5. COMPUTER ASSISTED DIAGNOSES IN MEDICINE
5. COMPUTER-ASSISTED DIAGNOSIS IN MEDICINE

Computers are being widely used for improving the quality of patient care. They enhance the decision-making, management, planning, and medical research. Medical informatics is developing at a great speed. It is imperative for the medical practitioners to integrate information technology into medical and health care management. The development of user-friendly interface to the Internet has resulted in an explosion of new applications. The new possibilities are being arisen. The technologies that primarily supported the administrative processes are now used for medical and health care management. Computer-based patient records and electronic communication are becoming part of routine medical practice.

The purpose of this review of literature is to have a systematic overview of the Knowledge-Based and Expert Systems. Expert system is the heart of almost all the systems from information management to computer-assisted instruction as well as surgical techniques to telecommunication-based systems. This era of rapid transition to the future is unprecedented in the history of mankind.

The rapid evolution of technology and clinical research makes it difficult even for the specialist to keep up. In the light of this ‘information explosion’, it has been demonstrated that physicians do not always make optimal decisions. The new developments have lead to the arrival of Knowledge-Based Systems (KBS) for our understanding of complex processes in medical decision-making. The work on entire range of patient monitoring systems and computer-assisted medical decision making is progressing rapidly.

A computer-assisted diagnostic support system (CAD) generates diagnostic hypothesis from a set of patient data. It can be used simultaneously with the doctor-patient consultation. The Knowledge-Based System (KBS) is designed to meet the knowledge gaps of the individual physician with specific patient problems. KBS and such
other Expert Systems (ES) can be a boon to the Rural Health Centers because the General Practitioners (GP) also can operate these systems.28

The main components of Information technology namely computers, communications, and structured data have undergone a sea change. There is increasing appreciation of the role that Information Technology (IT) can play in improving the overall health delivery systems333 in urban and rural areas. The role of computer in medicine has been expanded rapidly and continuing at the same pace in the new millennium26

I will review other knowledge base computer systems in medicine with especial emphasis on different available tools and various modalities of knowledge acquisition and representation. The terms such as Knowledge-Based Computer System (KBCS), Expert Systems (ES), Computer-Aided Diagnosis (CAD) and Computer-Assisted Medical Decision-Making (CMD) are more or less synonyms.

ARTIFICIAL INTELLIGENCE (AI)

ES and KBS are the branches of Artificial Intelligence305 (AI). AI is the branch of computer science that focuses on the development of computer systems to simulate the process of problem solving by duplicating the functions of human brain. The objective of AI applications is to enable computers to process information, gain knowledge, and understand their environment331. Due to the inherent limitations of the various approaches, researchers have become interested in AI. AI includes general problem solving, natural language processing, expert systems, robotics, machine vision, learning etc. A decision tree is an AI program that is adaptive and is closely related to a neural network. It can handle missing or non-decisive data in decision-making.204

Artificial intelligence has created new possibilities to neurotologic research.182-190 ES are capable of solving problems in a given domain by using the knowledge and emulating the behavior of specialists in that field. ES can be used as powerful tools for education since they are able to justify their own conclusions and to make the underlying reasoning explicit.236
WHAT IS AN EXPERT SYSTEM?

Computer-Aided Diagnosis (CAD) or Computer-Assisted Medical Decision-Making (CMD) is a type of Knowledge-Based System (KBS) or Expert Systems (ES). The definitions of KBS and ES vary, but the two terms are used interchangeably. The traditional computer program consists of data and algorithm. The ES is a type of computer programming that contains knowledge base and reasoning engine. The Expert System (ES) generates diagnostic hypothesis from a set of patient data. The shell of the ES allows the system to be linked with a processing unit. Here the input to the ES comes from the instrument and not from the end user.27

KBS has been developed from the insights of Artificial Intelligence, which tries to simulate human experts’ way of making decisions based on the knowledge of the domain. The KBS can converse about the patient’s illness. KBS is concerned with the problems of the representation and storage of knowledge and provides its access when needed. KBS integrates such stored knowledge with the data derived from specific problems to affect their solutions. The knowledge includes both factual or descriptive and problem-solving procedures or normative.204

So the CMD is an interactive computer system that directly assists doctors or other healthcare professionals with clinical decision-making tasks. CMD cannot replace doctors but just complement their natural abilities to make judgments with computer’s vast memory, reliability and processing capabilities. Physicians often have self-perceived knowledge gaps when they are seeing patients. Traditional continuing medical education is designed to meet the knowledge gaps of groups rather than individual physician with specific patient problems95.

NEED OF EXPERT SYSTEMS

The interest in the development of computer-assisted diagnostic support system began with a desire to overcome the problems of knowledge gaps so often felt by the doctors in dealing with some particular patient. Do physicians know when their diagnoses are correct? There are implications for decision support and error reduction104. Other motivations for developing ES include their potential educational value, superior patient’s
confidence, enhance productivity of the health care team, the computerized patient record (CPR) and their role as models of the diagnostic reasoning process.27

Rural people do not get the services of specialist doctors in their areas244. But a GP and other health workers can use ES. Thus it will be a boon to the less privileged people of remote areas. Even one can easily carry Laptop consultation system. It can serve as the function of second opinion to the consultant. Medical students can use it as a tutor. Doctors can expect better patient management. In the era of consumer protection, it will be a great asset to the consultants. Because the whole process is so transparent, one can easily win the confidence of the patients, which lacks so much in recent time.

Wolf and others344 examined the degree to which attending physicians, residents, and medical students stated desire for a computer based consultation on difficult-to-diagnose patient. They studied the changes in diagnostic decision-making based on perceptions of need and helpfulness. Wright & Wright345 found the Computer-assisted psychotherapy well accepted by the patients.

The human brain is unsurpassed in its ability to perceive, focus, think, analyze, imagine and create, but it is greatly limited in its ability to store a large collection of facts permanently, to recall the facts instantaneously and precisely, and to handle multiple variables at a time204. The rapid evolution of technology and clinical research makes it difficult even for the specialist to keep up. In the light of this ‘Information Explosion’, it has been demonstrated that physicians do not always make optimal decisions. Hence is the need of such ES.27

COMPONENTS OF EXPERT SYSTEM
The components of Expert system (ES) are Knowledge base, Inference engine, User interface and Database. The knowledge base is a collection of encoded knowledge of domain that is needed to solve problems in the patients. The inference mechanism is a computer program, that given a patient details, uses the information in the knowledge base to generate list of differential diagnosis about the patient. While these two components are viewed here as being conceptually distinct, they are interwoven in the system. Individuals who use Expert system to assist them with problem solving are referred to as users.27
Knowledge Representation

In developing ES, perhaps the most challenging part is to translate knowledge of domain into abstract representation that could be processed by computer. It can involve many approaches. Boolean logic, set theory and symbolic logic are used when clinician applies a branching logic, whether the symptom is present or absent. Operations are performed upon the set like cluster analysis and multivariate analysis.204

There are two distinct methods of knowledge elicitation28:

1. Classification or Scaling method.
2. The traditional Interview based approach.

There are three types of knowledge in ES27:

1. Declarative knowledge consists of factual knowledge of domain.
2. Procedural knowledge is the skill of knowing how to use declarative knowledge.
3. Heuristic knowledge consists of personal rules of thumb.

Personal rule formation is based on knowledge about particular problem to be resolved. Many have used IF-THEN form of problem solving personal rules of thumb. The success of a heuristic procedure that composes differential diagnosis dynamically has been demonstrated. These normative or procedural rules permit searching, focusing, scoring, clustering, discriminating, concluding and planning. These heuristic rules may be derived from interaction with the medical experts. The modular structure of Object Oriented Programming (OOP) allows the objects to contain both the declarative as well as the procedural code directly associated with that data27.

METHODS OF KNOWLEDGE REPRESENTATION

The various methods of Knowledge Representation employed in ES are: Algorithmic, Statistical pattern, Database comparison, Fuzzy Production rules, Frames forming semantic network, and OAV (Object, Attribute, Value) triplets. Each method has its own advantages and disadvantages. They all are very much inter-woven in the system. They are used judiciously according to the need of the time and subject matter. A decision tree is an artificial intelligence program that is adaptive and is closely related to a neural network, but can handle missing or nondecisive data in decision-making189.
Expert systems have been applied in medicine as diagnostic aids and education tools. The construction of a knowledge base for an expert system may be a difficult task; to automate this task several machine-learning methods have been developed. These methods can be also used in the refinement of knowledge bases for removing inconsistencies and redundancies, and for simplifying decision rules.\textsuperscript{336}

Juhola and others\textsuperscript{171} applied machine-learning methods based on artificial intelligence theory to the computer-aided decision making of some otoneurological diseases, for example Meniere's disease. Three methods explored were decision trees, genetic algorithms and neural networks. By using such a machine learning method, the decision-making program was trained with a representative training set of cases and tested with another set. The machine learning methods were useful also for their otoneurological expert system (ONE), which was based on a pattern recognition approach. The methods were able to differentiate most of the cases tested between the six diseases included, provided that a sufficiently large training set was available.

Translating the human mind's synthesizing process into rules and decision trees is a task that requires patience and insight. Managing a knowledge-based system is full of both rewarding and frustrating events\textsuperscript{27}. Some of the many methods have been described here:

**Production Rule Systems**

Medical knowledge in rule-based deduction is presented as a set of conditional rules or productions. Each rule/production has the basic form 'IF antecedents THEN consequent'. The systems developed on this approach are: MYCIN- selection of antibiotics for infections, GLAUCOMA- diagnosis and treatment of glaucoma\textsuperscript{339}.

Expressing medical problem-solving knowledge as a set of rules can be a fairly difficult task, as the diagnostic knowledge is intuitively known to the doctor and found in books as descriptive data. A set of fuzzy production rules connects the antecedents with consequences or conditions with actions. They are of the form 'if A, then B' where A and B are fuzzy sets\textsuperscript{27}. For example:

R 1: IF Age is >50 AND Hoarseness of voice of >15 days duration THEN Malignancy Larynx must be ruled out.

R 2: IF Age is > 50 AND Bilateral gradually progressive hearing loss AND Dislike to loud sounds OR Tinnitus THAN Presbyacusis is a possibility.
Hillman and others\textsuperscript{154} used a fuzzy logic approach to identify brain structures in MRI using expert anatomic knowledge that was coded in fuzzy set and fuzzy rules. The method first identifies major structures and then uses spatial relationships to these landmarks to recognize other structures. Goswami and others\textsuperscript{126} presented a rule-based reasoning augmented by case-based reasoning approach for neonatal resuscitation management. Fuzzy set theory has also been used for several medical problems including kidney failure and liver impairment\textsuperscript{27}.

**Algorithmic Method**

Knowledge acquisition, which consists of knowledge elicitation and knowledge representation, often is considered the weakest link in the design of expert systems. Systems frequently are built on the knowledge of one expert and require extensive use of knowledge engineering techniques to elicit this knowledge from the expert. Inductive algorithms are a potential alternative method of knowledge acquisition for expert system development.\textsuperscript{151}

Algorithmic methods are successful when the pathophysiology is clearly understood and categorical decisions can be made based upon reliable laboratory information. High-level FORTRAN and PASCAL languages have been used in Acid base, electrolytes problem and drug therapies. An algorithm is a step-by-step set of instruction on how to accomplish some tasks. Information specific to the problem is encoded in branching logic of the program statements. Inferences are generated by simply executing the statements in the program\textsuperscript{204}.

Kentala and others\textsuperscript{183} retrieved data on patients with Meniere's disease, vestibular schwannoma, traumatic vertigo, sudden deafness, benign paroxysmal positional vertigo, and vestibular neuritis from the database of otoneurologic expert system ONE for the development and testing of a genetic algorithm (GA). The accuracy of the diagnostic rules in solving the test cases was 81\%, 91\%, 92\%, 95\%, 96\%, and 98\% for the respective diseases. The best rules retrieved from the GA were described by a set of questions with the most likely answers. The most important questions concerned the duration of hearing loss and the occurrence of head injury. For rare diseases, some other reasoning process (such as case-based reasoning) can be used.
Object Oriented Knowledge

Object oriented database representation has been used for controlled medical terminologies\textsuperscript{160}. In object-oriented KBS, one has to identify the classes of objects. The class and its operations are defined as a single unit. Each object is a member of a class and each object has its associated attributes. The class 'physical examinations' can have typical objects like heart, abdomen, ear, eye, liver etc. A typical object, say ear, has the attributes like 'malformed pinna' or 'preauricular sinus'\textsuperscript{272}. In a practical system, one can extract hundreds of objects. The six selection characteristics for the actual inclusion of object are suggested\textsuperscript{72}: Retained information, Needed services, Multiple attributes, common attributes, common operations, and Essential requirements. One of the disadvantages of O-O technology is its long learning curve.

This method can be organized around the organ system such as Ear, Nose and Throat etc. Each of these areas is divided into more specific categories, which are in turn being further subdivided many times. Most of the entry process may consist of responses to menus of choices. A series of definitions can be offered on-line for the findings, meanings of those might not be fully clear to the user\textsuperscript{292}.

Data Base Comparisons

This approach is centered on the idea of comparing a new patient’s information to previous clinical knowledge database\textsuperscript{204}. For instance, consider a database of clinical information on F.B. Nose:

Child
Unilateral nasal obstruction
Unilateral nasal purulent or serosanguinous discharge
Unilateral nasal vestibulitis
Not responding to any medical treatment
Most common diagnosis: Foreign Body Nose
Uncommon diagnosis: Diphtheria Nose
Rare diagnosis: Tumor nose or paranasal sinuses

Kentala and others\textsuperscript{184} developed an interactive database for vertigo that could be used to assist in the diagnostic procedure and to store the data in a form of a database. The database offered the possibility to split and reunite the collected information in a
desired way. The database contained detailed information about patient history, symptoms and findings in neurotological, audiological and imaging tests. The symptoms were classified into three sets of questions: vertigo (including postural instability), hearing loss and tinnitus, and provoking factors. Confounding disorders were screened. The neurotological tests involved saccades, smooth pursuit, posturography and caloric test. In addition, findings in specified antibody testing, clinical neurotological tests, MRI, brain stem audiometry and electrocochleography were included. The input information could be applied in an expert system ONE for vertigo work-up. The database was claimed to be user-friendly. Besides diagnostic purposes the database was found excellent for research purposes, and combined with the expert system it worked as a tutorial guide for medical students.

Statistical Pattern Classification

When the clinician says that 'common things occur commonly' Bayes’s theorem of conditional probabilities can be used. Bayesian ES for diagnosis of 'acute abdominal pain' has been proved more accurate than physicians. It assumes that only one disease process is present at a time though patients can have multiple problems at a given time. It needs many different indicants concurrently, which at time are clinically unrealistic. The probabilities of one location may not be usable at other locations. Other techniques of this approach are Linear Discriminant Functions and Data Base Comparisons. Large patient databases are useful for decision-making.

Decision Analysis

It is a formal discipline for making decisions that in many respects resembles the informal strategies of clinicians. The model can be presented as a decision tree with several pathways along each of which are several nodes or decision points. Each intervention is a decision node. Other chance nodes are not under the physician’s control. The tree is progressively built, from signs, symptoms, laboratory tests, and diagnostic and therapeutic interventions. The tree is constructed in sufficient detail to make the representation realistic, and yet is constrained to prevent it from becoming unmanageably large.

Viikki and others employed decision tree induction to acquire diagnostic knowledge for otoneurological diseases and to extract relevant parameters from the
database of an otoneurological expert system ONE. The records of patients with benign positional vertigo, Meniere's disease, sudden deafness, traumatic vertigo, vestibular neuritis and vestibular schwannoma were retrieved from the database of ONE, and for each disease, decision trees were constructed. Their study showed that decision tree induction was a useful technique for acquiring diagnostic knowledge for otoneurological diseases and for extracting relevant parameters from a large set of parameters.

Kentala and others retrieved data on patients with Meniere's disease, vestibular schwannoma, traumatic vertigo, sudden deafness, benign paroxysmal positional vertigo, and vestibular neuritis from the database of the otoneurologic expert system ONE for the development and testing of the accuracy of decision trees in the diagnostic workup. Decision trees were constructed separately for each disease. The accuracies of the best decision trees were 94%, 95%, 99%, 99%, 100%, and 100% for the respective diseases. The most important questions concerned the presence of vertigo, hearing loss, and tinnitus; duration of vertigo; frequency of vertigo attacks; severity of rotational vertigo; onset and type of hearing loss; and occurrence of head injury in relation to the timing of onset of vertigo. Meniere's disease was the most difficult to classify correctly. The validity and structure of the decision trees were easily comprehended and could be used outside the expert system.

Cognitive Models
Cognitive psychologists and medical educators have discovered that an expert physician's diagnostic reasoning is a sequential hypothesis and test or abductive reasoning process. The history taking is mostly hypothesis-driven while examination of the patient is protocol-driven. The frames of associative knowledge in these KBS collectively form a complex semantic network. The system generates hypotheses and then recycles through the entire process again with additional information. A major technique of knowledge representation is the semantic net, in which facts and their relationships are shown both qualitative and quantitative. The most suitable languages for this work are LISP and PROLOG, ES-shell, Visual dbase.
Web-Based Knowledge Acquisition

WWW has created novel opportunities for sharing data via Internet. Samanta (1999) explored the use of web-based knowledge acquisition for the medical domain. A collaborative knowledge acquisition was possible in his approach. A suitable toolkit such as MedFrame was required to enable the medical experts to perform the knowledge acquisition tasks without support or with little support from knowledge engineer.

TOOLS

Dr. Roger Jellife developed pharmako-kinetically oriented methods for planning, monitoring and adjusting dosage regimens of powerful but potentially toxic drugs. Written in Interlisp language the ONCOCIN expert system advises on-line Cancer chemotherapy protocols.

Commonly used tools in CMD systems are AI Languages, Tool Kits, and ES-Shells. While most AI systems are written in LISP or PROLOG, The EXPERT, a domain-independent software tool or shell, is unusual because it is written in FORTRAN. AI/RHEUM system for diseases of joints was built using EXPERT. The INTERNIST system is composed of two basic types of elements: disease entities and manifestations (history, symptoms, signs and laboratory data). It was written in LISP and assembly language. For representing drug and laboratory knowledge in a clinical event monitor deployed in an inpatient setting, CLIPS has been selected as the basis for its KB and inference engine.

HYPERTENZ, the decision making program in treatment of hypertension used the Microsoft Access language of the Access database system. Due to the access Developers Toolkit it does not require Access to be installed on the users computer. It offers the user essential information and explanation of the decisions in a graded form. The user himself can update the price list of the equivalent medications. Marchevsky and others developed a rule-based expert system in EXCEL 4.0 (Microsoft, Redmond, WA) for the automatic classification of DNA. If-Than rules were used to classify histograms. The data was converted from list mode format into ASCII with the aid of CELLSHEET software (JVC Imaging, Elmhurst, IL).

In order to develop Expert System for the Assessment of Legal Capacity (ESALC), Hu-Z and others employed Visual Basic for Windows 3.0. They developed
the ESALC for assessment of criminal responsibility capacity of mentally ill offenders. Agarwal developed ‘Acuware’ in Client-Server computing environment, where she used Visual Basic 5.0 as front-end and MS-Access as back-end tool. Landmarks were scanned using Adobe Photoshop and the scanned images were stored in GIF format.

Computer-Aided Diagnosis (CAD) system developed by Chang and others could be easily implemented on existing commercial diagnostic digital Ultra-Sound (US) machines. It needs only a personal computer loaded with CAD software. They adopted the normalized auto-correlation coefficients as the texture features of a tumor. The Learning Vector Quantization 1 (LVQ1) learning algorithm was selected to train the proposed LVQ model. They used the LVQ Program Package (LVQ_PAK, Version 3.1; prepared by the LVQ Programming Team of the Helsinki University of Technology Laboratory of Computer and Information Science, Helsinki, Finland). The 2-dimensional normalized auto-correlation matrix was used as the input of the LVQ model. The dimension of the matrix can be fixed for any size of image. A 7363 556-pixel digital image is captured from the ultrasonographic scanner. In a 13 1-cm rectangle, there are 583 58=3364 pixels. The Region-Of-Interest (ROI) rectangle is 1.983 1.66 cm and 1153 96 pixels.

Knowledge Engineering System (KES)
The emergence of domain-independent software tools is a great boon to doctors. They can build KBS for a wide variety of applications. There is practically no need of knowledge engineer during the knowledge acquisition process. KES provides a pre-programmed user interface and a collection of implemented inference mechanisms like rule interpreter, Bayesian classifier, hypothesize-and-test model of diagnostic reasoning and so on.

Neural Networks
Neural networks are a computer-based reasoning method, which can be applied in expert systems created for clinical decision support. Neural networks have been used in medical imaging, in medical signal processing and to analyze both clinical and laboratory data. Principally, neural networks simulate the function of the brain. They have to be taught to make correct decisions from the input data. This learning process can be either supervised.
or unsupervised. The decision-making is based on mathematical transformations and it
occurs on a hidden level\textsuperscript{47}. Calculations are made on parallel manner and the decision-
making simulates pattern recognition method. The back propagation neural networks
have been applied to the problems in pathology and laboratory medicine\textsuperscript{11}.

Neural networks suit well in medical problems, which cannot be defined in simple
rules. A drawback of neural networks is that the decisions are irrational and cannot be
motivated to the user. Another problem is neural networks' difficulty to handle
incomplete input data, i.e., how to define some default or expected values for unknown
input parameters\textsuperscript{127}. In a complex medical area, which would require multilayered neural
networks, the neural networks require a large amount of solved cases for the learning
process\textsuperscript{185}.

A neural network consists of computer programs that learn to make diagnostic
predictions. The field of neural network has been growing considerably during this
decade. The construction of neural networks is simple. They learn by example and deal
with ambiguous data. They provide an educated guess, which conventional programs
could not do well, or at all. The neural networks in the expert systems assist physicians in
making the diagnosis. They have been applied to the CAD systems of the breast cancer\textsuperscript{14},
interstitial lung disease\textsuperscript{9} and ovarian malignancy\textsuperscript{43} using the database of clinical findings.
Diagnostic accuracy has been improved by using hierarchical neural network to model
decision subtasks\textsuperscript{340}.

The improvement of classification performance is achieved by connecting with
supervised learning rules for Learning Vector Quantization (LVQ) with a self-organizing
map of the neural network. The input samples along with correct classification labels are
given for these neural network models. The auto-correlation feature vector and a desired
result can be used as the input signals for the LVQ training process. The classification
label produced by the best-match neuron is used to decide whether a tumor image is
benign or malignant. The image of the region of interest (ROI) is selected with a region
that extends beyond the lesion margins by 1 to 2 mm in all directions and then saved as a
file for later analysis by the LVQ system. The texture correlation between neighboring
pixels within an ROI sub image is used to classify the tumor. To diminish the occurrence
of dead neuron in the LVQ model, the dead neurons are removed according to the training
set after a number of training iterations. The ambiguous code word would be split with
the members of the training set in the cluster to create 2 new code words. The steps would
be performed until the amount of code words reaches an acceptable percentage of the
training set\textsuperscript{295}.

Kentala and others\textsuperscript{185} did not find neural networks suitable for diagnosing vertigo and
they felt that a better choice would be either case-based reasoning or possibly genetic
algorithms or a combination of these.

APPLICATIONS

The current KBS have no potential to replace the doctors but are simply an aid to them.
The system is intended not to replace healthcare professionals but to support them.
Various CMD systems have been reported on medicine such as MYCIN, ONKOCYN,
DXPlain, ABEL, DIAGNOSES, EMERGE, CALBAN, HDDSS, GLAUCOMA,
INTERNIST, QMR, AI/RHEUM, and ONCOCIN etc.\textsuperscript{27,204} Computer-based consultation
helps even in managing electrolyte and acid base disorders\textsuperscript{46}.

The evaluation of empiric antibiotic therapy has also been modeled\textsuperscript{337}. Expert
Systems generate alerts and reminders, assists in diagnosis, and helps in therapy planning
and critiquing. These systems act as retrieval agents for medical and health care
information\textsuperscript{136}. ES can recognize and interpret the images. There are machine-learning
systems, which help in the development of new drugs and patho-physiological models
from data\textsuperscript{27}. Following are some of the various expert systems.

CD-ROM Decision Support Tools

A growing number of programs are available to aid the doctors in making a diagnosis.
Continuing Medical Education Association (www.medinfosource.com or
www.cmea.com) has come out with some good programs such as DiagnosisPro, Iliad 4.5,
and Quick Medical Reference. Others are Home Medical Advisor, DX plain, and Meditel
etc. These programs cover hundreds of diseases. A list of provisional diagnoses is
generated on the bases of clinical data. Some of the programs give references and tips for
coming to the final diagnosis. Problem Knowledge Couplers, an interactive program for
specific diseases provides suggestions for further investigations and diagnostic supports.
It accepts the clinical data of the patients. A review article\textsuperscript{41} compared Iliad, QMR, DX
plain, and Meditel. Authors found the programs fairly similar. The breadth of known
diagnosis and symptoms, the depth of knowledge about a disease, and the quality of the priority ranking of the diseases in the differential diagnosis were all differentiating factors.

Some of the other examples of such medical systems are: Epileptologists' Assistant, HELP (Knowledge-Based Hospital Information System), MDDB (Dysmorphic Syndrome). Jeremiah, Orthoplanner, and RaPID are decision support systems for dental surgeons. Clinical Event Monitor system generates alerts, interpretations, and screening messages etc. The hospital's personnel can be alerted for reportable infections by the help of Reportable Diseases Alerts system. Apache-3 helps in the evaluation of acute physiology and chronic health.

Rao designed a computer-based medical diagnostic system for logic formalisms of the Bayesian probabilistic belief networks. Data bank of about 35,000 disease-features is developed from text sources using MS access. The resident form gives information on many diseases, features, and their differential diagnoses using hyperlink word documents. He developed feature to disease, disease to feature, and feature-to-feature links.

**Rheumatology**

The EXPERT, a domain-independent software tool or shell, is unusual among the AI community on account of its being written in FORTRAN, while most AI systems are written in LISP or PROLOG. AI/RHEUM system for diseases of joints was built using EXPERT. The system will reason with whatever information is given and will tell the user if this information is not sufficient to trigger any of the disease conclusions. A disease criteria table consists of major and minor decision elements, required 'must have' elements and exclusionary 'must not have' elements. The table elements are combined as specified by the subject matter experts, to trigger conclusions at the definite, probable or possible confidence levels. Most of the entry process consists of responses to menus of eight or ten choices. A series of definitions are offered on-line for finding the meanings of the terms whose meaning may not be fully clear to the user.

The Austrian Society developed RHEUMexpert, a documentation and expert system for rheumatic diseases. In addition to this they developed a knowledge-based basic differential diagnosis support that differentiate between major groups of rheumatic diseases as inflammatory spine diseases, mechanical or metabolic reasons for spine
disorders, inflammatory joint diseases, degenerative or metabolic joint diseases and soft tissue diseases. They find that the system facilitates the systematized and standardized documentation of patient data.

Otolaryngology

'Vertigo', an expert system (ES) aimed at the classification and diagnosis of different forms of dizziness, was conceived mainly as a teaching tool in otoneurological departments. 'Vertigo' was tested on more than 200 cases of dizziness and was than used by ENT residents during their otoneurology stage.

An otoneurological expert system (ONE) was developed to help collect data and diagnose the work-up of vertigo of both central and peripheral diseases causing vertigo. Patient history and otoneurological and other examination results were used in the reasoning process. The history was interactively collected and was complemented with clinical examination results. The case history data could be either mandatory or supportive. Mandatory questions were used to confirm a diagnosis, and conflicting answers were used to reject an unlikely disease. Supportive questions supported or suppressed a diagnosis, but their presence was not obligatory. The reasoning procedure of ONE scored every question independently for different diagnoses, depending on how well they agreed with the symptom entity of a disease. Diagnostic criteria were set for each disease. In Meniere's disease, for example, the full triad was required. Graphic displays illustrated the linear and nonlinear correlation between the symptoms and diseases. For instance, both second-long Tumarkin-type attacks and attacks lasting hours gave a high score while intermediately long attacks scored much lower in Meniere's disease. To be able to take even rare diseases into consideration they tried to diminish the possibility of a wrong decision rather than maximize the likelihood of reaching only one right decision.

The database OtoNeurological Expert system (ONE) contained detailed information on the patient history, signs and test results necessary for the diagnostic work with vertiginous patients. The pattern recognition method was used in the reasoning process. Questions regarding symptoms, signs and test results are weighted and scored for each disease, and the most likely disease is recognized from the defined disease profiles.
Uncertainties in reasoning, caused by missing information, were solved with a method resembling fuzzy logic. They also applied adaptive computer applications, such as genetic algorithms and decision trees, in the reasoning process.

The decision-making ability of ONE neurotologic expert system was compared\textsuperscript{182,190} with the diagnoses of six physicians. Five of the physicians were residents and one was a specialist in the field of otolaryngology. The test patients were randomly selected from vertiginous patients referred to an otolaryngology clinic. The expert system and the physicians first had identical information on patient history, symptoms, and tests. During the second phase of the study the physicians were allowed to use the full medical records. The correct diagnoses were certified by an experienced specialist in neurotology.

The expert system did better in decision-making when both the expert system and the physicians had identical information on patients. However, when the physicians were allowed to use patient's complete medical records, they surpassed the expert system. The expert system diagnosed 65\% of the cases, while the physicians first diagnosed 54\% of the cases, and then with complete information, 69\% of the cases. From the patients' medical records, the physicians obtained information on the time perspective of the symptoms and the progression of the disease. These aspects should be used to further improve the expert system. The six diseases were detected with high accuracy also with adaptive learning methods and discriminant analysis. They aimed to construct a hybrid program for the reasoning, where the best reasoning method for each disease was used.

Auramo and Juholo\textsuperscript{13} compared the two different otoneurological expert systems, 'Vertigo' and 'One'. The expert systems were evaluated as regards their correctness in reasoning diagnoses. In the light of their data collected from randomly selected test patients, 'One' being a newer technique, was more effective, since it could infer more cases than 'vertigo' did. All the data was also evaluated and diagnosed by otoneurological specialists, independently of the expert systems, to guarantee objectivity in evaluation of the results of the expert systems. The follow-up should be implemented for the patients, since diagnosing sudden deafness and Meniere's disease during the first visit is often impossible\textsuperscript{187}.

The Sleep-EVAL\textsuperscript{255} system was found a valid instrument for the recognition of major sleep disorders, particularly insomnia and Obstructive Sleep Apnea Syndrome (OSAS) against polysomnographic data and clinical assessments by sleep specialists.
ICU
The bedside monitors, database information and the application of artificial applications need integration for efficient patient monitoring. Such integration helps in getting correct interpretations and in prescribing needed therapies. PATRICIA\textsuperscript{239}, an intelligent monitoring system, advises clinicians in the management of Intensive Care Unit (ICU) patients. The client server technology has been applied to take full advantage from information integration, shared resources and equipment networking. The architecture of the system is designed on the pattern of hospital health care systems and allows integration of bedside monitors to front-end computers, and through the data network to a central monitor that controls and manages all network operations. Electrocardiographic computer programs have been assessed with use of a reference database\textsuperscript{343}. Some other examples of acute care systems are: ACRON (Chest Pain), POEMS (Postoperative care), and VIE-PNN (Perinatal Nutrition)\textsuperscript{27}.

Pulmonology
Computer-controlled minute ventilation\textsuperscript{70} (CCMV) continuously adjusts the ventilator rate to changes in spontaneous respiratory drive and pulmonary mechanics to maintain preset total minute ventilation. CCMV may reduce barotraumas and chronic lung disease during long-term use. Burge and others\textsuperscript{63} developed Oasys an expert system for the interpretation of serial peak expiratory flow measurements in the diagnosis of occupational asthma. Oasys-2 is based on a discriminant analysis and achieved high sensitivity and specificity. Other systems related to the ventilation are: NeoGanesh (Mechanical Ventilation Management) and VentEx (Ventilator Therapy Monitoring). PUFF interprets pulmonary function tests\textsuperscript{27}.

Drug Therapy
A CMD was found improving the quality of control of warfarin therapy by a nurse practitioner over that by trainee doctors\textsuperscript{334}. ICONS\textsuperscript{150} utilizes case-based reasoning for medical decision support. As an application domain they have chosen the medical field of 'calculated antibiotic therapy' an intensive care medicine setting. ICONS runs on a PC and suggests adequate antibiotic therapy regimen satisfying medical and economic
conditions. Case-based reasoning is used for finding previously documented similar cases and for modifying them according to the requirements of the current patient.

Miller and others\textsuperscript{226} developed two Pharmacy ES: one for drug dosing and the other for adverse drug event prevention. They implemented a strategy for notifying clinical pharmacist of alerts generated in real-time. They found the system efficient and effective. An antibiotic decision support system QID was designed and developed to help physicians identify the antibiotic regimens with highest probability of covering the pathogens that are most likely to be present in individual patient. QID creates a list of antibiotics, ordered by potential benefit in treatment, for a patient with suspected infection before culture results are available.

Other examples of expert systems, which deal with drugs, are: SETH (Drug Poisoning), Dose Checker (Monitoring Drug Orders), SahmAlert (Efficacy of antibiotics), and ADE Monitor (Adverse effects of drugs). Colorado Medicaid utilization review systems review the drugs for Medicaid patients\textsuperscript{27}.

**Pediatrics**

IMM/serve\textsuperscript{227} is a computer program which implements the clinical guidelines for childhood immunization. It accepts as input a child's immunization history and then indicates which vaccinations are due and which vaccinations should be scheduled next. The clinical guidelines for immunization are quite complex and are modified quite frequently. Holzmann and others\textsuperscript{157} developed an Expert System for the classification of sleep/waking states in infants; i.e. active or rapid-eye-movement sleep (REM), quite or non-REM sleep (NREM), including its four stages, indeterminate sleep (IS) and wakefulness (WA). Macey and others\textsuperscript{216} described an expert system for the classification of events within an abdominal breathing signal as apnea or non-apnea in infants. The property measures are transformed into an appropriate form for input to a neural network. The neural network is trained to calculate the likelihood of the event being an apnea.

**Radiology**

The tumors and normal tissue on mammograms can be classified with the help of texture features of neural networks. The most useful features are derived from co-occurrence matrices of the images. The physician locates the Region Of Interest (ROI) of digital
images and uses the auto-correlation features of a tumor to make the diagnosis by using the Learning Vector Quantization (LVQ) neural networks.

Computer-Aided Diagnosis (CAD) system developed by Chang and others establishes an accurate preoperative diagnosis for surgical office-based digital ultrasound (US) of the breast. The diagnostic rate was even better than the results of an experienced radiologist. The performance comparison results included sensitivity, specificity, positive predictive value, and negative predictive value. The high negative predictive rate by the CAD system could avert benign biopsies. They retrospectively reviewed medical records of digital US images of the breast of pathologically proved benign breast tumors (fibroadenomas and fibrocystic nodules), and carcinomas (invasive duct carcinomas, invasive lobular carcinomas, and intraductal carcinomas). The digital US images were consecutively recorded. The physician selected the region of interest (ROI) on the digital US image. Then a Learning Vector Quantization (LVQ) model with 24 autocorrelation texture features was used to classify the tumor as benign or malignant. Surgeons may sometimes have difficulty in interpreting findings with confidence because some features overlap between benign and malignant criteria. The PERFEX interprets cardiac SPECT data and PHOENIX acts as a radiology consultant.

Tanaka and others applied fuzzy reasoning in a computer-assisted diagnostic system for ultrasonography and evaluated its clinical utility as a diagnostic aid for the unskilled clinician. They constructed a computer-assisted diagnostic system for ultrasonography to differentiate metastatic from inflammatory lymph nodes. The pattern of a skilled clinician's considerations was simulated with the fuzzy expert system. Three fuzzy production rules were set up according to the diagnostic criteria for lymphadenopathy. Each rule was transformed into a membership function. The max-min composition method was used for inference and the centroid method for defuzzification. The system was tested with 20 clinicians who were one to three years after graduation and inexperienced in ultrasonography. Accuracy, sensitivity and specificity were evaluated. They concluded that application of fuzzy reasoning in an expert system for ultrasonography improves the diagnostic performance of inexperienced clinicians.
Pathology

Urine single protein analysis is an ideal approach for screening and monitoring of the kidney disorders. In order to support clinical decision-making by an interpretative report, Ivandic and others\textsuperscript{167} developed Urine Protein Expert System (UPES). Based on a database having >500 excretion patterns, a modular knowledge base was extracted in production rules and implemented in a modern expert system shell. They thoroughly verified and validated the resulting interpretation system.

Can a laboratory-based expert system assist the physicians in solving patient problem outside their field of expertise by expertly interpreting hematological and biochemical data? Innis\textsuperscript{164} found that the expert laboratory system could present a list of possible diagnoses not thought of by the clinician. The ES, which uses fuzzy sets and pattern recognition as its inference mechanism coupled with a database comprised of hematological and biochemical responses to diseases and also analyzed data published in two leading journals.

Nathwani and others\textsuperscript{245} evaluated the diagnostic accuracy of pathologists with and without Pathfinder, an expert system on lymph node pathology. Pathfinder provides a differential diagnosis based on the initial histological features observed by the pathologist. It suggests additional histological features for observation that are likely to narrow the differential diagnosis. They found the Pathfinder a valuable tool that assisted pathologists in making accurate diagnosis. They observed that Pathfinder had superior attributes than pathologists to integrate information and to screen for observations incompatible with ant specific disease.

Bacton Dickinson systems deal with the hematology and MIC interpretation. Using culture-based criteria, Germ Alert assists in infection control. Germwatcher analyses Nosocomial infection whereas Hepaxpert 1, 2 interpret the tests for hepatitis A and B. Automatic phenotyping of dyslipoproteinemia is possible with LIPORAP. Pro.M.D. CFS Diagnostics interprets CSF findings\textsuperscript{27}.

Psychiatry

Expert System for the Assessment of Legal Capacity\textsuperscript{159} (ESALC) can be used as a supplementary instrument in forensic psychiatric assessment of criminal responsibility capacity of mentally ill offenders. EEG-Expert Automated Diagnostic System\textsuperscript{214} describes
and collects data of virtual analysis of electroencephalogram (EEG). It also makes an expert conclusion on the functional status of the brain and its particular regions. The system could be used for postgraduate training of young specialists as well as for the researches.

**Dermatology**
Gerbert and others\textsuperscript{114} discussed decision support software to help primary care physicians triage skin cancer and conducted a pilot study. They reported earlier detection of skin cancers with fewer office visits that led to better outcomes and decreased overall costs to the system. West and West\textsuperscript{340} investigated the decision accuracy of neural network models for the differential diagnosis of six erythematous skin diseases. They addressed conditions where a hierarchical neural network model could increase diagnostic accuracy by partitioning the decision domain into subtasks that were easier to learn.

**Cardiology**
Ischemic heart disease is one of the commonest causes of morbidity and mortality throughout the world. The risk factors are well known but unfortunately eligible patients do not get adequate drug treatment. Benson\textsuperscript{39} described a computerized monitoring system having expert system algorithm. It facilitates patient selection in primary prevention and encourage patient compliance to drug therapy. The system attempts to maximize the effectiveness and efficiency of dyslipidemia management.

The efficacy of several classes of anti-hypertensive medications is not always reliable indications of their selection. HYPERTENZ, a computer supported decision making in therapy of arterial hypertension, gives a sequence of decisions based on clinical experience using a series of parameters. This ES offers information and explanation of the decisions in graded form, which might be very useful for the general practitioners\textsuperscript{268}.

**Anesthesiology**
Meijers and others\textsuperscript{223} described a closed loop blood pressure controller to support the anesthetists during the cardiac surgery. The controller was based on a simple and robust proportional integral controller and a supervising rule based ES. The performance during automatic control showed the mean arterial pressure to be within 10 mm Hg of the set
point for 71.4+/- 15.5% of the time. One potential application of ES to anesthesia practice is a smart alarm to detect blood pressure liability. The study of Reich and others\textsuperscript{280} sought to derive and validate an ES to measure intraoperative mean arterial blood pressure (MAP). They observed that ES might provide a better tool to assess the relation between liability and outcome than had been available in past.

**GIT**

Trial\textsuperscript{281}, the real life data electronic diagnosis tool, delivers diagnosis probabilities based on Bayes’ theorem completed by Trial Algorithm (TA). Developed on the data of 7104 Euricterus patients, Trial can simultaneously calculate the resemblance of the patient’s signs and symptoms to each disease concomitantly (Bayesian Vertical, BV), and to any subset of a disease. It also calculates the probability of each diagnosis of the 17 disease categories as a percentage, as each significant finding is encountered (Bayesian Overall, BO). Any probability is further tested for compatibility using TA, a subset of BV. The Trial patients came from three jaundice databases: Euricterus Dutch, independent prospective and independent retrospective.

Morgan and others\textsuperscript{240} developed a personal computer-based expert system for the prescription of enteral formulas based on patient-need characteristics. They concluded that the use of an enteral expert system could be cost effective in the prescription of the enteral formulas for hospitalized patients. They project that the use of this program would save $27564/y in their hospital.

**Obstetric**

Keith and Green\textsuperscript{180} developed a prototype intelligent system, which applied captured expert knowledge to support clinical decision-making during labor. The system classified the same features from the CTG as experienced clinicians using numerical algorithms and a small neural network. This hybrid approach showed to obtain a comparable performance with experts. The CTG information, together with the patient information and labor events, were collectively passed to an expert system for processing. The expert system interpreted this combined data using a database of over 400 rules, which, are used to recommend action. Importantly, as the knowledge was rule-based, it allowed the system to explain the reasoning, which led it to recommend a certain action. After two
internal evaluations had found the system obtained a performance comparable with local experts, an extensive external validation was undertaken. Their study found that the majority of experts agreed well and were consistent in their management of the cases. The system obtained a performance that was indistinguishable from the experts, except it was more consistent, even when used by an engineer with little knowledge of labor management. Their study demonstrated the potential for intelligent systems to transform the cardiotocograph from a difficult-to-use, ineffective recorder of fetal heart rate, to an interactive and effective decision support tool capable of raising the skills of staff.

Web-Based Decision Support Tools

The National Guideline Clearinghouse (NGC), a free web-based (www.guidelines.gov) public resource for evidence-based clinical practice guidelines is one of the best available on Internet. Sponsored by Agency for Health Care Policy and Research, American Medical Association, and American Association of Health Plans, NGC wants to improve quality of healthcare, decrease cost, and enhance patient and clinical decision-making. Full-text of most of the guidelines are available on this web-site and the summary of guidelines are broken into several main components, which can be examined into detail such as sources in print, major recommendations, clinical algorithms, developers, endorses, and companion documents. Users can view the full content of list with scrolling facility or search by key words using Boolean operators such as AND, OR, and NOT. Many more other such sites are available on Internet.

ADVANTAGES AND RATIONALE

If properly studied, piloted, and implemented, expert systems have the potential to greatly increase the quality of care in the primary care setting. The implementation of expert systems leads to increase in the quality of care and decrease in the cost. Bates and others\textsuperscript{34} studied the effect of computerized physician order entry and a team intervention on prevention of serious medication errors. They found that a well-planned physician order entry implementation had decreased serious medication errors by 55%. Gerbert and others\textsuperscript{114} discussed decision support software to help primary care physicians triage skin cancer and conducted a pilot study. They reported earlier detection of skin cancers with fewer office visits that led to better outcomes and decreased overall costs to the system.
Kawamoto and others\textsuperscript{177} studied seventy Decision support systems (DSSs). DSS significantly improved clinical practice in 68% of trials. Graber and Mathews\textsuperscript{128} found that when key clinical features from 50 challenging CPC cases (reported in the New England Journal of Medicine) were entered into Isabel of Isabel Healthcare Ltd (http://www.isabelhealthcare.com/), the system provided the final diagnosis in 96% cases.

Johnston and others\textsuperscript{170} studied effects of computer-based clinical decision support systems on clinician performance and patient outcome. Three of 4 studies of computer-assisted dosing, 1 of 5 studies of computer-aided diagnosis, 4 of 6 studies of preventive care reminder systems, and 7 of 9 studies of computer-aided quality assurance for active medical care that assessed clinician performance showed improvements in clinician performance using a computer-based clinical decision support system (CDSS). Three of 10 studies that assessed patient outcomes reported significant improvements.

The provision of patient- and context-specific reminders has the potential to reduce diagnostic omissions across all subject grades for a range of cases. The study of Ramnarayan and others\textsuperscript{275} found a promising role for the use of future reminder-based CDSS in the reduction of diagnostic error. Kentala and others\textsuperscript{187,190} developed an OtoNeurological Expert system (ONE) to aid the diagnostics of vertigo and assist teaching. In the validation they found the expert system ONE to be a sound decision maker.

Schiffman and others\textsuperscript{299} conducted a systematic review of functionality and effectiveness of computer-based guideline implementation systems. Decision-support systems showed a positive effect on outcomes. The number of legitimate uses for rules-based processes in guiding physician behavior continues to grow and now includes such diverse functionality as reminders for when critical screening tests need to be performed and paging providers for abnormal laboratory results. Decision-support systems have led to such impressive statistics as a savings of $3 million per year in medication costs at a large academic teaching hospital and a 69% decrease in duplicative laboratory orders simply by informing providers of redundant orders\textsuperscript{198}.

The rationales for using ES are following\textsuperscript{27}:

\begin{itemize}
  \item Each consultant can now afford computer technology.
  \item Literate patients demand information and explanation regarding the diagnosis.
  \item Increasing popularity of Computers in public and medical professionals.
\end{itemize}
- Complete and accurate data entry.
- Helpful in consumer protection litigation and other legal matters.
- Enhanced productivity of the health care team.
- Confidentiality of patient's record.
- Wins the patient's confidence because of transparency.
- Educate and evaluate students, residents and other health care providers.
- Excellent tool for clinical research.
- Manage consultant's self perceived knowledge gap in managing particular patient.
- Mode of practicing Evidence Based Medicine.