ESTHER – expert system for the diagnostics of acute drug poisoning

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Abstract. In recent years, there have been a lot of cases of acute drug intoxication in Russia, and there exist a lack of qualified specialists capable of forming proper diagnosis of intoxication. That is why this research was aimed at developing of an expert system for diagnostics of poisonings caused by overdose or misuse of widespread medicines. Such medicines are available in every family and it is very easy to exceed the critical dosage that could lead to a fatal issue. According to some estimates about a half of all poisonings are provoked by improper use of medicines.

This paper presents the main concepts of an Expert System for Toxicological Help (ESTHER). The most widespread medicines were combined into 19 groups according to the similarity in poisoning diagnostics and treatment. More than 60 clinical signs used by an expert in diagnostics of intoxications were included. The system was deliberately designed to use only clinical signs of poisonings with the view of using it in ambulances and hospitals of small towns where accurate laboratory analyses are not available.

The system imitates reasoning of a physician – an expert in toxicology. The ideas of method for knowledge base construction are presented. The architecture of the expert system is discussed in detail as well.

1 Introduction

In recent years in Russia there was a trend toward fast increasing of a number of poisoning cases for adults as well as for children. This situation makes more urgent and important the problem of poisonings diagnostics and treatment. A considerable change in the acute poisonings pattern has occurred in the last decade. Pharmaceuticals (particularly psychotic drugs), alcohol and surrogates replaced as the main poisonings causes acetic acid and other corrosives, organophosphorous pesticides and other household agents. Approximately one half of all poisoning cases are connected with drug poisoning.

The critical situation with a large number of the intoxications could be significantly softened by the availability of good expertise in hospitals and in ambulance cars. But unfortunately the majority of physicians working in the ambulance service and in hospitals don't know enough about the reasons of intoxications, their diagnostics and treatment.

Therefore, the important aim of the research is development of an expert system based on the knowledge of experienced physician. Such system could be applied as a useful source of advices for young physicians and physicians of different specialisations.

This paper presents main ideas of ESTHER (Expert System for Toxicological Help). Now the system is in the process of testing at the Toxicological Centre of Russian Ministry of Health.

2 Particular features of diagnostics for acute drug poisoning problem

Specific features of diagnostics for drug poisoning problem are as follows:

1. There are a lot of different medicines. On the basis of their influence on human organism they could be allocated into 19 groups. Usually, a typical representative for each group can be defined.

2. A set of 5-12 diagnostic signs can be used for the diagnostics of poisonings caused by medicines belonging to one group. The total number of the diagnostic signs is more than 60. They can be divided into several groups: medical examination, patient’s complaints, anamnesis, state of central nervous system, cardiovascular system, respiratory system, urinary system, gastrointestinal tract. Each diagnostic sign has a scale of possible values. For example, pulse rate can be described as: tachycardia, normal pulse or bradycardia.

3. In the process of diagnostics a physician creates a holistic image of patient’s poisoning on the basis of poisoning’s description in terms of diagnostic signs’ values. Generally, knowledge about some subset of values is not sufficient for the diagnostics.

4. There are certain groups of drug poisonings described by similar diagnostic signs. For the differentiation among them it is necessary to solve differential diagnostics problems.

5. There are several courses of patient’s treatment depending on a type of a drug, severity of patient’s condition, and a degree of the affection on certain systems of human organism.

From the formal point of view, the diagnostics problem may be presented in the following way. There is a multi-dimensional space of combinations of diagnostic signs’ values. With 63 diagnostic signs having in average 3 values on each scale, the number of such combinations is equal to 3^{63}. It is necessary to allocate these combinations (clinical situations – CS) into different classes of poisonings. Let us note that such classes may intersect. Moreover, for each class it is necessary to distinguish among the degrees of intoxication: mild poisoning or severe poisoning.

3. The difficulties in the development of an expert system for the diagnostics of acute medicinal poisoning

From formal point of view, the diagnostic problem could be presented in the following way. There is the multi-dimensional space of combinations of diagnostic signs values. By 63 diagnostic signs having in the average 3 values on a scale, the number of such combinations equal to 3^{63}. It is necessary to allocate the combinations (clinical situations- CS) into different classes of poisoning. Let us note that such classes could be intersecting ones. Also, it is needed to differentiate for each class the degrees of intoxication: poisoning and severe poisoning, because a course of a patient’s treatment depends from it.

The main difficulties in the application of Artificial Intelligence approach to the solution of this problem are:

1. To be useful an expert system must closely imitate an expert reasoning in the process of diagnostics for each CS. However, direct presentation to an expert all CS is impossible due to big dimension of the problem.

2. One could not expect receiving from an expert in the explicit form rules used in the process of diagnostics. It is known that expert’s knowledge is predominantly unconscious.

3. A decision for each CS depends from a combination of diagnostic signs values (holistic image of a possible patient) and can not be imitated by asking an expert to nominate some coefficients of importance for each value of a diagnostic sign.

4. In any process of expert knowledge elicitation, an expert could make some errors. It is desirable to have means to discover errors and eliminate them.

Such specific feature of problem under consideration do not allow to use known approaches [1,2] and require to find a new approach.

4. Methodological approach to the construction of expert knowledge base

The main features of our approach to the construction of expert knowledge base for the diagnostics of acute for medicinal poisoning problem are the following:

1. 19 knowledge bases imitating an expert diagnostics skill are constructed successively for different classes of poisoning.

2. For given class an expert defines the subset of diagnostic signs and its values needed for the diagnostics. All combinations of the diagnostic sign values create the space of possible patient images.

3. An expert is asked to order values of each diagnostic sign by typicality par respect to given class of intoxication.

4. The expert's knowledge is elicited by the presentation on computer screen the description of different CS in the terms of diagnostic sign values. An expert is to give its classification into three classes: strong intoxication by a drag from the corresponding class; intoxication by such drag; no intoxication by a drag from the corresponding class (different cause of intoxication).

5. To save an expert efforts the utilization of binary relation of domination by typicality is done. If an expert allocates one CS to the class of intoxication, some others CS having all diagnostic signs values(from the subset used) not less typical for this class and at least one value-more typical, also belong to the class. Using such binary relation it is possible to classify several CS on the basis of one expert decision. In other words a cone of dominance by typicality is constructed in the space of diagnostic signs.

6. Fortunately such cones are intersecting ones. It creates the possibility for checking an expert information for the absence of contradictions and for finding the special cases of diagnostic signs dependence. For each contradictory case the corresponding information is presented on computer screen to an expert for the detail analysis.

7. The special algorithm is used for the choice of the next CS presented to an expert for the classification on the base of the criteria of minimum number of questions needed for the classification of all CS belonging to given class.

8. For the classes of medicinal poisoning described by similar diagnostics signs the special knowledge bases for differential diagnostics are constructed.

New approach in the problems of knowledge elicitation have been tested previously on different practical tasks [3,4].

There is the group of methods based on the approach [4,5]. More advanced of them allow to receive from an expert the classification of 700-800 CS per hour [5].

After construction, the knowledge bases were tested by the presentation of different difficult cases to the computer and to the expert. The results demonstrated the close imitation of expert reasoning.

5. Formal statement of the problem

Given:

$K = 1, 2, \ldots, N$ – the set of diagnostic signs; n_q – the number of values on the scale of the q-th diagnostic sign ($q \in K$).

L_1, L_2, L_3 – ordered decision classes. L_1 – severe intoxication with some medicine A; L_2 – mild intoxication with medicine A; L_3 – no intoxication with A.

X_q – the set of values on the scale of the q-th diagnostic sign; values on each scale are ordered by typicality for each decision class; the ordering by typicality on the scale of one diagnostic sign does not depend on the values of the other signs.

Cartesian product of the diagnostic signs' scales: $Y = X_1 \otimes X_2 \otimes \ldots \otimes X_N$ creates the set of clinical situations (CS). One CS may be represented as $y^i = (y_1^i, y_2^i, ..., y_N^i)$ and $y_q^i \in X_q$.

Needed:

On the basis of information obtained from an expert it is needed to construct the complete (all CSs are classified) and noncontradictory classification.

Let us explain the notion of noncontradictory classification. Having ordered diagnostic signs' scales, it is possible to define anti-reflexive and transitive binary relation *P* of domination by typicality (for one decision class):

$$P = \{(y^i, y^j) \mid \forall s \in K \; y^i_s \geq y^j_s, \exists s' \; y^i_{s'} > y^j_{s'}\},$$

where $\geq$, $>$ – weak and strong relations of domination by typicality between values on the diagnostic signs' scales.

If $(y^i, y^j) \in P$, then y^i cannot belong to lower class (in the order) than y^j does, and vice versa: y^j cannot belong to higher class than y^i. If this condition is true for any pair $(y^i, y^j) \in P$, then the classification is noncontradictory.

6. *Structure of the knowledge base*

Knowledge base of ESTHER system consists of 19 knowledge bases for the decision classes (different classes of poisonings) and 12 knowledge bases for differential diagnostics. After expert knowledge has been stored in the knowledge base of the system, it becomes possible for arbitrary CS with any combination of diagnostic signs' values to find out a decision class (or several) and severity degree of intoxication.

After the construction of complete and noncontradictory knowledge base, methods of questionnaire theory [6] have been used to produce an optimal decision tree for each class of medicines. Criterion of optimality here is a minimum average number of questions needed to arrive to a conclusion about the existence and severity of poisoning by the drug of this class [7]. Decision tree presents a strategy of putting questions about values of clinical signs with the goal to ascertain the fact of intoxication and state of a patient. Each node of the tree is a question about a value of a diagnostic sign. Depending on the answer the following node is chosen. One of the decision trees embedded into the ESTHER knowledge base is presented on Fig 1.

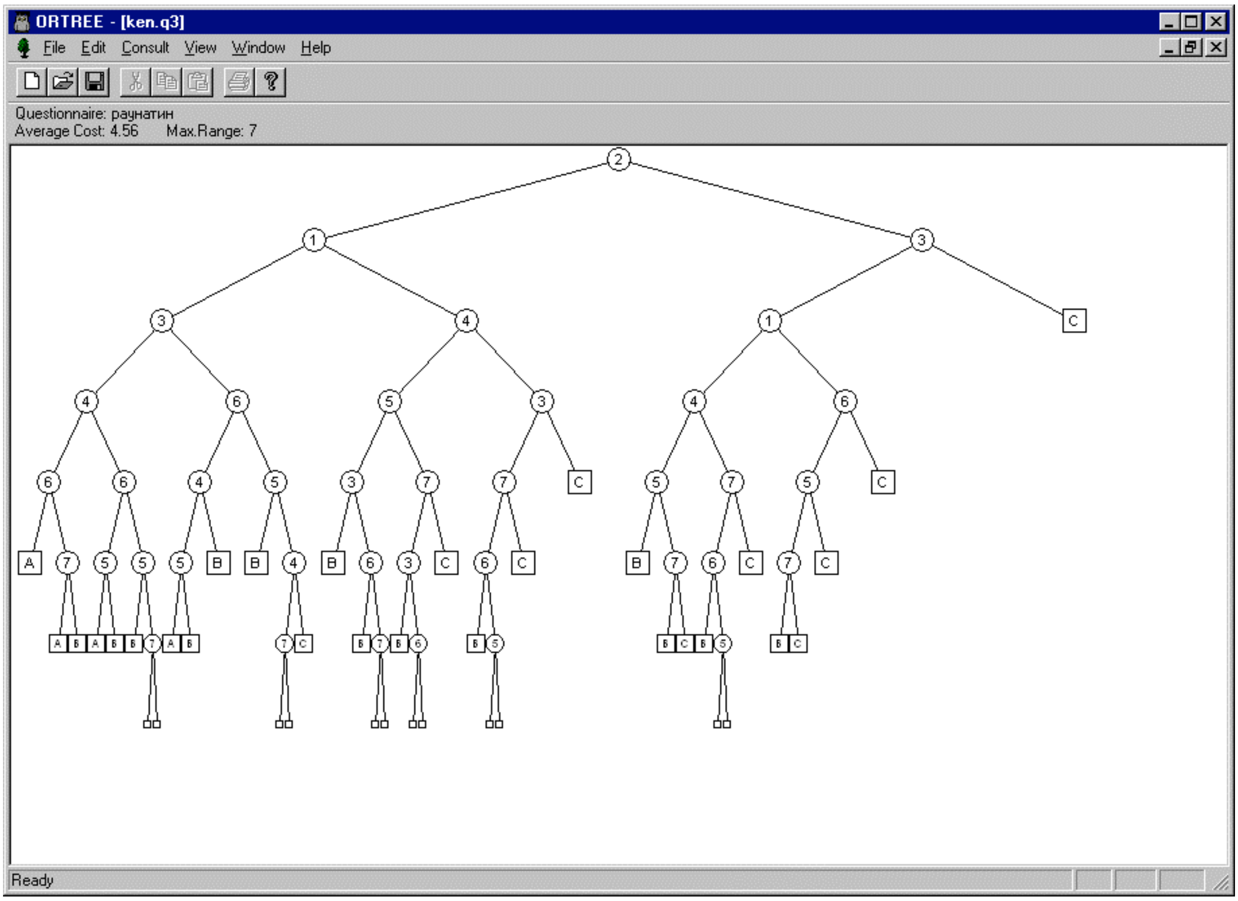

Fig. 1. The constructed optimal decision tree for diagnosing of poisoning by one of the medicines.

In the process of the knowledge base construction, the expert gave information about the most typical values of diagnostic signs for each decision class as well as impossible signs' values. Tables of prohibited values for pairs: "diagnostic sign – decision class" are the important constituent part of the knowledge base. Such tables allow speeding up the diagnostics process.

For the decision classes with similar sets of diagnostic signs the additional knowledge bases have been constructed. The corresponding optimal decision trees allow one to make decision in complex situations when intoxications by several drugs are possible. For such cases ESTHER gives the conclusions like "intoxication by drug A is more probable than one by drug B", "intoxication by drugs A and B is possible". An expert who tested the system noted that these answers increase the quality of system's answers in difficult cases of poisonings.

7. System architecture

Principal modules of ESTHER system and their interactions are represented at the diagram (see Fig. 2).

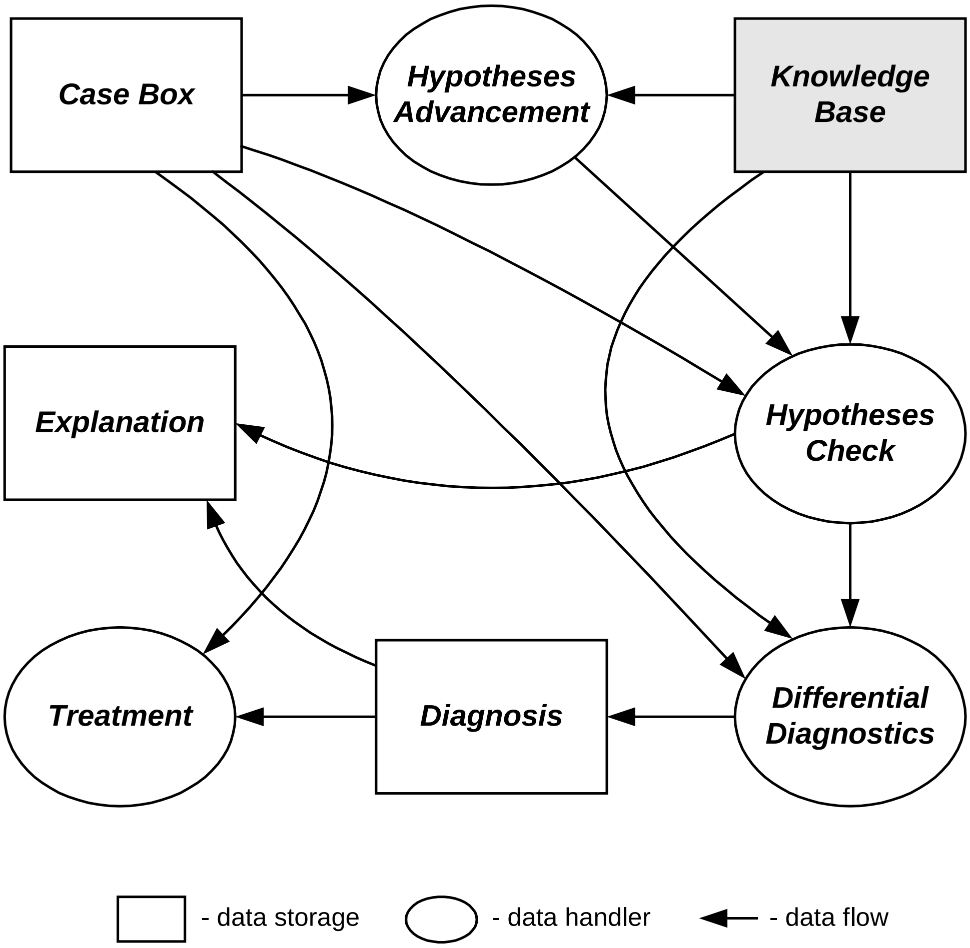

Fig 2. ESTHER principal modules and their interactions

There are two basic modes of a user's work with ESTHER system – data input mode and consultation mode. In the data input mode a user sees a list of clinical signs grouped under the titles: "External examination data", "Anamnesis", "Cardiovascular system", etc. All information about a patient including his/her state, illness history, complaints and so on is stored in the "**Case Box**" module. A user, for example an ambulance physician, successively enters values of clinical signs that are relevantto a particular case. "**Hypotheses Advancement**" module monitors this information and makes suppositions about a possible poisoning cause. If such a supposition arises, it notifies a user and suggests switching to consultation mode for hypotheses checking.

Hypotheses advancement module examines a patient's case with the aim to discover typical signs of poisoning by one or another drug. If there are several concurrent hypotheses it selects one that is supported by the largest number of typical signs' values. When a hypothesis for checking is formed, the hypotheses advancement module either notifies a user about its readiness to switch to consultation mode when system is in the data input mode at the moment or transfers the arisen hypothesis to the "**Hypotheses Checking**" module when system is in the consultation mode.

In the consultation mode the system successively checks and puts forward new hypotheses. It takes initiative upon itself and asks the user about values of clinical signs that are needed to confirm or to reject a hypothesis. While checking a hypothesis about a poisoning by some drug, the system uses the constructed optimal decision trees. A pass through the tree is accomplished and at the nodes, where values of clinical signs are still unknown, a user is questioned about values of appropriate signs to reach a conclusion. As a result of this pass one of the following conclusions is drawn: "Serious poisoning by medicine *A*", "Mild poisoning by medicine *A*" or "No poisoning by medicine *A*". The last means that either the poisoning was caused by the medicine other than X or there is no drug poisoning at all.

At any time user can break the mode of consultation, switch back to data input mode, add and/or change values of any clinical signs and after that resume the consultation.

While advancing and checking hypotheses the so-called exclusions are used intensively. Exclusion is a rule formulated by the expert in the following form: "Poisoning by the medicine *A* cannot cause the clinical signs' values *a, b, c…*" Our practice revealed that such rules decrease significantly the number of hypotheses to be checked as well as the time necessary to reach a diagnosis.

In general case it may happen as a result of hypotheses checking that several hypotheses about poisonings by different medicines are confirmed. This may be the case if patient actually has taken several medicines as well as when different medicines result in similar clinical pattern. In order to refine the diagnosis the "**Differential Diagnostics**" module is applied. There are special expert rules stored in the knowledge base of the system. They allow distinguishing among medicines similar in clinical patterns in difficult cases. These rules are also stored as optimal decision trees. An oriented graph is constructed in the "**Differential Diagnosis**" module. Nodes of the graph correspond to confirmed hypotheses and arcs correspond to the relations of poisonings' probabilities between different medicines. For example, if differential diagnostics rules state that poisoning by medicine *A* is more probable than poisoning by medicine *B*, then nodes *A* and *B* in the graph are connected by the arc, which originates at node *A* and enters node *B*. After that, the graph is condensed, that is a kernel of undominated nodes is extracted. For each node *A* belonging to the kernel the string "Poisoning by medicine *A* is most probable" is written to the final diagnosis (module "**Diagnosis**"). For the other nodes *B* the string "Poisoning by medicine *B* is not excluded" is written to the diagnosis. Our discussion with expert revealed that these two wordings are sufficient for practical purposes and there is no need in more precise distinguishing among poisonings' probabilities.

The ESTHER system allows explaining the diagnosis. While passing through a decision tree in the "**Hypotheses Check**" module information about passed tree nodes is stored. That is information about values of clinical signs that were used in diagnosing is recorded. The "**Explanation**" module stores arguments "pro" for each confirmed or rejected hypothesis as well as arguments "contra". The system provides explanations in the following form: "*There is poisoning with medicine A with degree of gravity X* ***because*** *sign* S_1 *has value* s_{11}*, sign* S_2 *has value* s_{21} *...* ***in spite of*** *the fact that sign* S_3 *has value* s_{32} *etc.*". This allows explaining in a natural way from the user's viewpoint both confirmed and rejected hypotheses. It is important to remark, that physicians use this explanation style as well when explaining their own decisions – usually they enumerate symptoms of poisoning and then say that these symptoms are sufficient for diagnosing.

There is also the module of recommendations on treatment as a constituent part of the ESTHER system ("**Treatment**" on the diagram). It can be used as a reference manual for getting acquainted with basic methods of treatment of poisonings by one or another medicine. Another, more important feature is its ability to give recommendations on the particular given case of poisoning. Using a diagnosis made by other modules of the system and extracting clinical pattern of poisoning from the "**Case Box**" module it is able to recommend treatment with regard to the gravity of poisoning, degree of damage to the systems of human organism. It can also prescribe a symptomatic therapy. Moreover, when prescribing treatment methods and dosage of antidote medicines it is possible to take into account age, weight and illness history of the patient.

Openness of ESTHER system's architecture was an important objective of its designing. Openness principle was followed when designing the knowledge base of the system, inference, explanation and treatment subsystems. Therefore, for example, it is a rather simple task now to include new groups of medicines that could be the cause of poisoning. This task is of great importance, because new medicines are emerging continuously.

The system's design provides for separation and encapsulation of a user interface environment shell and the system's knowledge base that was implemented in a specialised high-level scripting language. This guarantees high reusability of the knowledge base handling components and allows easy modification of rules and algorithms included in the system.

7 Conclusion

From our point of view the ability of expert system to behave like a human is the critical factor for its application. The developed ESTHER system includes large knowledge base that closely imitates expert knowledge and reasoning in the problem of drug poisonings diagnostics.

The system gives to a user a possibility to use active and passive ways of interaction. When ESTHER takes initiative upon itself and starts questioning a user he or she can have a lesson for self-education. A user can compare his/her preliminary conclusion with one of the expert – the author of the knowledge base.

It is important to note that the open architecture of ESTHER provides a possibility to add new decision classes (causes of intoxications) and new diagnostic signs for such classes. A revision of individual knowledge bases is also possible for any decision class using knowledge of more experienced (for this class of poisonings) physician.

The expert system for the diagnostics of acute drug poisonings is the example of "knowledge distribution" for large groups of specialists. We believe that appearances of new diseases and new drugs make the problem of "knowledge distribution" for large areas more important.

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