Two approaches: 
atomic vs. molecular

Molecular (=pre-coordinated =enumerative )
- A single name/code and value
  - Left patellar deep tendon reflex intensity is 2 +
- Advantage
  - Concise in data storage
  - Easy to execute decision support logic
  - Don’t allow non-sensical statement

Atomic (=post-coordinated =compositional)
- Deep tendon reflex intensity is 2 +
  - Anatomic site is *patella*
  - Laterality is *left*
- Advantage
  - Better domain coverage & compositional flexibility (expressivity)
  - Requirement for compositional rules to avoid Combinatorial explosion, and anatomically implausible occurrence

Recommendation
- System should allow conversion: Atomic $\Rightarrow$ Molecular

Medical Injuries
- As many as 44,000 to 98,000 Americans die each year from medical errors
- More people die from medical injuries than from Breast Cancer or AIDS or Motor Vehicle Accidents
- Direct health care costs totaling $9 - 15 billion per year
- A systems approach utilizing information technology (clinical decision support systems) is needed

Definition: Medical Informatics
- Medicine is fundamentally an information science
  - Clinicians and researchers spend a great deal of time acquiring and analyzing it
  - There is evidence it is not used optimally
    - e.g., misuse of services, medical errors, etc.
  - There are scientific ways to determine how to use information better
- The scientific field that deals with biomedical information, data, and knowledge —their storage, retrieval, and optimal use for problem solving and decision-making.
**Fundamental Theorem of Medical Informatics**

An intelligent practitioner working in combination with information resources/technology is “better” than the practitioner without such support.

> Creating an environment of “supported practice”

Adapted from Hersh WR. Health/Medical/Biomedical Informatics: A general introduction. 2003

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**Clinical Informatics Applications**

- Can classify by the type of information they use
  - **Patient-specific**
    - The core application: the electronic medical record
    - Another application: telemedicine
  - **Knowledge-based**
    - Information retrieval systems
  - **Combining the two**
    - Decision-support systems

---

**Definitions**

- **Clinical decision support system**
  - Any computer program designed to help health professionals make clinical decisions
  - Tools for information management: information retrieval
  - Tools for focusing attention: alerts, reminders
  - Tools for providing patient-specific recommendations: diagnostic system


- **Expert system**
  - A model of decision process
  - To represent, in an approximate form that is executable by a computer, the logical processes employed by an expert in a particular subject area to decide among 2 or more alternative conclusions


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**Classical Expert System**

A computer program that, given case description, uses the information in the KB to generate new information about the case


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**Fundamental problems in designing medical expert system**

- **Knowledge acquisition**
  - How to translate human knowledge (e.g. textbook, journal, clinical database etc) into abstract representations in a computer
- **Knowledge representation**
  - How to represent human knowledge in terms of data structures that can be processed by a computer
- **Inference generation**
  - How to use the abstract data structures to generate useful information in the context of a specific case
Decision Support Tools

- **Rule Systems**
  - If A and B or C Then D

- **Bayesian Systems**

- **Neural Nets**

- **Logistic Regression**

- **Protocols**

More Jargons

- **Type of learning in data mining**
  - Supervised learning: prediction
    - Inputs & correct outputs
    - Algorithms
      - Regression, Bayesian method, decision tree, neural network, nearest neighbor, genetic algorithm
  - Unsupervised learning: association, clustering
    - Inputs
    - Wallmart example: Beer and diapers
    - Algorithms
      - Association rules
      - Clustering

Types of Clinical Decision Support

- **Rule based system**
  - If ~ then ~
  - E.g.: MYCIN, most CDSS system in clinical practice

- **Probability based system**
  - Ilia, QMR

Types of Clinical Decision Support System

- **Isolated system**
  - Adverse event surveillance
    - ADE (adverse drug event), Nosocomial infection, Decubitus ulcer surveillance system
  - Antibiotics prescription management
  - Renal dosing system

- **Comprehensive system**
  - CPOE (Computerized Physician Order Entry)
**Architecture of Clinical Decision Support System**

- Select patient
- Record observation
- Enter order

**Event Monitor**

**Rules Engine**

**Alert/Reminder**

**Clinical Workstation**

**Common Data Repository**

**CLAS (critical laboratory alerting system)**

**Goal**
- Notify as rapidly as possible health-care personnel of laboratory values

**System description**
- Alert logic: 11 alerting conditions (high/low/falling) developed by a medical panel
- Alerts were generated when test results transferred from the lab to the EMR
- Alerts were sent to health care personnel via pager, EMR, or fax

**Evaluation (before and after)**
- Appropriate treatment for alerting condition: 68.1% → 83.8%
- Time spent in life threatening condition: 30.4hrs → 15.7hrs

**CLAS (critical laboratory alerting system)**

**Data Used: Laboratory Results, Blood Gases**

<table>
<thead>
<tr>
<th>Alerting Condition</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyponatremia (NAL)</td>
<td>Na⁺ &lt; 130 mEq/l</td>
</tr>
<tr>
<td>Falling Sodium (NAS)</td>
<td>Na⁺ &lt; 130 mEq/l in 24 hrs and Na⁺ &lt; 130 mEq/l</td>
</tr>
<tr>
<td>Hypernatremia (NAS)</td>
<td>Na⁺ &gt; 155 mEq/l</td>
</tr>
<tr>
<td>Hypokalemia (KL)</td>
<td>K⁺ &lt; 2.7 mEq/l</td>
</tr>
<tr>
<td>Falling Potassium (KLF)</td>
<td>K⁺ &lt; 2.7 mEq/l in 24 hrs and K⁺ &lt; 3.2 mEq/l</td>
</tr>
<tr>
<td>Hypokalemia, patient on digoxin (KLD)</td>
<td>K⁺ &lt; 2.7 mEq/l and patient on digoxin</td>
</tr>
<tr>
<td>Hyperkalemia (KH)</td>
<td>K⁺ &gt; 6.0 mEq/l</td>
</tr>
<tr>
<td>Metabolic acidosis (CO₂L)</td>
<td>CO₂ &lt; 15 and BUN &lt; 50 or CO₂ &lt; 18 (BUN unknown)</td>
</tr>
<tr>
<td></td>
<td>CO₂ &lt; 18 and BUN &gt; 50</td>
</tr>
<tr>
<td></td>
<td>CO₂ &lt; 18 and BUN unknown</td>
</tr>
<tr>
<td></td>
<td>CO₂ &lt; 18 and BUN &gt; 50</td>
</tr>
<tr>
<td></td>
<td>CO₂ &lt; 18 and BUN &lt; 50</td>
</tr>
<tr>
<td>Metabolic alkalosis (CO₂H)</td>
<td>CO₂ &gt; 25 and BUN &lt; 5</td>
</tr>
<tr>
<td></td>
<td>CO₂ &lt; 25 (BUN unknown)</td>
</tr>
<tr>
<td></td>
<td>CO₂ &gt; 25 (BUN unknown)</td>
</tr>
</tbody>
</table>

**Alerting Criteria for CLAS**

- Data Used: Laboratory Results, Blood Gases

<table>
<thead>
<tr>
<th>Alerting Criteria</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia (GL)</td>
<td>Glucose &lt; 45 mg/dL</td>
</tr>
<tr>
<td>Hyperglycemia (GES)</td>
<td>Glucose &gt; 150 mg/dL</td>
</tr>
</tbody>
</table>
**Antibiotic Prescription Management**

**Goal**
- Support optimal decision about the use of antibiotics and other anti-infectives
- Why?
  - Require access to a large amount of complex information

**Ordering Antibiotics: Computerized Support**

**Supporting Information: Recycled Data**

**Antibiotic Prescription Management**

**Supporting Logic: An Explanation**

**Antibiotic Prescription Management**

**Supporting Information: Recycled Data**

**Antibiotic Prescription Management**

**Supporting Logic: An Explanation**

**Antibiotic Prescription Management**

**Supporting Information: Recycled Data**
**Blood Ordering Program**

**System description**
- Ask a reason for the order when the order is entered
- Verify the reason entered is consistent with other data in EMR
- Physicians must enter a reason (free-text) if an override is necessary

**Evaluation**
- Failed meet criteria 19% (871/4357)
- According to QA reviews, only 0.4% (17/4357) were found to be true exception.

---

**Criteria for Ordering Red Blood Cells**

**Used in a Blood Ordering Application for Physicians**

- Hemoglobin < 12 g/dl or hematocrit < 35% if age ≥ 35 years
- Hemoglobin < 10 g/dl or hematocrit < 30% if age < 35 years
- Oxygen Saturation (SaO2) < 95%
- Active bleeding
- Blood loss > 500 ml
- Systolic blood pressure < 100 mm Hg or heart rate > 100 bpm
- Adult respiratory distress syndrome (ARDS)

---

**Computerized Physician Order Entry (CPOE)**

**Definition**
- Allows physicians to enter orders into a computer rather than write them on paper
- Improve medication process and decision-making

**CPOE Incorporate**
- Relevant patient information
- Decision logic
- Into ordering process

---

**Computerized Protocols for Standardization of Clinical Decisions**

A protocol for management of intravenous fluid & hemodynamic factors in patients in the intensive care unit.
CPOE Application Features

Structured Orders: Dose List

Structured Orders: Dose Frequency List

Screen Display of Brigham Integrated Computing System’s Renal Dosing

Drug Allergy Checking

Alert review and therapeutic action screen


Drug Knowledgebase

Computerized ADE Surveillance System

Incidence of ADE

- 19% of medical errors (Harvard Medical Practice Study)
- 2-5 ADEs per 100 admissions
- Not recognized by clinician: ~80%


Voluntary Reporting vs. Computerized ADE Surveillance

Logic of Computerized ADE Surveillance

- Knowledge-based
  - As an antidote, vitamin K is given when a patient has bleeding tendency due to warfarin medication
- Patient-specific
  - E.g.> Vitamin K order stored in EMR
- Computerized ADE surveillance: Combining the two
  - E.g.> Vitamin K order can be used as a signal to detect ADEs

Voluntary Reporting Computerized ADE Surveillance


Computerized ADE Surveillance System (CSS)

Pharmacy Data
Lab Data
Clinic Documentation

Generate ADE alerts
Independent Verification by Clinical Pharmacist or Trained Nurse

Verified ADE DB

Voluntary Reporting

Computerized ADE Surveillance

Store Information

Create ADE Alert

Trigger Condition Met

Verify ADE Condition

Create ADE Alert

Verify ADE Condition

Verify ADE Condition
**ADE Signals: Core of CSS**

- **Data Type**
  - Medication orders
  - Laboratory
  - Laboratory-order results
  - Notes

- **Trigger Type**
  - Order for or without therapy
  - Laboratory test
  - Laboratory medication

- **Example**
  - Order for anticoagulation

**Improving PPV ADE Signals: Rules Behind Signals**

- **Positive Predictive Value**

**Computerized ADE Surveillance System (CSS)**

- **Review & Data Collection**
  - **Review methods**
    - Reviewing the chart
    - Talking with the clinicians caring for the patient
    - Interviewing the patient, when possible
  - **Causality Assessment**
    - Naranjo Score
  - **Severity**
  - **Relevant data for verified ADEs**
    - Type of ADE
    - Drug causing ADE
    - ADE signal
    - Others: diagnosis, number of drugs given, ADE symptom, Time of ADE first noticed

**Gold Standard for ADE Detection?: Chart Review vs. Computerized ADE Surveillance**

- **ADE surveillance methods**
  - Voluntary reporting
  - Chart review
  - Computerized ADE Surveillance system
    - Detect more severe ADEs than chart review (51% vs. 42%)

**Computerized Surveillance System: Gold Standard for ADE Detection?**

- **Scenario(1)**
  - **Hives** to **radio-contrast dye** were developed and fixed with **Benadryl**.
  - The CSS was particularly good at identifying events associated with quantitative changes.

- **Scenario(2)**
  - **Patient** became **drowsy** due to **Benzodiazepine**, and it was resolved when Benzodiazepine was discontinued.
  - Chart review was better at identifying events associated only with symptoms.

- **There is no single “Gold Standard” in ADE detection.**
Diagnostic systems

- Backgrounds: assessed the diagnostic capabilities of four internal medicine diagnostic systems
  - Meditel, Iliad: Bayesian
  - Dxplain, QMR: non-Bayesian, probabilistic association

- Methods: Ten expert clinicians created a set of 105 diagnostically challenging clinical case summaries involving actual patients. Each of the systems produced a ranked list of possible diagnoses for each patient, as did the group of experts.

Results: No single computer program scored better than the others on all performance measures. Among all cases and all programs, the proportion of correct diagnoses ranged from 0.52 to 0.71, and the mean proportion of relevant diagnoses ranged from 0.19 to 0.37.

Conclusions: The programs should be used by physicians who can identify and use the relevant information and ignore the irrelevant information that can be produced.

Discussion

- Accuracy: Diagnostic system vs. physician
- Usefulness: for primary care physicians or medical students


Input variables

Bayesian network structure (output: pneumonia probability)

Blood gas interpretation

Developed with a data set of 32,000 emergency department patients.
yesterday released the results of a survey, All hospitals were required to put in disaster plans for Y2K. Beth Israel has such a plan in place, but because systems evolve so quickly, it was already outdated. The crisis began when a researcher installed software to analyze data, and a large number of information started flowing over the network. Doctors noticed when they fail.

California's legislative mandate

Inherent complexity of medicine

- Poorly understood pathophysiological process
- Notoriously idiosyncratic
- Lack of objective gold standard

Beth Israel Deaconess Medical Center's computer system crashed repeatedly over 31/2 days last week, periodically blocking access to patient records, prescriptions, laboratory reports, and other information, and forcing the hospital to revert to the paper-based systems of what one executive called 'the hospital of the 1970s.'

Hospital and public health officials are calling the incident a wake-up call for hospitals across the country, whose computer systems may not be able to keep up with their growing workload. At Beth Israel, the systems handle 40 terabytes of data - slowed or stopped and stayed down for two hours.

Software Oversight Committee (SOC)

- To make sure there is ongoing monitoring to detect adverse events, address them, and to insure that the overall system performs as designed

FDA regulation

- 1976 medical device act
- 1995 FDA regulates blood bank software
- 2002 General principle of software validation

Two Approaches

Software Oversight Committee (SOC)

- To make sure there is ongoing monitoring to detect adverse events, address them, and to insure that the overall system performs as designed

FDA regulation

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- 1995 FDA regulates blood bank software
- 2002 General principle of software validation

Leapfrog survey finds limited use of CPOE in U.S. hospitals January 18, 2002

The Leapfrog Group yesterday released the results of a survey conducted last spring, that assessed hospitals' use of computer physician order entry (CPOE) and other patient safety initiatives.

The survey was offered to more than 500 hospitals in Atlanta, California, East Tennessee, Minnesota, Seattle-Tacoma- Everett, and St. Louis. Complete results of the survey are available on the Leapfrog Group's Web site (NewsPoints/Reuters, 1/18).

The Leapfrog Group is a coalition of 96 large health care purchasers that aims to reduce medical errors and health care costs by steering its members' employees to hospitals that implement the three patient safety practices. The group plans to extend the survey to an additional 1,000 hospitals this year (Martinez, Wall Street Journal, 1/17).
**Decision Support Standards: Arden Syntax**

- Arose from the need to make medical knowledge available for decision making at the point-of-care
  - Make knowledge explicit

- Allow knowledge sharing within and between institutions

- Standardize the way medical knowledge is integrated into hospital information systems

- Inventors
  - Columbia Presbyterian
  - Regenstrief
  - LDS

**Arden Syntax-Rationale**

- A Medical Logic Module (MLM) is an independent unit in a health knowledge base.
- Each MLM contains maintenance information, link to other sources of knowledge, and enough logic to make a single health decision.
- The MLM is an stream of text stored in and ASCII file in statements called slots.

**Medical Logic Module**

- A Medical Logic Module (MLM) is an independent unit in a health knowledge base.
- Each MLM contains maintenance information, link to other sources of knowledge, and enough logic to make a single health decision.
- The MLM is an stream of text stored in and ASCII file in statements called slots.

**Simple MLM**

- **Logic:**
  
  IF Chest_Pain is present and (ECG_Result = Acute_MI or CK-MB is greater than 5% or Troponin is greater than 2)
  
  THEN conclude true;

  **Action:**
  
  Write "Acute MI is present".

**Decision Support Standards**

- **HL7 Standards**
  - Arden Syntax
  - Guideline Interchange Format
MLM: Structure (Categories and Slots)

- **Maintenance category**
  - Title, mlmname, version, institution, author, date, validation

- **Library category**
  - Purpose, explanation, keywords, citation, link

- **Knowledge category**
  - Type, data, priority, evoke, logic, action, urgency

Knowledge: Data Slot

- **Purpose**
  - Terms in MLM must be mapped into a database
  - Use of curly braces ( ) allows flexibility in mapping to the institution's local database
  - "Curly brace problem" also hinders sharing of knowledge

- **Example**
  - Last_creatinine:=read last (select "OBSER_VALUE" from "LCR" where qualifier in "creatinine")

Knowledge: Logic slot

- **Includes**
  - Set of medical criteria
  - End with a "conclude statement"
  - Logical algorithm: If ~ then--conclude true;

- **Example**
  - If last_creatinine is not present then
    - alert text:="No recent creatinine available. consider ordering creatinine before giving IV contrast."
    - conclude true;
  - else conclude false;
  - endif;

Knowledge: Action slot

- **Functions**
  - Carry out actions if logic slot concludes true
  - Examples of action
    - Write a message to screen
    - Store a message in a file
    - Call another MLM

- **Example**
  - Action:
    - write "Last creatinine:"
    - last_creat
    - "on:"
    - time of last_creatinine
  - Appears as
    - Last creatinine: 2.36 on: 2003-09-23T06:30:00

Arden syntax sample

- **Library**
  - purpose:
    - Warn the health care provider of hypokalemia in the setting of digoxin therapy:
  - explanation:
    - Whenever a serum or whole blood potassium value is stored, it is checked for hypokalemia (less than 3.3). If hypokalemia is present, then if the patient has a non-zero serum digoxin level within the 3 months or an active order for digoxin administration, then an alert is generated (using the later of the level or the order). It warns that hypokalemia may potentiate digoxin arrhythmias. Repeat alerts are not generated if there has not been a new digoxin level or order since the last alert:
  - keywords: hypokalemia; digoxin; arrhythmia;
  - citations: ;

http://csl.sintra.com.csmc.edu/hl7/arden/
Arden syntax sample

title: Screen for hypokalemia with digoxin therapy (triggered by potassium storage);
filename: astm_hypokalemia_and_digoxin;
version: 1.00;
institution: ASTM E31.15; Columbia-Presbyterian Medical Center;
author: Robert Jenders, M.D., M.S. (jenders@cucis.cs.columbia.edu) with modifications by Harm Scheppler MD;
specialist: 

date: 1995-02-20;
validation: testing;

Knowledge:
type: data_driven;
data:
/* evoke on storage of a serum or whole blood potassium*/
storage_of_potassium := EVENT {storage of potassium};
/* read the potassium that evoked the MLM */
potassium := READ LAST {potassium level};
/* get the last active digoxin or digitoxin order */
digoxin_order := read last {digoxin order};
/* evoke */
storage_of_potassium;

logic:
/* exit if the potassium value is invalid */
if potassium is not number then
conclude false;
endif;
/* exit if there is no hypokalemia */
if potassium >= 3.3 then
conclude false;
endif;
/* exit if indication of digoxin use cannot be found */
if (digoxin_order is null) then
conclude false;
endif;
/* send an alert */
conclude true;

action:
write "The patient's potassium level (" ||potassium|| " mEq/l on " ||time of potassium|| ") is low. If the patient is currently taking digoxin, then the hypokalemia may potentiate the development of digoxin-related arrhythmias."
; urgency: 50;
end;

What is the issue?

We want to share:
• Data
• Decision support logic
... and we want semantic understanding
• So computers can understand and use the data not just people
• S2AGE
  • Electronic exchange and deployment of medical knowledge
  • Overcome curly brace problem

Goal of the S2AGE project

Collect the evidence
Build the guidelines
Publish the guidelines
Download the guidelines
Develop local consensus
Import the guidelines
into local clinical information system
• Convert to executable structure via a complier
• Guidelines in practice
  • Impact and local adjustments
• Providing feedback
  • Central organization responsible for the management of guidelines

Gartner Group Predictions

Vendors currently using Arden:
• SMS [Siemens]
• McKesson-HBOC
• Eclipsys
• IBM

Gartner predicts that through 2002, >75% of healthcare organizations will implement rule-based technologies
Beginning in 2000, computer-based patient record systems and data repositories that do not support an Arden Syntax-based, user-definable rules-processing system will lose market share.
Selected Bibliography of CDSS: Reading Assignment


Questions?