations (about 75/hypothesis)
 - *Evocation* like $P(H|M)$
 - *Frequency* like $P(M|H)$
 - *Importance* of each M
 - *Causal relations* between H's
- Diagnostic Strategy:
 - Scoring function
 - Partitioning
 - Several questioning strategies

QMR Database

Explore DataBase

Disease

- ANEMIA DUE TO ABNORMAL MATURATION
- ANEMIA OF CHRONIC DISEASE
- ANEMIA OF DECREASED VITAMIN B12 ABSORPTION
- ANEMIA OF FOLATE DEFICIENCY
- ANEMIA OF VITAMIN B12 DEFICIENCY
- ANEMIA SECONDARY TO MARROW DAMAGE
- ANGINA PECTORIS**
- ANGINA VARIANT <PRINZMETAL>
- ANGIOIMMUNOBLASTIC LYMPHADENOPATHY
- ANKYLOSING SPONDYLITIS
- ANORXIA NERVOSA

Finding

- TREMOR PILL-ROLLING
- TREMOR RESTING
- TREMOR WING-BEATING
- TREPONEMA FLUORESCENT ANTIBODY POSITIVE
- TREPONEMA PALLIDUM IMMOBILIZATION POSITIVE
- TRIAMTERENE THERAPY RECENT HX
- TRICHINELLA BENTONITE FLOCCULATION TEST POSITIVE
- TRICHINELLA SKIN TEST POSITIVE
- TRIGEMINAL NEURALGIA
- TRIGLYCERIDE <S> SERUM INCREASED**
- TRICHINELLA SKIN TEST POSITIVE

Findings:

- 1 3 TRIGLYCERIDE <S> SERUM INCREASED**
- 0 2 TACHYCARDIA
- 0 3 SKIN SWEATING INCREASED GENERALIZED
- 1 1 SHOULDER PAIN RIGHT
- 1 1 SHOULDER PAIN LEFT
- 0 4 SEX MALE
- 0 2 SEX FEMALE
- 0 2 PALPITATION <S>
- 2 2 MYOCARDIAL INFARCTION HX
- 2 3 MYOCARDIAL INFARCTION FAMILY HX
- 2 3 LIPOPROTEINEMIA TYPE IV
- 2 2 LIPOPROTEINEMIA TYPE III
- 2 3 LIPOPROTEINEMIA TYPE II
- 2 1 LEG <S> CLAUDICATION INTERMITTENT HX
- 2 2 HYPERTENSION HX
- 1 1 HEMORRHAGE GASTROINTESTINAL ACUTE RECENT
- 1 1 HEMORRHAGE ACUTE RECENT HX
- 1 2 HEART SOUND <S> S4 LEFT ATRIAL GALLOP

- 1 2 PEDIATRIC DRUG HYPERSENSITIVITY CHOLESTATIC REF
- 1 2 PEDIATRIC EXTRAHEPATIC BILIARY ATRESIA
- 1 2 PEDIATRIC BILIARY CIRRHOSIS SECONDARY
- 1 2 PEDIATRIC BILIARY CIRRHOSIS PRIMARY
- 1 2 PEDIATRIC FATTY LIVER SECONDARY
- 1 2 OBESITY
- 1 1 WEBER CHRISTIAN DISEASE
- 1 2 ATHEROMATOUS EMBOLISM
- 1 4 DIABETIC KETOACIDOSIS
- 2 3 DIABETES MELLITUS
- 1 3 GOUTY ARTHRITIS CHRONIC
- 1 4 GOUTY ARTHRITIS ACUTE
- 1 3 ABDOMINAL AORTIC ANEURYSM <UNCOMPLICATED>
- 1 3 VENTRICULAR ANEURYSM LEFT
- 1 3 ARTERIOSCLEROTIC HEART DISEASE
- 1 3 MYOCARDIAL INFARCTION ACUTE
- 1 3 CRESCENDO ANGINA
- 1 3 ANGINA PECTORIS
- 1 3 PANCREATITIS CHRONIC

QMR Scoring

- Positive Factors
 - Evoking strength of observed Manifestations
 - Scaled Frequency of causal links from confirmed Hypotheses
- Negative Factors
 - Frequency of predicted but absent Manifestations
 - Importance of unexplained Manifestations
- Various scaling parameters (roughly exponential)

Example Case

Internist Data Summary

Internist Reconstruction -- Data Summary

Diagnose

Manifestations PRESENT:

- ABDOMEN DISTENTION
- ABDOMEN FLUID WAVE
- AGE GTR THAN 55
- ALKALINE PHOSPHATASE BLOOD GTR THAN 2 TIMES NORMAL
- AMMONIA BLOOD INCREASED
- ANOREXIA
- ARTHRITIS HX
- ASCITIC FLUID PROTEIN 3 GRAM <S> PER DL OR LESS
- ASCITIC FLUID WBC 100 TO 500
- ASTERIXIS
- BILIRUBIN BLOOD CONJUGATED INCREASED
- BILIRUBIN URINE PRESENT
- CHEST PAIN LATERAL EXACERBATION WITH BREATHING
- CHEST PAIN LATERAL SHARP
- DEPRESSION HX
- DYSPNFA ARR IPT CNSFT

Remove Present

Manifestations ABSENT:

- ALCOHOLISM CHRONIC HX
- ASCITIC FLUID AMYLASE INCREASED
- ASCITIC FLUID CYTOLOGY POSITIVE
- ASCITIC FLUID LDH GTR THAN 500
- DIARRHEA CHRONIC
- ESOPHAGUS BARIUM MEAL VARICES
- FECES BLACK TARRY
- FEVER
- HEMATOCRIT BLOOD LESS THAN 35
- PRESSURE VENOUS CERVICAL INCREASED ON INSPECTION
- STOMACH BARIUM MEAL ULCER CRATER <S>
- T3 RESIN UPTAKE INCREASED
- T4 FREE BLOOD INCREASED
- UREA NITROGEN BLOOD 30 TO 59
- URIC ACID BLOOD INCREASED

Remove Absent

Initial Solution

Diagnostic Results

Problem:

- 94 HEPATITIS CHRONIC ACTIVE
- 119 PEDIATRIC HEPATITIS CHRONIC ACTIVE
- 136 MACRONODAL CIRRHOSIS <POSTNECROTIC>
- 158 BILIARY CIRRHOSIS PRIMARY
- 178 PEDIATRIC BILIARY CIRRHOSIS PRIMARY

Explained:

- AGE GTR THAN 55
- ALKALINE PHOSPHATASE BLOOD GTR THAN 2 TIMES NORMAL
- ANOREXIA
- BILIRUBIN BLOOD CONJUGATED INCREASED
- BILIRUBIN URINE PRESENT
- FECES LIGHT COLORED
- HAND <S> PALMAR ERYTHEMA
- IMMUNOELECTROPHORESIS SERUM IGA INCREASED
- IMMUNOELECTROPHORESIS SERUM IGG INCREASED

Absent:

- DIARRHEA CHRONIC
- FEVER
- HEMATOCRIT BLOOD LESS THAN 35

Unexplained:

- ABDOMEN DISTENTION
- ABDOMEN FLUID WAVE
- AMMONIA BLOOD INCREASED
- ARTHRITIS HX
- ASCITIC FLUID PROTEIN 3 GRAM <S> PER DL OR LESS
- ASCITIC FLUID WBC 100 TO 500

Complementary:

- 143 MICRONODAL CIRRHOSIS <LAENNECS>
- 162 HEPATITIS ACUTE VIRAL
- 170 CHOLANGIOCARCINOMA <INTRAHEPATIC NON HILAR>
- 178 HEPATIC AMYLOIDOSIS

Shelf:

- ABDOMEN DISTENTION
- ARTHRITIS HX
- CHEST PAIN LATERAL EXACERBATION WITH BREATHING
- CHEST PAIN LATERAL SHARP
- FECES GUAIAC TEST POSITIVE
- PLEURAL FRICTION RUB
- WEIGHT INCREASE RECENT HX

Askable:

- ABDOMEN PAIN CHRONIC
- ABDOMEN PAIN EPIGASTRIUM
- ABDOMEN PAIN EPIGASTRIUM UNRELIEVED BY ANTACID
- ABDOMEN PAIN EXACERBATION WITH MEAL <S>
- ABDOMEN PAIN NON COLICKY
- ABDOMEN PAIN PRESENT
- ABDOMEN PAIN RIGHT UPPER QUADRANT
- ABDOMEN TENDERNESS PRESENT
- ABDOMEN TENDERNESS RIGHT UPPER QUADRANT
- ACTIVATED PARTIAL THROMBOPLASTIN TIME INCREASED
- AGE 16 TO 25
- AGE 26 TO 55
- ALBUMIN SERUM DECREASED
- ALKALINE PHOSPHATASE BLOOD INCREASED NOT OVER 2 TIMES NORMAL

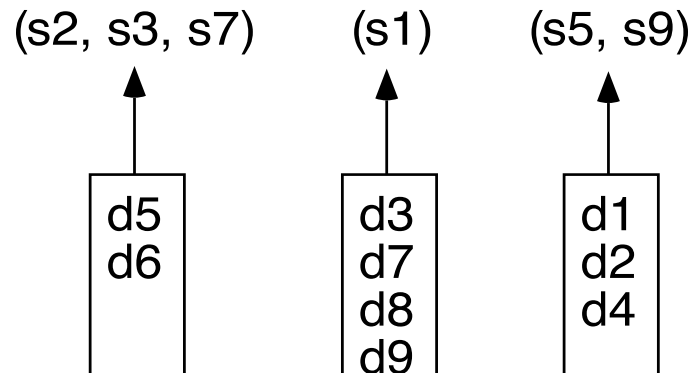
Symptom Clustering for Multi-Disorder Diagnosis

— Tom Wu, Ph.D. 1991

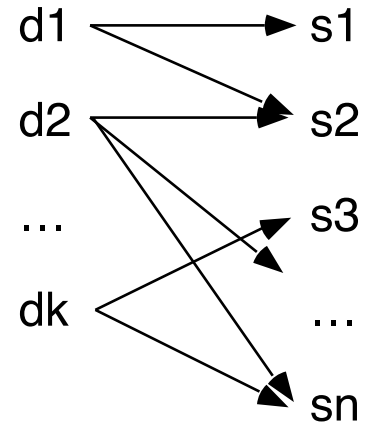
Assume a bipartite graph representation of diseases/
symptoms

Given a set of symptoms, how to proceed?

If we could “guess” an appropriate clustering of the
symptoms so that each cluster has a single cause ...

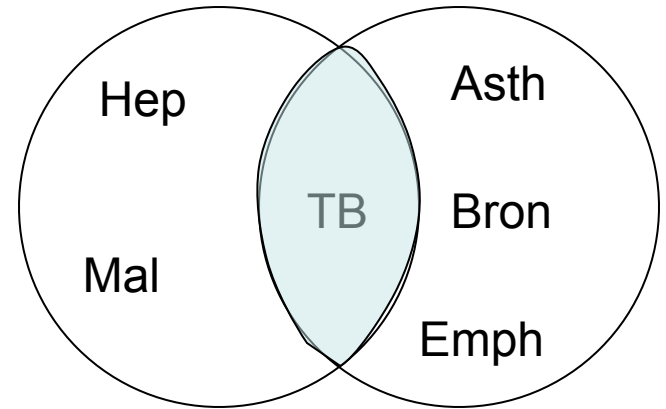


... then the solution is (d5, d6) x (d3, d7, d8, d9) x (d1, d2, d4)



Clustering Alternatives

Symptom	Possible Causes
Fever	TB, Hepatitis, Malaria
Cough	TB, Asthma, Bronchitis, Emphysema

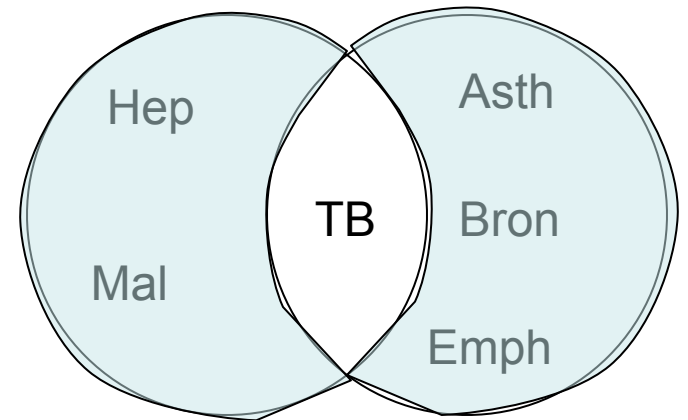


H1

H2

Fever, Cough
TB

Fever	Cough
Hep Mal	Asth Bron Emph



Synopsis in Renal Disease

- Diseases

- Hypertension (HTN)
- Acute glomerulonephritis (AGN)
- IgA nephropathy (IgA)
- Prerenal azotemia (PRA)
- Hepatorenal syndrome (HRS)
- Renal vasculitis (RV)
- Congestive heart failure (CHF)
- Aldosteronism (Aldo)
- Constrictive pericarditis (Peri)
- Diabetic ketoacidosis (DKA)
- Analgesic nephropathy (AN)
- Hypokalemic nephropathy (HKN)
- Chronic renal failure (CRF)

- Symptoms

- High urine osmolality (Osm \uparrow)
- High urine specific gravity (Sg \uparrow)
- Low urine sodium (Na \downarrow)
- Low urine pH (pH \downarrow)

	HTN	AGN	IgA	PRA	HRS	RV	CHF	Aldo	Peri	DKA	AN	HKN	CRF	RTA
Osm	X	X	X	X	X	X								
Sg \uparrow	X	X	X	X	X	X	X							
Na \downarrow				X	X		X	X	X					
pH \downarrow		X		X						X	X	X	X	X

After Osm ↑

Osm ↑
HTN
AGN
IgA
PRA
HRS
RV

	HTN	AGN	IgA	PRA	HRS	RV	CHF	Aldo	Peri	DKA	AN	HKN	CRF	RTA
Osm	X	X	X	X	X	X								
Sg ↑	X	X	X	X	X	X	X							
Na ↓				X	X		X	X	X					
pH ↓		X		X						X	X	X	X	X

Osm↑, Sg↑

Add Sg↑

Cover

HTN

AGN

IgA

PRA

HRS

RV

	HTN	AGN	IgA	PRA	HRS	RV	CHF	Aldo	Peri	DKA	AN	HKN	CRF	RTA
Osm	X	X	X	X	X	X								
Sg↑	X	X	X	X	X	X	X							
Na↓				X	X		X	X	X					
pH↓		X		X						X	X	X	X	X

Add Na↓

Restrict

Append

Osm↑, Sg↑, Na↓
PRA HRS

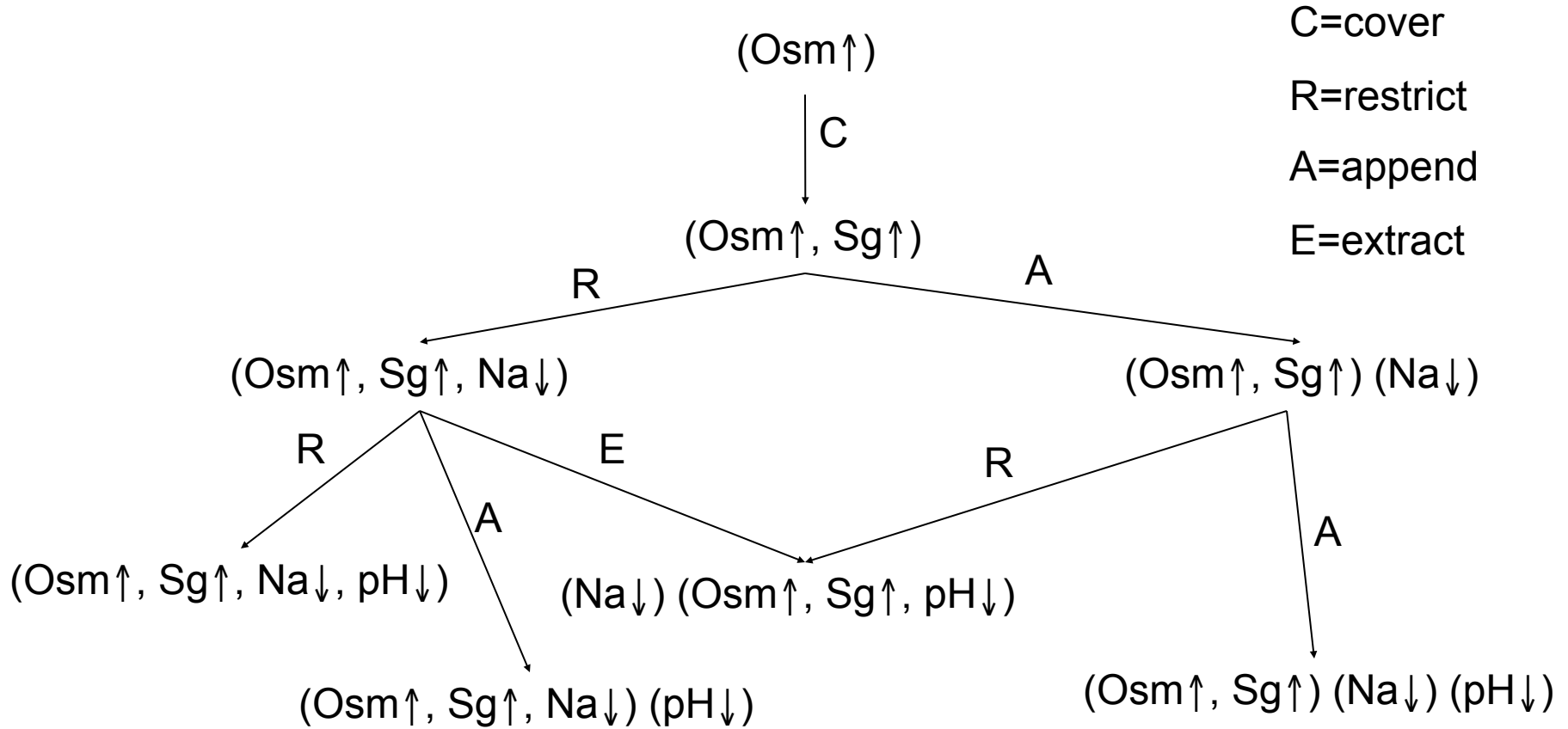
or

Osm↑, Sg↑
HTN AGN IgA RV

Na↓
Aldo CHF Peri

	HTN	AGN	IgA	PRA	HRS	RV	CHF	Aldo	Peri	DKA	AN	HKN	CRF	RTA
Osm	X	X	X	X	X	X								
Sg↑	X	X	X	X	X	X	X							
Na↓				X	X		X	X	X					
pH↓		X		X						X	X	X	X	X

Search Space



	HTN	AGN	IgA	PRA	HRS	RV	CHF	Aldo	Peri	DKA	AN	HKN	CRF	RTA
Osm	X	X	X	X	X	X								
Sg↑	X	X	X	X	X	X	X							
Na↓				X	X		X	X	X					
pH↓		X		X						X	X	X	X	X

Symptom Clustering is Efficient

- Like in any “planning island” approach, reducing an exponential problem to several smaller exponential problems vastly improves efficiency, *if it captures some insight into the problem.*
- Wu's algorithm (SYNOPSIS) will keep a compact encoding even if it overgenerates slightly.
 - E.g., suppose that of the set of diseases represented by $(d5, d6) \times (d3, d7, d8, d9) \times (d1, d2, d4), d6 \times d8 \times d1$ is not a candidate. To represent this precisely would require enumerating the 23 valid candidates. Instead, the factored representation is kept.

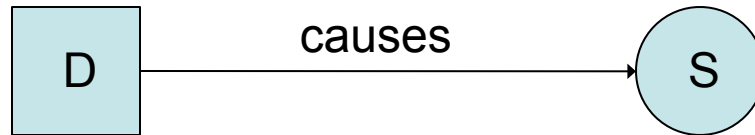
In a diagnostic problem drawn from a small subset of the Internist database, it is a *power of 3* faster and a *power of 5* more compact than standard symptom clustering.

Guide search via probabilities, if we have a reasonable model(!)

More Expert Systems

- Causality?
- What's in a Link?
- Temporal reasoning
- Quantitative reasoning
- Model-based reasoning
- Workflow

Meaning of Representation?



- Always? → probability
- Magnitude? → severity; bad cold → worse fever?
- Delay? → temporality
- Where? → spatial dependency
- Under what conditions? → context
- Interaction of multiple causes → physical laws
- Cross-terms → high-dimensional descriptions

Temporal Reasoning

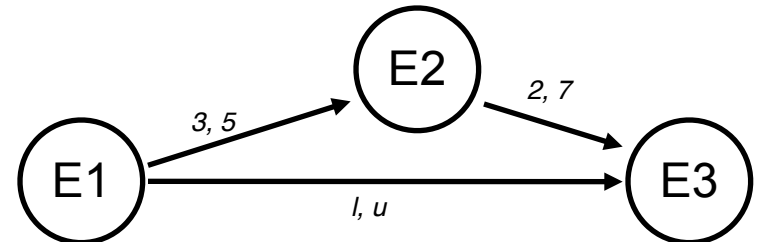
- **Keeping track of multiple forms of temporal relations (Kahn '75)**
 - **The time line**
 - “On Dec. 12 last year . . .”
 - **Special reference events**
 - “Three days after I was hospitalized in 1965 . . .”
 - **Temporal Ordering Chains**
 - “It must have been before I graduated from high school.”
- **Constraint propagation (Kohane '87)**
 - **Primitive relation: e1, e2, lower, upper bounds**
 - **Heuristics for propagation based on semantic grouping**

$$3 \leq T(E2) - T(E1) \leq 5$$

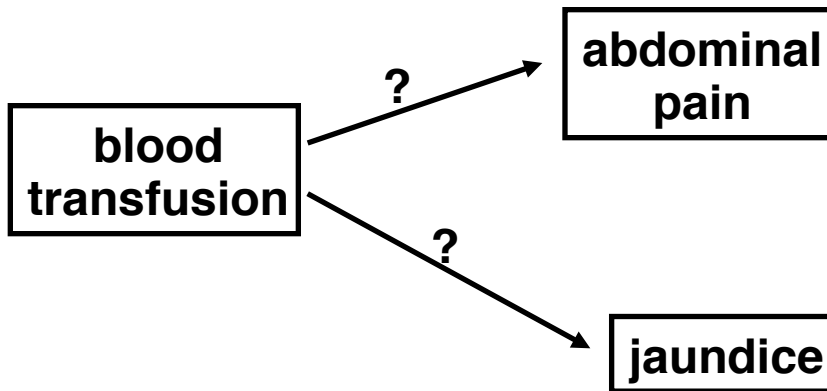
$$2 \leq T(E3) - T(E2) \leq 7$$

Therefore

$$l=5 \leq T(E3) - T(E1) \leq 12=u$$

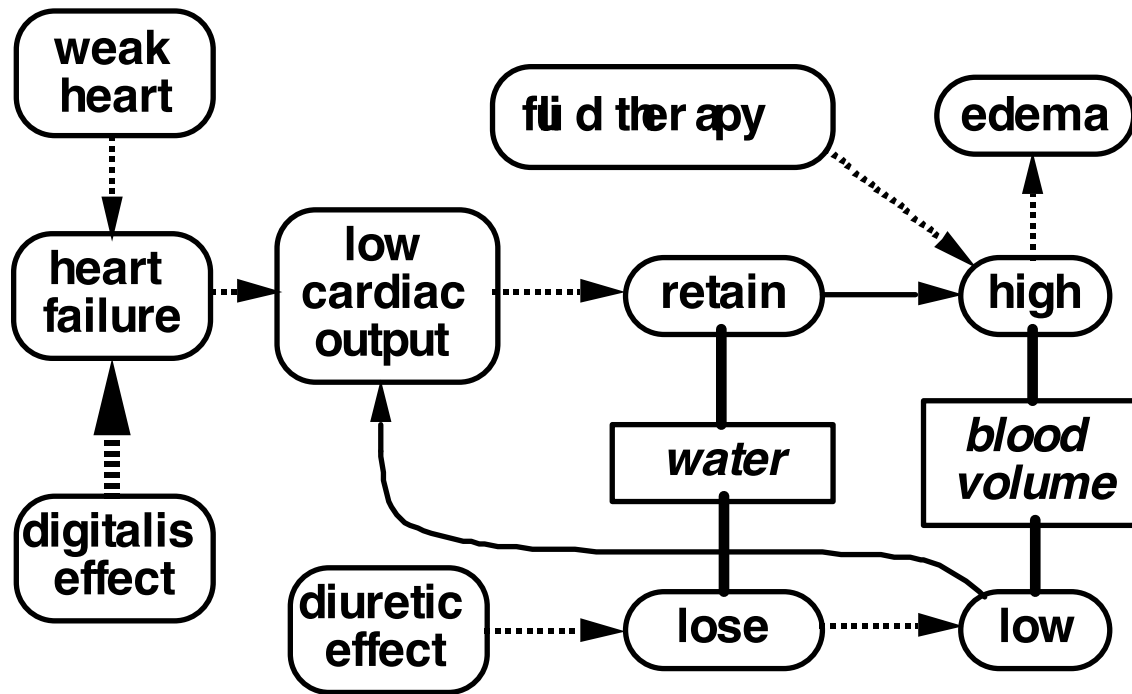


Exploiting Temporal Relations



- transfusion precedes both abdominal pain and jaundice *implies* transfusion-borne acute hepatitis B
- as in 1, but only by one day
- jaundice occurred 20 years ago, transfusion and pain recent
- Can be very efficient at filtering out nonsense hypotheses.

Interpreting the Past with a Causal/Temporal Model



- ▶ definite cause
-▶ possible cause
- ||||▶ possible correction (not all shown)

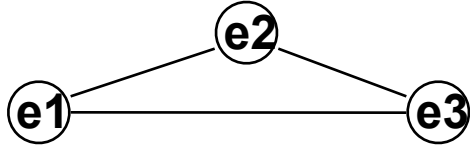
Temporal Representation can be Complex

Figure of EKG data from heart removed due to copyright restrictions.

Time

The usual:

- point, intervals, constraints



- timelines, reference events, fuzz, ...

The unusual

- cyclic edema

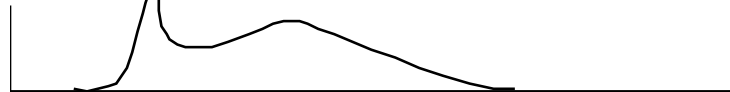


- focal glomerulonephritis



- patterns of fever

Systems issues



- flow of "now"
- supporting the illusion of "instantaneous" decision-making within a temporal reasoner
 - correcting the past
 - reasoning by hindsight

The Surprisingly Normal pH

- Diarrhea causes bicarbonate (alkali) loss
- Vomiting causes acid loss
- Therefore, normal pH is a manifestation of {diarrhea + vomiting}!

Multi-Level Causal Model

Figure of three-level causal model removed due to copyright restrictions.

Reasoning from Models

- Model handles all possible interactions, without having explicitly to anticipate them all
- Reasoning: Fit parameters to a physiological model, then predict consequences to suggest
 - other expected findings
 - reasonable interventions
- Qualitative models
- Combining associational and model-based reasoning

Guyton's Model of Cardiovascular Dynamics

Figure removed due to copyright restrictions.

Long's Clinical Model of Heart Failure Predictions for Mitral Stenosis with Exercise

Figure removed due to copyright restrictions.

Physiological

"All variations in myocardial contractile activity can be expressed as displacements of the force-velocity curve. However, there are two fundamental ways in which the force-velocity curve can be shifted. Figure {left} shows a family of force-velocity curves obtained from an isolated cardiac muscle; each curve was obtained at a different preload, i.e., with a different degree of stretch on the muscle. Note that changing the preload has altered the intercept of the force-velocity curve on the horizontal axis; i.e., it has increased the isometric force developed by the muscle. However, these alterations in preload have not altered the intrinsic velocity of shortening, since all the curves extrapolate to the same intercept on the vertical axis. Thus, a change in initial length of heart muscle shifts the force-velocity curve by altering the total force which can be developed by the muscle.

This type of shift in the force-velocity curve may be contrasted with that obtained when a positive inotropic agent, such as norepinephrine or digitalis, is added to the muscle while the initial length is held constant (Fig. {right}). These agents not only increase the force which the muscle is capable of lifting, i.e., the intercept of the force-velocity curve on the horizontal axis, but also increase the velocity of shortening of the unloaded muscle, i.e., the extrapolated intercept on the vertical axis."

— Harrison's (6th ed.)

Figures

Normal cat-muscle

Inotropic Agent

Figures removed due to copyright restrictions.

Clinical Knowledge

"... from the clinical point of view, heart failure may be considered to be a disease state in which an abnormality of myocardial function is responsible for the inability of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues. Though a defect in myocardial contraction always exists in heart failure, this disorder may result from a *primary abnormality* in the heart muscle or it may be secondary to a *chronic excessive work load*. It is important to distinguish heart failure from (1) states of *circulatory insufficiency* in which myocardial function is not primarily impaired, such as cardiac tamponade, hemorrhagic shock, or tricuspid stenosis, (2) conditions in which there is *circulatory congestion* because of abnormal salt and water retention but in which there is no serious disturbance of myocardial function, and (3) conditions in which the normal heart is suddenly presented with a load which *exceeds its capacity*, e.g., accelerated hypertension."

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