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Comparing Bayesian inference and case-based reasoning as support techniques in the diagnosis of Acute Bacterial Meningitis

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ABSTRACT

The amount of information available for physicians has dramatically increased in the recent past. In contrast, the specialist's ability to understand, synthesize and take into account such information is severely constrained by the short time available for the appointments. Therefore, systems reusing available knowledge and implementing reasoning processes become critical to support the tasks of the doctors. As a number of different techniques for building such systems are available, contrasting their effectiveness becomes a major concern. This is especially important in the case of infectious diseases that can be lethal within hours such as the Acute Bacterial Meningitis (ABM) for which implementing and contrasting different techniques allows for an increased reliability and speed in supporting the process of diagnosis. This work focuses on the construction of diagnosis support tools for ABM, reporting a comparative assessment of the quality of a Clinical Decision Support System (CDSS) resulting from the application of Case Based Reasoning (CBR), to that of an existing CDSS system developed using a Bayesian expert system. Although both approaches proved to be useful, the one based in CBR techniques show some interesting capabilities as higher precision, automatic learning or experience capturing, and also a better response to lack of input data. The three developed systems perform with high levels of accuracy– e.g. propose correct diagnostics based on a certain set of symptoms – but the one based on CBR present some additional capabilities that look very promising for implementing these kind of systems in a real world scenario.

1. Introduction

During everyday's clinical practice of evaluating a patient and making a clinical diagnosis, the problem of the analysis of patient's signs and symptoms requires the use of available reference information (related to similar cases with their respective analysis and diagnosis) together with the procedures and tools that support the decision-making process. In virtue of this and taking into account reference information, the physician develops and tests a series of hypotheses, eventually reaching a diagnosis or a group of differential diagnoses. Based on these clinical pictures, and generally also on protocols as well as standardized or commonly accepted guidelines, the doctor designs and indicates an appropriate treatment, or else orders subsequent examinations.

The amount of information related to similar cases and the recommended diagnosis and procedure for each of them as well as its complexity has increased drastically. Although this represents a great help to the doctor when it comes to making a clinical assessment and diagnosis, it requires the doctor's availability of attention and concentration on the information in order to be able to synthesize, analyze and finally benefit from it. In addition, it also requires a fair deal of time, which is not usually at the disposal of doctors during the clinical assessment. According to the interviewed physicians, in most cases the available time in a doctor appointment has not changed significantly in the last few years; if there has been any slight change, it has not increased but reduced available time. These restrictions can be summed up in two problems: limited time and resources to process all the potentially available information.

Computer-based techniques have been applied in different ways in order to timely and effectively take advantage of the available related information (Hopgood, 2005). Multiple Artificial Intelligence techniques such as Pattern Analysis, Neuronal Network, Expert Systems and Bayesian Networks among others have been put into practice (Pandey & Mishra, 2009).

Infectious diseases like the one used as case study for this research, usually require a fast and precise initial clinical diagnostic, which in turn would lead the next, more detailed (and eventually

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more risky or even with a higher cost) studies. Different intelligent techniques can be applied to develop these kinds of systems, each one presenting different basis requirements and outcomes. This paper reports on the contrast of two of these techniques: case-based reasoning and Bayesian inference. The final objective in this comparative research is to identify a suitable technique that performs with acceptable precision, degrades slowly in the absence of input information, helps the experts in their own way of working, and can start functioning based on a limited amount of gathered experience.

This paper is organized as follows: In Section "2. "Application context – Diagnosis of Acute Bacterial Meningitis" the case study is presented, briefly describing the illness, its symptoms and signs, and the differential diagnoses that can be produced by a clinical physician. As it is detailed in Section 3, several systems have been developed to help with clinical decision in a wide variety of applications. However, there are only a few that apply to the specifics of diagnosing Acute Bacterial Meningitis. In the following Section "3. "Clinical Decision Support Systems" a brief description of the field in which the intelligent techniques are assessed is given. The intelligent techniques being compared are exposed next (Bayesian Inference and CBR), together with the detailed description of two systems built using each of these techniques. Having described the prototype applications, the experiment design, case base construction process and simulations performed are explained in Section 4. Finally, based on the obtained results obtained, conclusions are drawn and future work detailed research directions are provided in Section 5.

2. Application context – Diagnosis of Acute Bacterial Meningitis

This research is developed using as application case the Acute Bacterial Meningitis (ABM) diagnosis in paediatric patients.

ABM, that has a high rate of morbidity in paediatric patients and also produces important sequels, can present itself either in an isolated way or epidemically, and it is of utmost importance to make both an early diagnosis and an immediate treatment.

Based on the assessment of the signs and symptoms related to this disease, doctors must develop the corresponding diagnosis, distinguishing between the different possible differential diagnoses. As described in (Ocampo, Herrera, Machado, & Ruibal, 2003), there are at least 24 signs and symptoms that can be found in a patient with ABM, in an independent or combined form and that have different levels of significance in the composition of the clinical presentation that leads to the diagnosis of the disease. In (Ocampo et al., 2003), it can also be found the combinations of these signs and symptoms according to the way they are assessed by the corresponding doctor, for infants and over 2-years-old patients.

For this research, an intensive analysis of signs and symptoms to be considered has been performed. Eventually, a set of 84 signs and symptoms were defined and grouped into sections according to the different stages of the clinical examination that the expert usually carries out as shown in Table 1.

The ABM diagnosis is complicated as other diseases present a combination of similar signs and symptoms, i.e., *differential diagnoses*. Alternative diseases among which the doctors must clearly identify the existence of ABM include: Acute Viral Meningitis, Tuberculous Meningitis, Encephalitis – Brain Abscess, Meningism, Meningeal reaction to nearby inflammation, Meningeal Hemorrhage and Brain Tumor.

3. Clinical Decision Support Systems

A Clinical Decision Support System (CDSS) is (Berner, 1998) "*an algorithm based on computer science that helps the clinical doctor in one or more steps during the process of diagnose*". These systems provide information, to help and advice physicians in the process of making an optimal diagnosis decision. One of the first CDSS that appeared in the marketplace was the MYCIN system developed at Stanford University. MYCIN was designed to diagnose and recommend a treatment for blood infections. The knowledge was represented as a group of IF-THEN rules which were associated a certainty factor. Another historically relevant decision support system, although not applied to the medical field, was PROSPECTOR. The PROSPECTOR system was applied to geology and allowed the assessment of places according to diverse criteria: presence of beds and deposits, assessment of geological resources and the selection of a drilling spot. It uses the Bayes theorem as the main mechanism to assess the probability of the occurrence of a certain event.

Table 1
Groups of symptoms and signs.

yGroups	Symptoms
Symptoms or interrogatory	Fever, somnolence, nasal secretion, vomits, liquid deposition
Skin and mucosa physical examination	Pale skin, cyanotic skin, cold skin, skin, skin purpuric syndrome.
Lymphoganglionar physical examination	Cervical adenopathy
Face and skull physical examination	Hyper tense fontanelle, depressed fontanelle, pain in facial sinuses, mastoid inflammation (mastoiditis)
Abdominal physical examination	Hepatomegaly, esplenomegaly
Cardiovascular physical examination	Tachycardia, lowered cardiac tones, weak peripheral pulse, arterial hypertension
pleuropulmonary examination	Polypnea, grunting, flatness to percussion, distant alveolar sound, humid stertors, tubal bruit, pleural bruit
Buccopharyngeal physical examination	Congestive pharynx
Nose and eyes physical examination	External ear secretion, Congestive eardrum, purulent secretion in the middle ear, serous nasal secretion, purulent nasal secretion
Neurological and physical examination	Comma, depression, lethargy, irritability, facial paresis, facial paralysis, spinal sector paresis, paralysis, muscular hypo tonicity, increased deep tendon reflexes, babinski sign.
Meningeal signs	Nape stiffness, trunk stiffness, kernig sign, brudzinski sign.
Cephalous Spinal Fluid analysis (CSF)	Cloudy aspect, hemorrhagic aspect, crystalline aspect, low glucose, positive pandy's reaction, augmented proteins, red blood cells present, augmented white blood cells, bacteria (Meningococcus, Neumococcus, Hemophilus, Streptococcus)
Blood test	Altered leukocytosis, diminished hemoglobin concentration, diminished hematocrit, diminished platelet recount, augmented segmented leukocytes, augmented band leukocytes, augmented lymphocytes, high erythro sedimentation rate, positive C-reactive protein.
Blood culture	Blood culture with bacteria (Meningococcus, Neumococcus, Hemophilus, Streptococcus), Blood culture with other bacteria
Pharyngeal exudates	Streptococco in pharynx, Other bacteria in pharynx.
Other symptoms, signs or analysis results	Koch's bacillus in CSF, purified protein derivative, convulsion
Computed Tomography	Hemorrhage, tumors, abscesses, edemas, hydrocephalia
Transfontanellar ecography	Hemorrhage, tumors, abscesses, edemas

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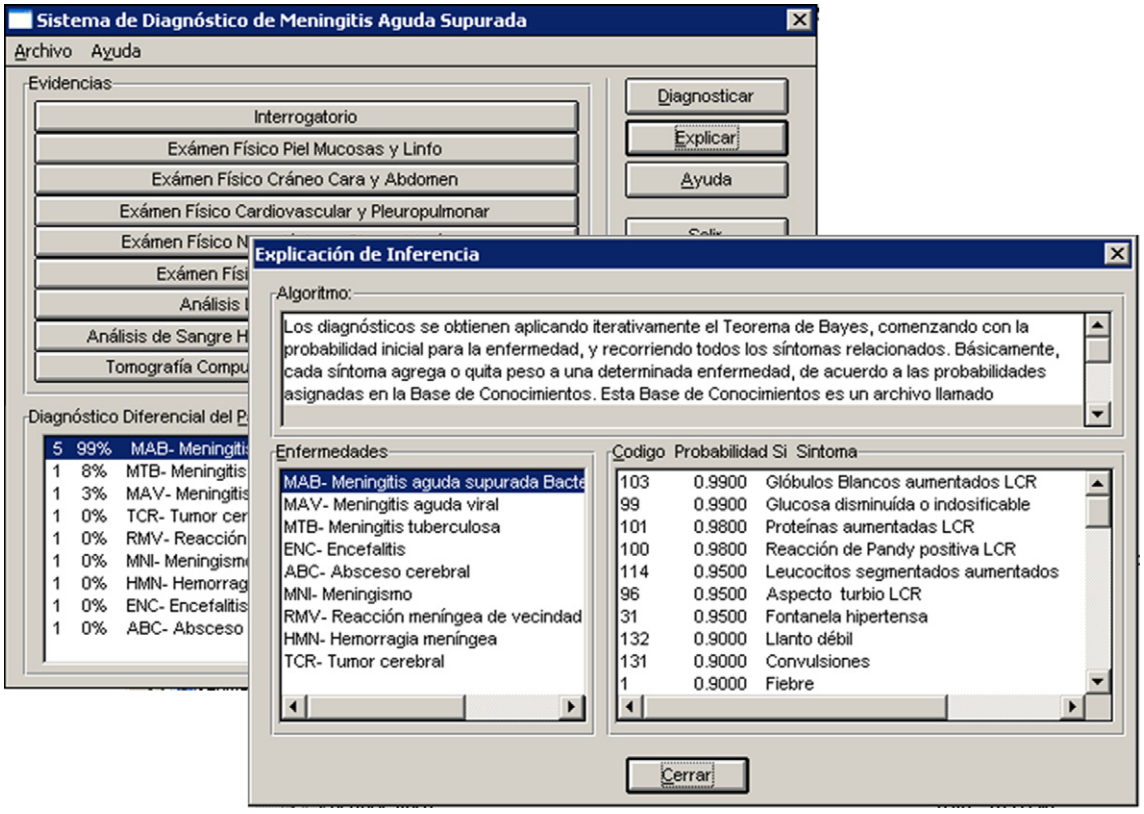

Fig. 1. AMBDES (Spanish interface), main window and inference explanation.

When using CDSS, the role of the clinical expert is fundamental. These systems provide support to the decision making process, but do not indicate the decision to be taken. The interaction between the expert and these systems is paramount as the system cannot work by itself.

The complexity of CDSS lies not only in the elicitation and modelling of expert knowledge, but also in the processing of large amounts of information, conciliating information from the patient with information from the doctor. Besides, there is a great complexity associated to the handling of the natural uncertainty degree of every decision in the medical field. From a group of diagnoses and/or signs that are taken as inputs, these systems suggest a group of diagnoses, possibly with their respective associated certainty degrees.

Only if the system is fed with enough, clear and precise information, experts will be able to adapt that information, using their knowledge and experience in the derivation of a definitive diagnosis. The differentiated specific diagnosis is the result of an elaboration made by doctors combining their own knowledge and experience with the information provided by the CDSS. Signs and symptoms shown by the patient are received as input. A list of possible diagnoses, eventually considered according to their certainty, is then built using the knowledge incorporated in the system and the experience and reasoning of the expert (Chohra, Kanaoui, & Madani, 2007).

In the rest of this section we describe the three CDSS systems that have been developed to help physicians diagnose the ABM, under two completely different AI approaches: Bayesian inference and CBR.

3.1. Bayesian Acute Bacterial Meningitis Diagnosis Expert System (ABMDES)

The Acute Bacterial Meningitis Diagnosis Expert System (ABMDES), thoroughly described in (Ocampo et al., 2003), uses a Bayesian inference engine to propose the differential diagnosis with their corresponding certainty degree, based on the symptoms and signs group that a patient presents. ABMDES uses a database composed of real paediatric patients that have attended a consultation in order to work.

The disease probabilities and the symptoms and signs – associated with each disease – probabilities have been extracted from this database. Through a user interface (Figs. 1 and 2) the physician registers the signs and symptoms assessed in the patient. Based on this data, by applying the Bayes' Theorem repeatedly in its inference engine, the system calculates the accumulated probabilities of existence of the different possible diseases.

The database of indicative data has the following structure:

3.1.1. SYMPTOM CODE/SYMPTOM DESCRIPTION

Where SYMPTOM CODE is a unique code assigned to each indicative datum;

The diseases database has the following structure:

DISEASE CODE/DISEASE DESCRIPTION/PI/{SYMPTOM CODE/PS/PN}. In which *DISEASE CODE* is a unique code assigned to each disease, *PI* is the probability that a patient arriving to the clinic shows the disease, having no other information – this probability has been calculated based on national statistics and physicians real expertise-; *{SYMPTOM CODE/PS/PN}* denotes 1 or more records where *SYMPTOM CODE* is a unique symptom or sign identifier, *PS* is the probability that this indicative datum presents if the disease exists, and *PN* is the probability that this indicative datum presents if the disease does not exists.

The indicative data have been grouped in the way used by field experts as a method. This makes easier for physicians with little or no experience to use the support system. In this way, not only the correct performance of the system can be achieved, but also – and even more important – higher accessibility and usability levels can

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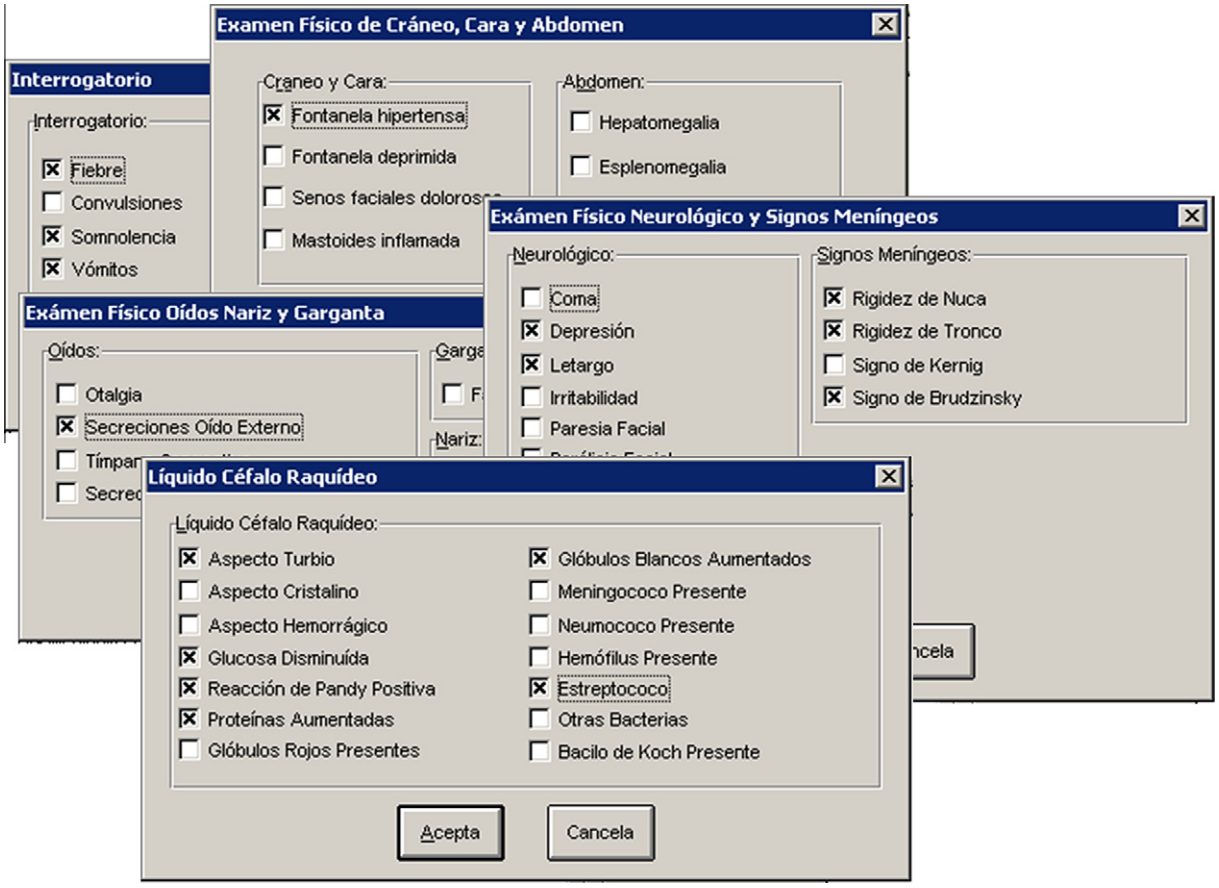

Fig. 2. ABMDES symptoms and signs registry.

be reached in contexts where there is shortage of adequately trained or experienced physicians.

Bayesian Inference systems are a kind of expert systems in which the experience or knowledge base is modelled expressing different probabilities. These probabilities represent a causal model. The inference engine then, based on the causal model applies the Bayes' Theorem iteratively to obtain a conclusion.

The Eq. (1) represents the renowned Bayes' theorem, using in the expression the events M and X (Russel & Norvig, 1995; Szolovits, 1995):

$$P(M/X) = \frac{P(X/M) * P(M)}{P(X/M) * P(M) + P(X/no\,M) * P(no\,M)} \quad (1)$$

Where M denotes the fact *"the patient suffers from Acute Bacterial Meningitis"* and X is a particular combination of symptoms and signs of the patient.

Then, the probability *"the patient suffers from meningitis"*, given the symptoms combination X, is equal to the probability of X supposing the disease exists, multiplied by the overall probability of existence of the symptoms X, whether the disease exists or not. Statistically, we know that

$$P(X/M) = \frac{P(M \cap X)}{P(X)}$$

And

$$P(X/M) = \frac{P(M \cap M)}{P(M)}$$

therefore:

$$P(X \cap M) = P(X/M) * P(M) = P(M/X) * P(X)$$

from which we obtain:

$$P(M/X) = \frac{P(X/M) * P(M)}{P(X)}$$

$$P(M/X) = \frac{P(X/M) * P(M)}{P(X/M) * P(M) + P(X/no\,M) * P(no\,M)}$$

Using the structures detailed above, a calculation of the most probable diagnosis is carried out applying the Bayes' theorem iteratively.

In this case it can be appreciated that the probability of a certain hypothesis, given a certain element of evidence, can be calculated from the *a priori* probability of such hypothesis (that is to say, without knowing anything about the evidence) and the probabilities that the evidence exist given that the hypothesis is true and given that the hypothesis is false.

Considering the diseases and indicative data mentioned, the Bayes' theorem can be expressed in the following way:

$$P(H/E) = \frac{PS * PI}{PS * PI + PN * (1 - PI)}$$

It is started by doing $P(H) = PI$ for each disease, where $P(H)$ will hold the likelihood of the patient suffering from the illness, and here it is initialized with PI. While the program requests indicative data information (through several questions to the user), the $P(H|E)$ is calculated according to each of these data. When an indicative datum exists, the previous formula is applied; and when it does not, the same formula is applied but substituting PS by $(1–PS)$ and PN for $(1–PN)$. The effect of each indicative datum is then the substitution of the a priori probability $P(H)$ by $P(H/E)$.The process goes on in this way, continuously updating the $P(H)$ of all diseases as the user inputs new indicative data values.

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Other Bayesian systems in medicine include the following:

BayPAD (Luciani et al., 2007) is a system based on a probabilistic model that uses a Bayesian network for the diagnosis of pulmonary embolisms. Besides, the system applies case-based reasoning for the management of hospital resources.

MENTOR (Mani, Valtorta, & McDermott, 2005) is another system in which a Bayesian model was built from a medical dataset regarding mental retardation.

PROMEDAS (Kappen, Wiegerinck, Akay, Neijt, & van Beej, 2003), based on Bayesian inference rules, takes as input the patient's group of symptoms and test results, and gives as an output the main diagnoses to take into account, with their corresponding certainty levels.

Finally, *DIAVAL* (Diez, Mira, Iturralde, & Zubillaga, 1997), a system for the diagnosis of heart diseases, uses a Bayesian network as knowledge base, and it computes the "*a posteriori*" probabilities of each diagnosis it considers, selecting the most probable and relevant ones.

3.2. CBR System for ABM

3.2.1. CBR systems in a Nutshell

In general, Case Based Reasoning (CBR) is a methodology utilized for the solution of problems and learning within the AI area which dates back to the late 1970s (Kolodner, 1993); certain results could be tracked down from psychology, where it was demonstrated that on numerous occasions human beings solve their problems based on their past experiences, rather than on a profound knowledge of the topic in question. For instance, doctors look for groups of known symptoms, engineers take many of their ideas from previously successful solutions, and programmers reutilize abstract schemes they already know (Díaz Díaz Agudo, 2002). The fundamental concept on which this methodology is based is *"similar solutions correspond to similar situations or problems"*.

From a base of experiential knowledge in which previous cases are correctly identified with their corresponding solutions, a Case Based Reasoning System (CBRS) consists in analysing the existing correlation of such knowledge base with the new suggested problem and, in virtue of the correspondences, adapt and propose the nearest solution. Instead of using an explicit model of the problem for the inference process, it simply utilizes the experience captured in the same way the expert usually inputs and processes it. Another characteristic that differentiate these systems from other approaches of expert systems is the increasing learning, that is given in an automatic and almost transparent way due to the fact that the retained cases are stored as new cases (Aamodt & Plaza, 2004; Kolodner, 1993; Pal & Shiu, 2004; San Miguel Carrillo, 2007).

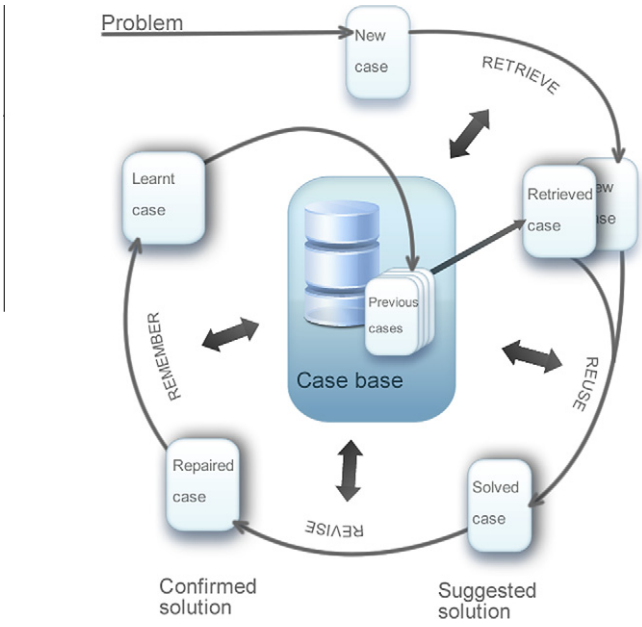

Fig. 3. The "four Rs" CBR cycle.

When a new problem appears, the CBRS looks for a previously occurred problem, i.e., case, whose description is the most similar taking into consideration the presented characteristics. The solution to that problem is used as a basis to generate the solution to the new problem. According to Watson (1997). "*a case is a contextualized piece of knowledge representing an experience*". It contains the previous lesson and the context in which that lesson can be applied It can also be defined as "*a complete description of the problem, with its respective solution and also an assessment of the solution's efficiency*" (Otavio Alvares, 2006).

The CBRS can be defined as a cyclic process named "*the four Rs*" (Fig. 3): (i) *R*ecover the most similar cases, (ii) *R*eutilize the cases that might solve the problem, (iii) *R*evise the proposed solution if necessary, and (iv) *R*etain the new solution as part of a new case (Aamodt & Plaza, 2004; Lopez de Mantaras et al., 2006). A more detailed description of this process is as follows:

- *Case recovery.* This process of recovering a case can be divided into three tasks: Identifying the characteristics or the indices that describe the new problem; locating the relevant cases and choosing the best candidate, or candidates, among the most relevant cases. Two of the most currently used techniques are: recovery of the closest neighbour, and inductive recovery (Kolodner, 1993), (Pal & Shiu, 2004).
- *Solution adaptation.* Usually, when a case is recovered, an analysis is carried out to determine the similarity with the presented problem. The adaptation consists in identifying the differences between the recovered case and the current case and afterwards, applying mechanisms (formulas, rules or others) to those differences as to obtain the final solution. Generally, there are two types of adaptation: (i) structural adaptation, which consists in applying rules and formulas directly to the stored solution, and (ii) the derived adaptation, which consists in reutilizing the rules and formulas that generated the recovered solution in order to generate the new solution (Watson, 1997).
- *Case revision.* After the case has been adapted, it is convenient to verify that the differences with the new one were taken into account. If the obtained solution to the new problem is not the correct one, it is feasible to repair it and in this way, learn from mistakes. Basically two steps are taken: (i) the solution is assessed and its applicability to the real case is determined, and (ii) the case to be stored is repaired.
- *Retention.* This process consists in incorporating what is useful from the new solution to the knowledge. This involves: (i) selecting the case information to be retained, in which way to retain it, and (ii) how to integrate it to the structure of the memory (Aamodt et al., 2004).

There are some aspects that need to be taken into account when creating a case base as they have a direct impact on the design of the CBRS such as the structure and representation of the cases, the memory model used to organize the case base and the selection of indices used to identify each case (Pal & Shiu, 2004). The case base needs to be organized in manageable structures that support efficient searches and recovery methods. For this purpose, a wide range of possibilities can be used in text files, relational databases or XML files and in order to access them rapidly. Cases may represent different sorts of knowledge that can be stored in different representation formats, such as objects, semantic webs, and tables.

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Table 2
Existing CBR systems applied to CDSS.

System	Description
SHRINK	Diagnosis of psychiatric diseases (Kolodner & Kolodner, 1987)
MEDIC	Diagnosis of pulmonary diseases (Turner, 1989)
ALEXIA	Hypertension analysis scheduling (Bichindaritz & Seroussi, 1992)
ICONS	Antibiotic therapy and intensive treatment scheduling (Gierl, 1993)
BOLERO	Pneumonia diagnosis (Lopez & Plaza, 1993)
FLORENCE	Healthcare scheduling (Bradburn & Zeleznikow, 1993)
MNAOMIA	Diagnosis, treatment scheduling and clinical investigation assistance for psychiatric diseases (Bichindaritz, 1995), (Bichindaritz, 1996)
MACRAD	Image analysis (Macura et al., 1994) (Macura & Macura, 1995)
IMAGECREEK	Image analysis (Grimnes & Aamodt, 1996)
CADI	Medicine students' tutorial (Fenstermacher, 1996)
SCINA	Diagnosis of cardiac diseases (Haddad, Adlassnig, & Porenta, 1997)
CARE-PARTNER	Diagnosis and treatment scheduling of stem cells transplant (Bichindaritz, Kansu, & Sullivan, 1998)
CAMP	Diary menu scheduling
AUGUSTE	Diagnosis and scheduling of Alzheimer treatment (Marling & Whitehouse, 2001)
T-IDDM	Treatment scheduling of diabetes (Montani, Bellazzi, Portinale, & Stefanelli, 2002)
CASEY	A system applied to the medical diagnosis of heart failures, that offers a causal explanation of the patients' pathology. This system combines the Case Based Reasoning methodology with the usage of IF-THEN rules (Koton, 1988a), (Koton, 1989), (Koton, 1988b)
PROTOS	A system that enables the user to classify auditory disorders based on the Case Based Reasoning methodology and a semantic knowledge network that manages structures and categories (Bareiss, 1989), (Bareiss, Porter, & Murray, 1989), (Bareiss, Porter, & Wilson, 1988), (Porter, Bareiss, & Holte, 1990), (Porter & Bareiss, 1986)

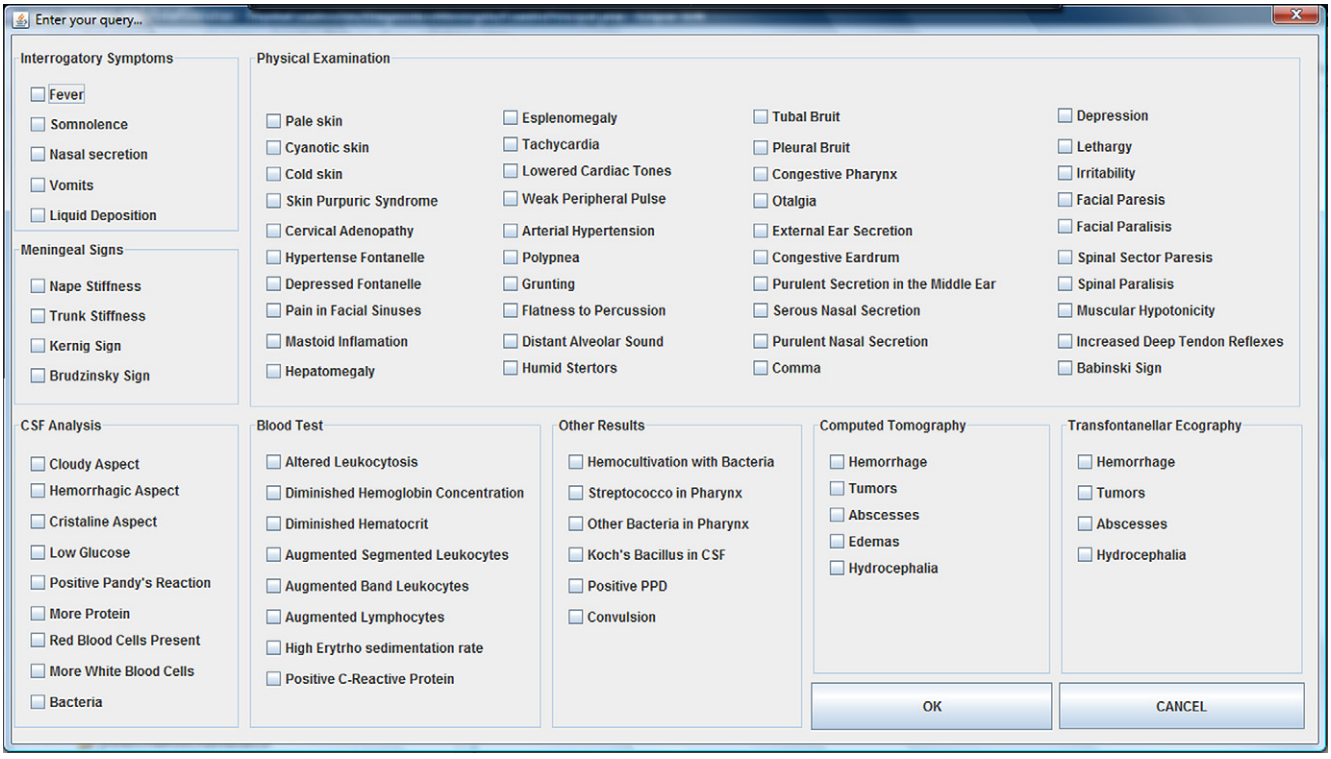

Fig. 4. ABMCBDS entry of a new consultation.

As with medical Bayesian systems, there are numerous CBRS that have successfully been applied in general context and diagnosis in particular. Table 2 shows some reference examples of CBRS applied to CDSS.

3.2.2. Implementation of CBR CDSS for the diagnosis of ABM (ABMCBDS)

In order to assess the applicability of the CBR methodology to the studied case, a CBRS applied to the diagnosis of the Acute Bacterial Meningitis of children under the age of 12 months was developed (hereafter ABMCBDS). Previous to its construction, a subgroup of signs-and-symptoms was selected according to what is specified in the section "2. Application context – Diagnosis of Acute Bacterial Meningitis".

Table 1 indicates the signs and symptoms being considered, grouped in the way the medical expert usually carries out the examination. As in *ABMDES*, the *ABMCBDS* represents the examination groups in this way, in order to facilitate the consultation data entry by the doctor.

The similarity between cases is given basically by the absence or presence of symptoms and signs. The differential diagnoses group that is to be taken into account by the system is then selected. These are the ones referred to in the Section 2.

The *ABMCBDS* was developed using the *JColibri 2.1* framework (Recio García, Diaz Agudo, & González Calero, 2008) following

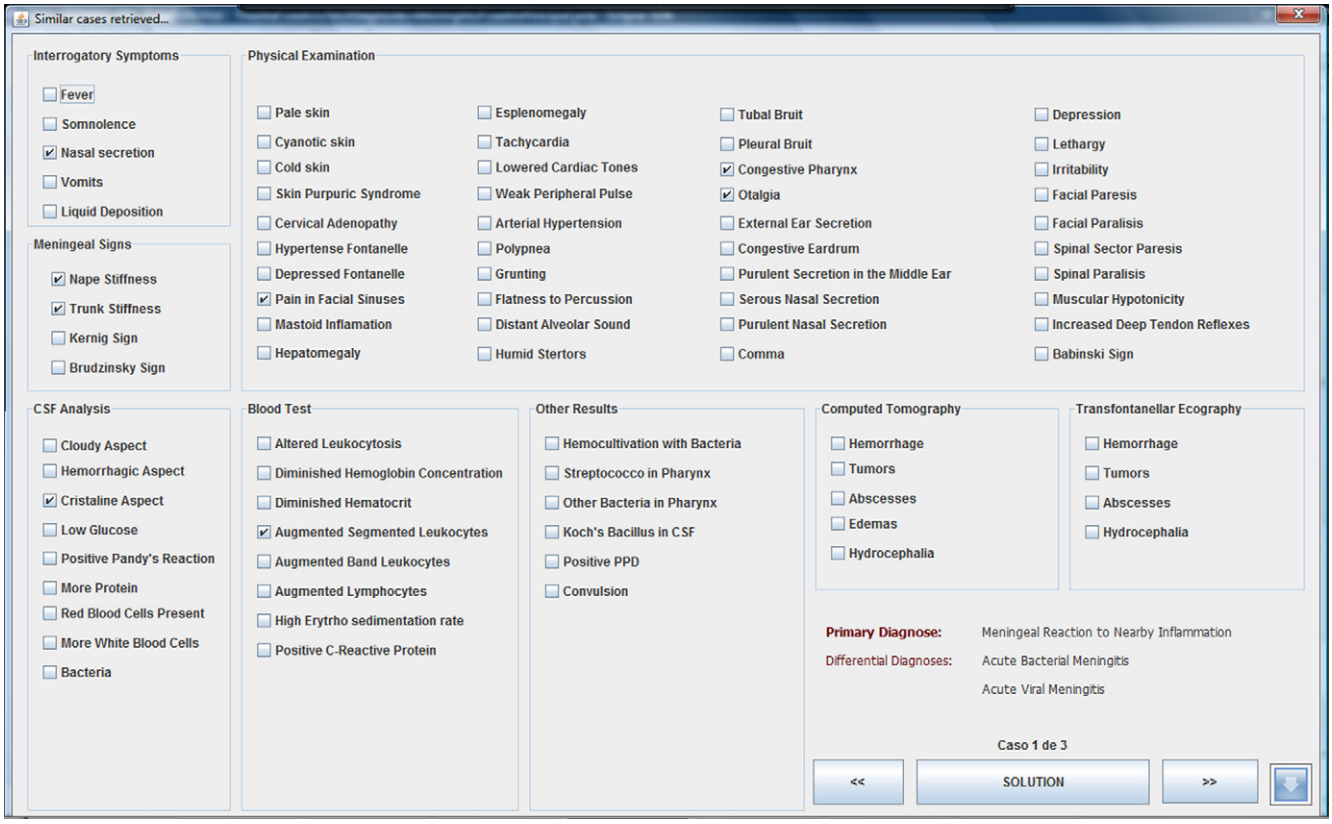

Fig. 5. ABMCBDS– similar recovered cases.

previously mentioned *four R* cyclic process consisting, i.e., (i) *Recovery* of the most similar cases, (ii) *Reutilization* of such cases, (iii) a *Revision* of the proposed solution and, (iv) the *Retention* of the new solution.

In *ABMCBDS*, each case represents the situation of a medical consultation: the *problem* consists of the description of the signs and symptoms shown by the patient (clinical feature). The *solution* represents the diagnosis given by the doctor in that particular situation; and the *assessment* indicates how accurate a diagnosis is the one given, that is to say, if the system has proposed the diagnosis the expert was expecting, and not a differential diagnosis.

Fig. 4 shows the user interface used to enable the doctor to entry the information for a new consultation.

During the *ABMCBDS* execution, a new visit is registered by the expert, i.e., the doctor, as a new case. This new case has only the *problem* part, the clinical feature. The *ABMCBDS* then proceeds to the recovery of the most similar case/s. In order to do this, the clinical feature of the visit is compared to all other clinical features that compose the *Knowledge Base*, calculating the similarity to each of them. This similarity calculation is accomplished using a global similarity function for taking into account all of the attributes, and local similarity functions for each attribute. The similarity function used for single attributes is that of equality. The global function is calculated as the weighed summation of the local functions.

Given two cases or situations T and S, the similarity between both is given by:

$$Similarity(T,S) = \frac{1}{n} * \sum_{i=1}^{n} f(T_i, S_i) * w_i$$

where n is the number of signs and symptoms of each case; f is the local or global similarity function for the attribute i (simple or compound attribute) in cases T and S, and w is the weight of the symptom or sign i.

The technique initially used to recover cases is the one known as closest neighbour recovering the k most similar cases (k is an adjustable parameter).

Fig. 5 shows the user interface used to display the similar cases recovered. Note that it contains both the "description" of the case (with the values of the present signs and symptoms) and its "solution" (diagnosis).

Once the similar cases are recovered, the user is given the chance to select the case considered as the most similar, which is to be reused. Then the solution indicated by the previous case turns into the solution of the current case. This new solution is then to be revised. In this stage the expert physician gives her decision with regard to the possible differential diagnoses, also providing the information about the accuracy assessment about the *ABMCBDS* system proposed diagnose. The doctor will then indicate whether the proposed solution is the correct one or not, and, when it is not, she will also indicate the correct diagnosis. The system's learning ability is based not only in success but also in failures and mistakes.

Once the case is revised, the diagnosis and its corresponding assessment are obtained, and it is ready to be incorporated to the knowledge base.

For the implementation of *ABMCBDS*, a relational database has been used to store the cases (MySQL).[1] The Hibernate framework[2] has been used to implement the cases object-relational mapping.

3.2.3. Implementation of CBR CDSS with adaptation for the diagnosis of ABM (ABMCBDS-Adapt)

As was described before, *ABMCBDS* behaves with a high accuracy rate, even when it lacks of automatic capabilities for the adap-

[1] http://www.mysql.org/.
[2] http://www.hibernate.org/.

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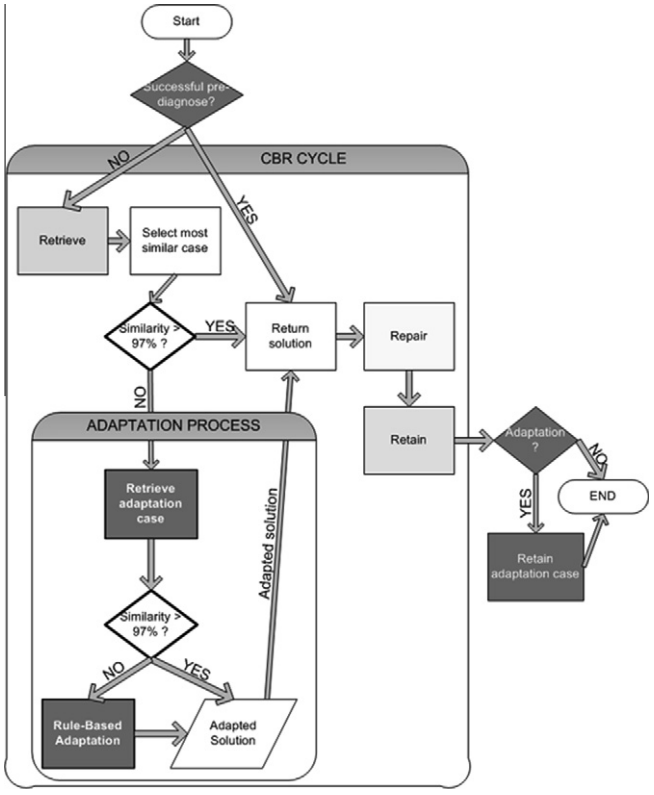

Fig. 6. The adaptation process.

tation of previous solutions. The eventual differences in the descriptions of the problems are not being fully taken into account. In order to assess the feasibility of improving the system by incorporating automatic adaptation processes, a third system has been developed.

The *ABMCBDS-Adapt* is an extension of the *ABMCBDS* that implements the reutilization step. This is achieved by integration of Case Based Reasoning and rule based expert systems.

Instead of reusing directly the most similar case selected by the user, the previous and current cases are compared to assess the similarity between them. If the similarity is higher than a certain threshold then the solutions of the previous case can be directly reused – differences between cases are negligible -.On the other hand, if the similarity factor is lower than the threshold, an adaptation process is carried out.

Adaptation cases are then introduced. These cases store *adaptation experiences*. The *description* part of these cases is composed by the *differences* that exist between the clinical situation represented in the base (consultation, real) cases, and by the solution of the retrieved consultation case. The *solution* of the adaptation case consists of the *adapted solution*. Thus, an adaptation case is a representation of a *change experience*.

The adaptation process depicted in Fig. 6 starts by automatically creating a new *query* (based on the symptoms differences of the consultation cases and previous consultation case solution); this *query* is used to retrieve the most similar adaptation case. The similarity between the query and the recovered case is again assessed. If the similarity factor is higher than a certain threshold the solution offered by the recovered case is directly reused. This means that the solution of the current diagnosis case corresponds to the solution of the retrieved adaptation case. If the similarity factor is lower than the threshold then the adaptation case cannot be reused (the current situation does not apply) and the previous solution is *transformed* using a rule based system. Each rule indicates a transformation to be made (add or retract a diagnose), taking into account the differences existing in the clinical situations of the previous and current cases.

Thus, the system can store and reuse previous adaptation cases, but can also learn new experiences by different means: reutilization of an adaptation case; rule based adaptation and adaptation made by the user in the repair step.

Besides the adaptation process, a pre-diagnosis step has been implemented. This step checks for situations in which the Case Based Reasoning process does not offer a major benefit because the only presence of a certain symptom indicates the existence of the corresponding differential diagnose. These situations are detected by a rule based system.

4. Experimental work and evaluation

In order to populate the Case Base for both *ABMDES* and *ABMCBDS* and *ABMCBDS-Adapt* systems, large amounts of historical documentation about real consultations of real paediatric patients and the corresponding occurrences of the varied symptoms and signs, as well as the diagnoses of ABM and differential emitted diagnosis were used. Then, based on this data collection, synthetic consultation cases derived from a population of 10,000 patients are randomly generated, using the occurrence probabilities of diseases and symptoms previously described. Each potential case is generated through the application of standard Montecarlo method using the existing probabilities. Having no deeper knowledge about the probability distribution of each illness in the population, or about the probability distributions of the symptoms or signs, Montecarlo rounds were developed using uniform distributions. Each round has been taken independently of the others, assuming no relationship between arriving patients (social, economic, or any other that could effectively imply dependencies between the probability distributions).

Once the first group of potential cases has been obtained, the duplicated or extreme situations were deleted. The next step is the validation of *virtual consultations* by the medical experts, so as to count with a group of consultations effectively representative of the normal population (the case database is "cured"). In order to do this, a specifically designed program is used, through which the medical experts indicate the verisimilitude of the case (and thus its usefulness as a real case for the system), the primary diagnosis and the differential diagnoses Fig. 7.

In this way a cured population of 216 cases was obtained, and their respective expert diagnosis, which will be useful to compare the behaviour of both intelligent systems.

Through the application of the usual statistical calculations to determine the size of the sample for the experiment, 30 cases were extracted from the case base (taking the higher sample size obtained for both systems, based on the means and standard deviations calculated for both using well-established statistical processes).

In order to determine the size of the sample for the experiment, the usual statistical sample size calculations were applied. To find the average and variance of both systems, 25 cases were randomly selected from the case database (a standard set of 10 cases is the commonly accepted practice for this kind of experiments and populations, according to National Institute of Statistics advisors). Each of these cases was applied to both systems and their results compared against the expert-issued diagnostic. Both systems proved to have a Bernoulli distribution and showed a success average of $p = 0.88$. The expected mean and variances were then $E[X] = p = 0.88$ and $V(X) = p(1-p) = 0.88 * 0.12 = 0.1056$.

The null hypothesis and alternate hypothesis based on the calculated averages are:

$$H_0 : \mu 1 = \mu 2 \rightarrow \mu 1 - \mu 2 = 0$$

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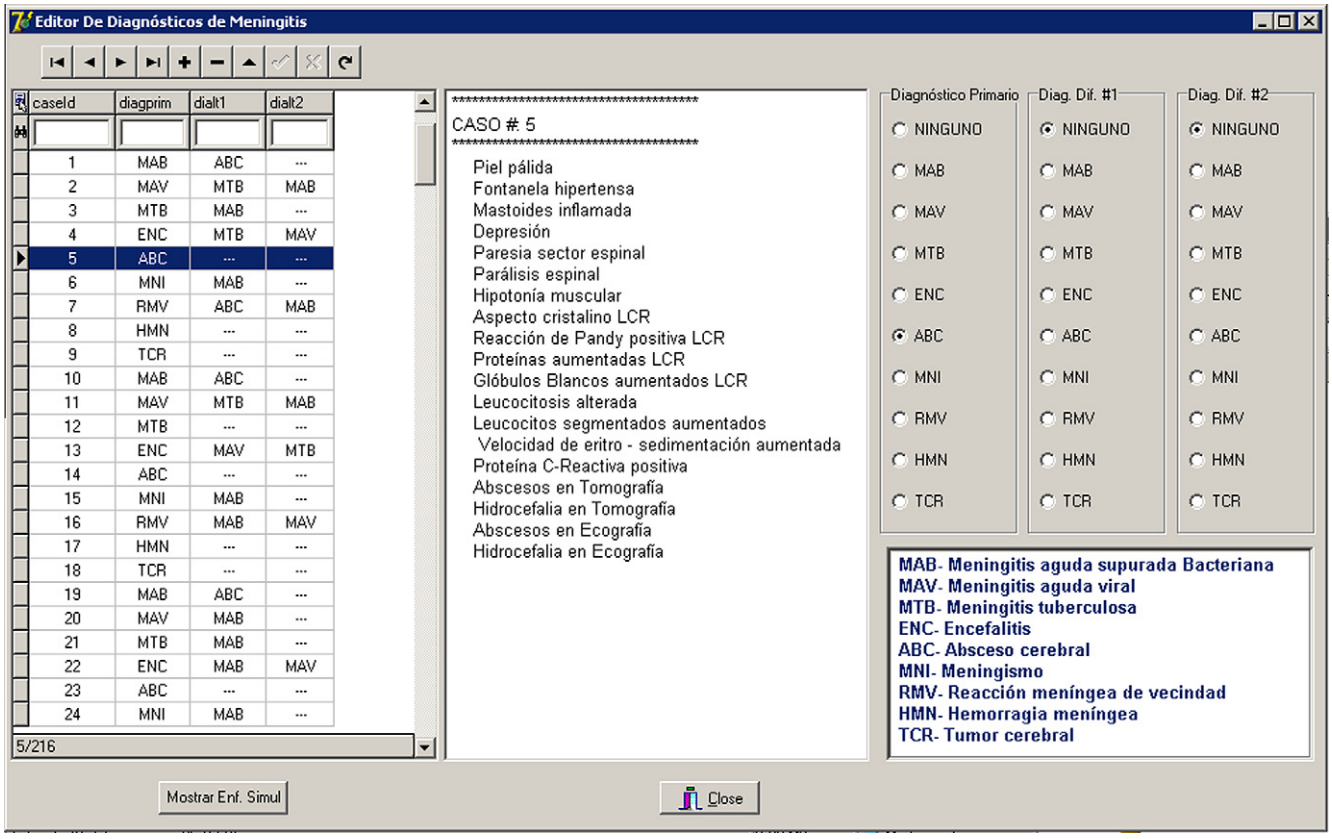

Fig. 7. Program used by the physicians to diagnose of ABM in the database cases.

$$H_A : \mu 1 > \mu 2 \rightarrow \mu 1 - \mu 2 > 0$$

The Normal probability distribution has been used for the samples distribution, as it provides enough accuracy balanced with an acceptable calculations cost.

For this experiment it has been considered enough to use an α probability of 1.0% ($\alpha = 0.01$), which implies a value of $Z_\alpha = 2.33$.

In this research it is expected that the RBC system outperforms the bayesian one, regarding the accuracy, in at least 20%. Thus, the minimum distance between estimations and real values should be $d = 0.2$.

Then,

$$Z\alpha = \frac{(X'_1 - X'_2)(\mu_1 - \mu_2)}{\sqrt{\frac{\sigma_1^2 + \sigma_2^2}{n}}}$$

Having that $(X'_1 - X'_2) - (\mu_1 - \mu_2) = d$, and that $\sigma_2^2 = \sigma_1^2$ the sample size n is:

$$N = \frac{Z\alpha^2 * 2 * \sigma_1^2}{d^2}$$

$$N = \frac{2.33^2 * 2 * 0.1056}{0.2^2} = 28.66$$

As a result, in this research a sample size of $n = 30$ was considered.

These sample cases were applied as entries in both systems. For each applied case, the result was registered (proposed diagnosis) by each of the three systems, and the results were contrasted with the correct diagnosis emitted by the medical expert to determine if the result matched the diagnosis expected by the expert or not. With these data the *precision* or *accuracy* of each system could be measured.

The second test regarded tolerance. The aim of this test was to analyze the impact that the user's experience may have on the system's performance, because one of the main objectives of this kind of CDSS is that they must be useful for a wide range of physician (in regard to their specific experience in coping with the target illness). In other words, CDSS should be useful both for expert and novice physicians. In this research's context, we define *novice* as the condition that would determine a difficulty in assessing some important symptoms. From the point of view of the CDSS, this is similar to say that the *input information is degraded.* In collaboration with expert physicians, a subset of symptoms was defined, that included those that are usually more difficult to detect, or those whose correct interpretation largely depends on the physician's experience.

The most difficult components (signs or symptoms) to assess were started to be withdrawn increasingly (one by one) from the cases of the group used for the test, until all of them were removed. In each iteration, the group of cases was applied to both systems and the results were registered, analyzing its correction in the usual way, in order to determine the flexibility or tolerance of both systems.

The precision or accuracy of the system is simply defined by the proportion of right answers the system gives back.

As can be noticed in Table 3 and Table 4, the precision of the systems is above 90%, and *ABMCBDS-Adapt* slightly overcomes the other two.

Regarding accuracy, a differential characteristic between the systems must be particularly taken into account: while *ABMDES* does not become more accurate in time (as inference is carried out based on 10,000 cases, and there is no learning or automatic incorporation of knowledge built into this system), it is expected that *ABMCBDS* and *ABMCBDS-Adapt* progressively increases their accuracy.

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Table 3
Accuracy results for ABMDES, ABMCBDS, and ABMCBDS-Adapt.

System	Successes	Success proportion
ABMDES	27	0.9
ABMCBDS	28	0.93
ABMCBDS-Adapt	29	0.97

This is due to the fact that incorporation of new experience is an implicit part of the normal Case Based Reasoning process and therefore of the *ABMCBDS* and *ABMCBDS-Adapt* as well. This means that, while the system is being used and new cases gradually incorporate to the case base (more accumulated and documented experience available for the inference), the system must behave with higher precision and accuracy in the proposed diagnoses as long as the experience keeps on the increase.

Furthermore, actual performance of the Bayesian system is based on an extensive set of illness and symptoms / signs probabilities, derived from a 10,000 arrivals to the emergency room. In contrast, the CBR systems only count on an experience base of less than 200 cases.

The *flexibility* of a system is defined as the tolerance it presents towards the lack of specificity of a case. This can occur due to the

Table 4
Results of the accuracy test.

Case Id	Real diagnose	*ABMDES*	*ABMCBDS*	*ABMCBDS-Adapt*
131	Acute viral meningitis	Meningeal reaction to nearby inflammation	Acute Viral Meningitis	Acute Viral Meningitis
168	Brain Tumor	Brain Tumor	Brain Tumor	Brain Tumor
71	Meningeal reaction to nearby inflammation	Meningeal reaction to nearby inflammation	Meningeal reaction to nearby inflammation	Meningeal reaction to nearby inflammation
113	Brain Tumor	Brain Tumor	Brain Tumor	Brain Tumor
194	Meningeal reaction to nearby inflammation	Meningeal reaction to nearby inflammation	Meningeal reaction to nearby Inflammation	Meningeal reaction to nearby inflammation
79	Acute Bacterial Meningitis	Acute Bacterial Meningitis	Acute Bacterial Meningitis	Acute Bacterial Meningitis
203	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage
135	Meningism	Meningism	Meningism	Meningism
176	Meningeal reaction to nearby inflammation	Meningeal reaction to nearby inflammation	Meningeal reaction to nearb Inflammation	Meningeal reaction to nearby inflammation
82	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage
44	Brain Tumor	Brain Tumor	Brain Tumor	Brain Tumor
174	Acute Bacterial Meningitis	Acute Bacterial Meningitis	Acute Bacterial Meningitis	Acute Bacterial Meningitis
166	Meningeal reaction to nearby inflammation	Meningeal reaction to nearby Inflammation	Acute Bacterial Meningitis	Acute Bacterial Meningitis
86	Meningeal reaction to nearby inflammation	Meningeal reaction to nearby Inflammation	Meningeal reaction to nearby Inflammation	Meningeal reaction to nearby inflammation
98	Brain Tumor	Brain Tumor	Brain Tumor	Brain Tumor
83	Brain Tumor	Brain Tumor	Brain Tumor	Brain Tumor
65	Meningism	Meningism	Meningism	Meningism
155	Meningism	Meningism	Meningism	Meningism
143	Tuberculous meningitis	Brain Tumor	Acute Viral Meningitis	Tuberculous Meningitis
68	Brain Tumor	Brain Tumor	Brain Tumor	Brain Tumor
23	Brain abscess	Brain Abscess	Brain Abscess	Brain Abscess
118	Brain Tumor	Brain Tumor	Brain Tumor	Brain Tumor
213	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage
185	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage
156	Acute Bacterial Meningitis	Meningeal reaction to nearby Inflammation	Acute Bacterial Meningitis	Acute Bacterial Meningitis
179	Meningism	Meningism	Meningism	Meningism
211	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage
49	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage	Meningeal Hemorrhage
69	Acute Bacterial Meningitis	Acute Bacterial Meningitis	Acute Bacterial Meningitis	Acute Bacterial Meningitis
138	Brain Tumor	Brain Tumor	Brain Tumor	Brain Tumor

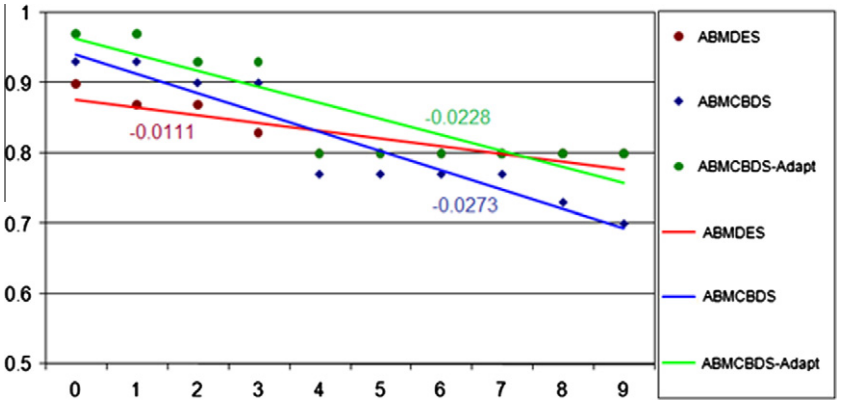

Fig. 8. Results of the flexibility test.

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different abilities of physicians to detect signs and symptoms, or to the doctor's experience.

In order to analyze the response of each system to this condition, same cases were applied to both systems. Each time it was withdrawn one important symptom or sign (considering important signs for this task those that would be difficult to assess by novice physicians) and the accuracy of both systems assessed in these diminished conditions.

Fig. 8 shows the results of the experiments carried out for testing the systems' flexibility. The ABMDES and ABMCBDS-Adapt systems both present less degradation in accuracy than ABMCBDS. On the other hand, the ABMCBDS-Adapt system has showed to be more sensitive to the absence of a symptom, compared to the Bayesian inference-based system.

For every simulation and experiment, the considered test cases were built by experienced practicing physicians. These experts clearly stated the correct diagnosis for each case, based on the combination of symptoms and signs.

5. Conclusions and future work

In this paper, three approaches of application of Intelligent Systems for the development of Clinical Decision Support Systems have been presented.

It has been verified that prototype systems produced using both techniques, applied over a group of cases representative of a real population, have a behaviour that can be considered effective for supporting Clinical Decisions.

The experiments carried out with *ABMCBDS* and *ABMCBDS-Adapt,* and the verification by medical specialists with wide experience in the diagnosis of the considered diseases, allow us to conclude that this Artificial Intelligence approach for the construction of Clinical Decision Support systems is particularly interesting, given its effectiveness and particularly its ability to incorporate knowledge and experience from the field experts.

All things considered, the results obtained from the realized experiments in order to compare the systems developed using CBR (*ABMCBDS, ABMCBDS-Adapt*) and simple Bayesian Inference (*ABMDES*) for the diagnosis of the same diseases, allow us to state that:

- *ABMCBDS* and *ABMCBDS-Adapt* are more precise than *ABMDES*.
- *ABMCBDS-Adapt* is more precise than *ABMCBDS*.
- *ABMCBDS-Adapt* is more flexible and robust than *ABMCBDS*, which indicates one of the benefits of *implementing* the adaptation step, and combining *Case Based* Reasoning with rule based expert systems.

As part of our future work, we plan to make use of ontologies for deeper semantic interpretation of symptoms and signs. In this first approach to the diagnose of ABM, the set of symptoms and signs selected has been such that each one is modelled as an independent event (from the statistical point of view, and also from the clinical point of view). The gathered probabilities are based in this assumption. No eventual interrelationships between different symptoms have been taken into account. Those would have led to very complex conditional probabilities, which would probably have been too difficult (or even impossible in some cases) to elicit. Furthermore, the existing bayesian inference engine would require a drastic reengineering to cope with these relationships.

Ontologies could be a means to implicitly model those interrelationships, without the need to explicitly model the conditional probabilities.

This would apply with major benefits to CBR- based system, because these kind of system do not relay on an explicit mathematical model, in contrast with the bayesian ones.

Another future work concerns the application of CBR techniques to design more complex CDSS, e.g., a treatment proposal system for paediatric HIV-AIDS disease. The research group has been working now for several years on the application of different computational techniques in the construction of systems to help with the HIV-AIDS diagnose and, mainly, antiretroviral treatment proposal. This problem seems to be more complex than the one analyzed in this research, as there are many more symptoms and signs involved, but mainly because it is a rather new illness, with no real cure, and with a very limited set of treatment alternatives to use.

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