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A Study on Controlling Hospital Acquired Infections: A Knowledge Based System Approach

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Abstract: Nosocomial infections or hospital acquired infections are diseases that develop during an admission to hospital and are a consequence of treatment, procedures of treatment or work of hospital staff. These infections are dangerous because they are caused by bacteria that are developed and transmitted within the hospital, where they may reach a high level of resistance to antibiotics. The goal of this study is to identify such infections for a single patient or hospital units and to create a real time information system for analyzing the microbiological data and to control the infections. In order to attain this objective, we introduce a knowledge based system approach for microbiological investigation to select the most suitable antibiotic therapy. The knowledge base of the proposed system has been obtained from international standard guidelines for microbiological laboratory practice, from experts' suggestions. Also we present the overall structure of the system and its implementation. This system will help medical practitioners and physicians to adopt appropriate methodology for controlling nosocomial infections.

Key words: Antibiogram, knowledge based system, antibiotics, microbiology

INTRODUCTION

Nosocomial infections or hospital acquired infections are diseases that develop during an admission to hospital and are a consequence of treatment, not necessarily a surgical one, or work by the hospital staff. Usually a disease is considered a nosocomial infection if it develops 72 h after the admission to the hospital. These infections are much more dangerous than community infections because they are caused by bacteria which have a dangerous resistance to antibiotics. These infections are an important cause of increased morbidity, mortality and health care costs world wide. These have steadily grown for nearly two decades, in spite of many measures-such as shorter hospital stays-they were expected to have an attenuating effect (Paxton, 1999) and it's one of the five leading causes of death in the United States (Haley *et al*., 1985).

Antibiotics are the drugs that are commonly used to fight against infections caused by bacteria. However, according to the center for Disease Control and Prevention (CDC) statistics, more than 70% of the bacteria that causes hospital-acquired infections are resistant to at least one of the antibiotics most commonly used to treat infections.

The general approach of the treatment of Nosocomial Infection consists of the following phases.

- A normal microbiological investigation will be conducted.
- Pathogens will be isolated and for each isolated bacterium an antibiogram (represents bacterium's resistance to a series of antibiotics) to be built.
- The result of the test will be presented as an antibiogram.
- The information included in the antibiogram will be used to prescribe an antibiotic with a desired level of resistance for the isolated pathogen.

This study is focused on the validation of microbiological data and selection of the suitable antibiotic therapy for the complex task of controlling the infection. To manage the different aspect of the problem, we propose a knowledge based system, which will support physicians to take precise decisions of the treatment.

The proposed intelligent system consists of two modules, first one is knowledge base that contains the domain information from experts and the next is inference

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engine that contains the general problem solving knowledge. The knowledge about the problem is translated into special data structures and rules in the knowledge base as defined by Patterson (1990) and Rich and Knight (1991). The inference engine applies these rules to the available data in order to produce solutions of the problem.

The systems knowledge base has been obtained from NCCLS (National Committee for Clinical Laboratory Standards, 2005) guidelines and from experts' suggestions. NCCLS is an international standard organization recognized by almost all laboratories as the reference in routine work and it publishes an annual compendium containing testing guidelines for microbiological laboratories.

THE LITERATURE REVIEW OF INTELLIGENT SYSTEMS FOR ANTIBIOTIC AND INFECTIOUS DISEASES

During the last few years many infection event surveillance system have been developed to monitor microbiological analysis results and to early identify infection and epidemiological events early. Significant examples of these systems are discussed here.

Germ Watcher/Germ Alert (Khan *et al*., 1996) is a family of expert systems designed to support infection control specialists in detecting, tracking and investigating infections in hospitalized patients. Its knowledge base was obtained by the analysis of some documents written by CDC's NNIS (Center for Disease Control, National Nosocomial Infection Surveillance), (NNIS, 2004) providing explicit culture-based and clinical based definitions for the most significant Nosocomial infections.

DNSev is a knowledge based system has been developed to support the laboratory physicians during the process of validation of bio chemical analysis. The objectives of DNSev are: Support of the validation of analysis results, help for laboratory automation, clarity, flexibility, reliability and time saving. During the development of DNSev, the knowledge acquisition and elicitation task was performed by interviewing laboratory physicians and also by using available documents and laboratory guidelines.

VALAB, a knowledge based system, that permits real time validation of data, is designed to be equivalent to validation by the Laboratory Chief. The decision produced by the expert system is based on several factors, including correlation between repeated Laboratory Results, Physiological association between different variables, the hospital department from which the test was ordered and patients age and sex. The VALABsystem incorporates (Fuentes and Lacambra, 1997) greater than 4000 rules. Operational since November 1988, it has validated greater than 50,000 medical patients reports in real time. The goals of VALAB are to reduce the time between the arrival of the samples to be analyzed and the despatch of the validated results and to increase the reliability of the results of analysis.

Pro. M.D stands for Prolog system for the support of medical diagnostics. With this system, the Laboratory Physician is able to convert his own theoretical understanding and efficient problem solving strategies into the rules of knowledge base. The most important part of its knowledge base are condition or production rules in the form IF (condition) THEN (action). The Pro. M.D. Access System offers an automatic conversion of the knowledge base into Microsoft Access database tables and forms.

VITEK Advanced Expert System (AES) (Livermore *et al*., 2002) an expert system for antibiogram validation, that is integrated in particular analytical instruments. AES interprets the results of antibiotic susceptibility tests using a knowledge base that contains most of the known resistance mechanism. The AES system starts from the minimum inhibitory concentration levels given by the instruments and classifies them into three levels: Susceptible, intermediate and resistant.

Toxo Net is a knowledge based system (http://medexpert.imc.akh.wien.ac.at/ToxoNet.) intended to support the clinician in analyzing the test results of routinely made toxoplasmosis tests with the objective of not only facilitating routine laboratory work but also assuring quality by settling standards for therapy. The knowledge base of Toxo Net comprise knowledge that enables the system to either detect or exclude an infection by analyzing the results of several investigations carried out to detect the specific antibodies in serum.

WHONET is an information system (O'Brien and Stelling, 1995) developed to support the world health organizations goal of global surveillance of bacterial resistance to anti microbial agents. Microbiologists, physicians and infection control workers may use its software to enhance monitoring of drug resistance in their hospitals and communities and to merge their files into national regional and global networks for surveillance of drug resistance. WHONET only performs statistical evaluation of long term infection evaluation inside the hospital and does not take care of antibiogram validation, patient infection monitoring.

THE KNOWLEDGE BASED SYSTEM

The objectives of the knowledge based system are the validation of microbiological data, the identification of critical situation for a single patient or for hospital units and warn the microbiologist, provide reports about the amount of nosocomial infection in various areas of the hospital.

To achieve these objectives, we should analyse the microbiological aspects and problems related to the treatment of microbiological data inside a hospital in more detail. As a part of this study, we have identified some subproblems which will be described in three different time periods. The three categories are summarized here.

- The problems mainly involve the validation of antibiotic test results according to international guidelines.
- The problems involves the monitoring of the patients status and the evaluation of infections.
- The problem is the one of identifying sudden outburst of an infection.

Knowledge base: Knowledge base is the part of a knowledge based system that contains the domain knowledge, which consists of The Microbiological Laboratory Guidelines, Microbiological data, Bacteria classification data, Antibiotic Informations and Hospital discharge summary of the patients.

Microbiological laboratory guidelines: The knowledge regarding the tests performed by microbiological Laboratories has been elicited from NCCLS guidelines. NCCLS guideline are basically composed of a list that specifies the antibiotics to be tested, a list that specifies antibiotic test interpretation and a list of exceptions regarding particular antibiotic test results.

Microbiological data: For the microbiological analysis the bacterial infections data includes:

- Information about the patient: Sex, age, hospital unit where the patient has been admitted.
- The kind of material (specimen) to be analyzed (e.g., blood, urine, saliva, pus, etc.) and its origin (the body part where the specimen was collected)
- The data when the specimen was collected (often substituted with a analysis request date)
- For every different bacterium identified, its species and its antibiogram.

Bacteria classification data: One of the problems that the intelligent system tries to address is the classification of the infecting bacteria into strains. The strain classification is very important to correlate different infection events which are instead caused by the same bacterium. This strain identification module of the system is deeply described here.

Antibiotic information: Antibiotics are represented hierarchically following the ATC specifications (Anatomical Therapeutic Chemical, (ATC) index with Defined Daily Doses (DDD), 2002) the ATC5 code specifies which active principle characterizes each antibiotic. Other information recorded for each antibiotic is: The Daily Defined Dose (DDD), the cost of the DDD, the way of administration and other characteristics used by the system to compute the list of the most effective antibiotics to use for each infection.

Hospital discharge summary: For each patient stay into the hospital, a hospital discharge summary (Hudson and Cohen, 2000) should be collected with the following information: Patient demographical data, Days spent in ICU, Days spent in the hospital before test, clinical therapies performed and the hospital ward and identified pathogens namely:

Staphylococcus (A Spherical gram-positive parasitic bacterium of the germs, usually occurring in grapelike clusters and causing boils, septicemia and other infections). *Enterococcus* (Usually a nonpathogenic streptococcus that inhabits the intestine). *Entrobacteria* (Any of various gram-negative rod-shaped of the family enterobacteriaceae that includes some pathogens). This kind of information should be collected by every hospital. These features are summarized in Table 1.

Structure of the system: The knowledge based system collects the microbiological data from a Laboratory

Table 1: Hospital discharge form

Demographical and hospitalization data	
Patient name	
Sex	(Male, Female)
Age	Integer
Recurring stay	(True, False)
Days of stay in ICU	Integer
Days of stay in ICU before specimen was received	Integer
Bacterium is isolated when patient is in ICU	(True, Flase)
Department of stay (departments +ICU)	……
Pathogens	
Pathogen name	(Pat.name1, Pat.name2...)
Gram(+)	(True, False)
Staphylococcus	(True, False)
Enterococcus	(True, False)
Enterobacteria	(True, False)
Nonfermenters	(True, False)
Antibiotics	
Antibiotic name	(Ant.name1, Ant.name2…)
Group1, 2…	(True, False)
Sensitivity	(Sensitive, Intermediate, resistant)

Information System (LIS), the Domain Expert. The LIS collects the analysis results from automatic analyzers connected to the system or from manual input. The data from the LIS are stored by the system's internal database and organized in infection events, in which the information is coded following the most widely recognized international standards.

The system data base structure is designed to store all the information regarding infection events that are acquired in real time from different LISs. The database associates infection event data, according to the typical design of dataware house, to other information such as antibiotic knowledge, hospital discharge summary and international microbiological laboratory guidelines. All the information is coded according to the ICD-9-CM international standard, obtained from National center for Health Statistics, Center for Disease Control standard. This microbiological information is analysed by several system modules shown in Fig. 1. The bacterium species classification, the antibiogram and a strain identification module.

Each infection event is analyzed by the strain identification module that, starting from the bacterium species and antibiogram, classifies the bacterium into corresponding strain. The strain classification is very important to correlate different infection events that instead are caused by the same bacterium. The most precise classification method is the genetic analysis of the bacterium. Such an investigation, however, is currently too costly: Therefore, the most common classification uses the antibiogram associated to the bacterium. According to this information, a strain is a combination of a bacterium species and a particular set of results in the associated antibiogram. For a particular bacterium species, it may be necessary to restrict the set of antibiotics (inside the antibiogram) to be used for identifying a strain. The strain identification module follows these considerations in order to analyse each isolated bacterium and assign the relative strain to it. This information is used by the other modules in order to find co occurrence between different infection events. This strain identification module is also used to improve the quality of the reports. To compute more effective reports on the microbiological data, it is necessary to count each infection event only once.

After strain classification, each infection event is analyzed by the Inference Engine, the part of the

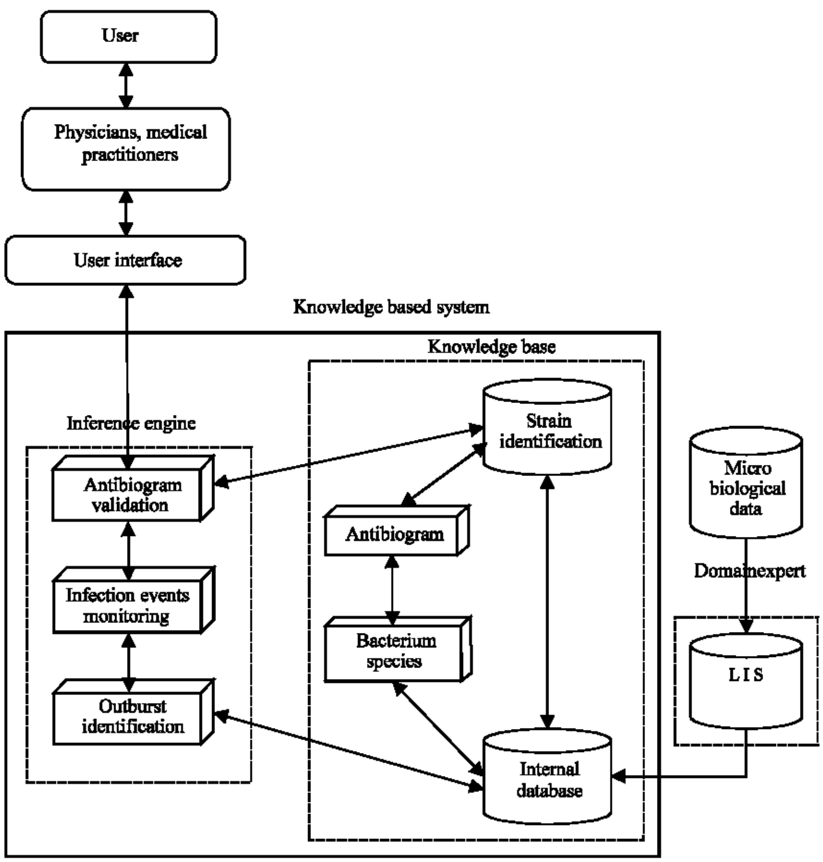

Fig. 1: Components of the expert system

knowledge based system that contains general problem solving knowledge.

Now the infection events are enriched by the inference engine, that are shown to the microbiological laboratory physician, who has to decide which is the correct bacterium antibiogram to be presented to the physician for therapy definition and which alarms should be issued to be shown to him. To reduce the human and machine error, every time the microbiological laboratory physician changes an antibiogram result, the antibiogram is reprocessed by the knowledge base modules.

Inference engine: The Inference Engine is built to solve three different categories of problems, which will be described as follows:

The inference Engine finds untested but necessary antibiotics, identifies impossible antibiotic results for particular species and tests common relationship among antibiotic results. The quality of antibiogram results is critical because physicians use them directly from therapy definition. The system should check that all the necessary antibiotics have been tested and that the results of the tests are correct according to NCCLS rules. The results can be wrong if they are not in accordance with predictions based on the results of other antibiotics. For example, Oxacillin is representative for all Oxacillines: If a bacterium is found resistant to Oxacillin, then it is resistant to all the Oxacillines.

The next problem is mainly involve the monitoring of the patient's status and the evaluation of infection. The Alarms should be raised in the case in which dangerous events are discovered by comparing the result of the current analysis with the result of previous analysis. For example, an alarm should be raised if a bacterium is found with a significant change in its antibiogram with respect to the previous test: This change may be explained by an error in the previous or actual antibiogram by a new bacterium infection. This event should immediately passed to a repetition of the antibiogram to verify the correct bacterium species and response. The physician will react to this alarm by changing the therapy.

Another alarm should also be raised if a bacterium infection persists for a relatively long period, also in this case the actual therapy is not suitable and should be changed.

We generate the alarm rules which will be frequently occurring in the database.

The following is the Mathematical Statement of the association rule method (Agarwal and Srikant, 1994). Let $I = (i_1, i_2, i_3)$ be the set of items. e.g., drug codes, organisms isolated, wards etc., Let D be a set of transactions. e.g., Culture reports, where each transaction T is a set of items such that $T \subseteq I$. We say that a transaction T, contains X, where $X \subseteq T$. An association rule is a rule that states X associates with Y, denoted by $X \Rightarrow Y$, where $X, Y \subseteq I$ and $X \cap Y = \phi$ (empty set). We define support of rule $X \Rightarrow Y$ as the proportion of transactions in D with both X and Y i.e., $X \cup Y$. We define confidence of a rule $X \Rightarrow Y$ as support $(X \cup Y)$/Support (X). Support is the percentage of transactions that the rule can be applied to or the percentage of transactions in which it is correct. Confidence is the number of cases in which the rule is correct, relative to the number of cases in which it is applicable.

These rules are related to each other according to the following generality relation: Rule one is more general than rule two if they have the same consequent. For example.

1. Amoxicillin+Clavulanic Acid = S, clindamycin = S→ Oxacillin = S
2. Amoxicillin+Clavulanic Acid = S, Clindamycin = S Trimethoprin+Sulfamethoxazole = S → Oxacillin = S

rule 1 is most general and rule 2 is intermediate.

If associations rule (Lui and Chung, 2000.) such as $X \Rightarrow Y$ represents the regular situation. The rule X, not(Y) $\Rightarrow$ alarm(Y) represents the abnormal situation. When X and not(Y) occur simultaneously, an alarm has to be raised because the value of Y should be true instead of false, when X is true. The condition not(Y) is obtained in the following way: When Y is a singleton condition, we consider the result for an antibiotic in an antibiogram as two valued, where R (resistance) is the complementary value of S (sensitive) and vice-versa.

For example, the alarm rule formed from rule 1 is

Amoxicillin+Clavulanic Acid = S
Clindamycin = SOxacillin = R →alarm (Oxacillin = S)

After the consultation of experts in this field, the similar alarm rules will be constructed from association rule and will be recommended to the microbiologist.

The third one is to identifying outburst of an infection. An outburst happens when the same bacterium causes a number of new infection events significantly greater than the normal. To this purpose, the number of infection events found is compared to the number of events predicted using neural network techniques, which will be a separate study. If the number of infections found is above the predicted one, then immediately the alarm is raised and communicated to the epidemiologist.

System implementation: The process discussed here has been implemented using an expert system programming approach. To choose the best instrument for implementing the system, we suggest Kappa-PC 2.4 (http://www.intellicorp.com) because it offers good features, cost ratio and a simple and powerful programming language. Moreover it works in interpreted and compiled mode, can reason both forward and backward and communicates easily with databases. Regarding the systems knowledge base, since the guidelines of NCCLS compendium can change the rules that are designed as templets: rules are general and are dynamically instantiated referring to database entries that represent NCCLS guideline. Therefore the rules can be updated with the last guidelines version by simply updating the corresponding database table. Thus the need to have qualified people continuously updating the knowledge is not necessary since it is sufficient to update NCCLS table entries which are stored in the system's database.

CONCLUSIONS

Through this study, a vivid discussion about the knowledge based expert system has been presented. This system will be of great help to the society by enabling physicians and researchers to adopt the most relevant policies for controlling nosocomial infections. To be more specific, the objectives of this system are the complete analysis of microbiological data and the formation of a real time information system. The intelligent system which has been developed to meet the above mentioned objectives is clearly described with system structure and the care functioning. Also in this study, a reliable programming language for the system functioning has been recommended. After the successful software representation of the knowledge base rules and alarm rules for Antibiotic dose adjustment, will expose how the computerized expert system can enable or guide the physicians in making the correct choice of choosing the comparatively absolute therapy in the monitoring of patients' infection.

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