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With a little help from a computer: discriminating between bacterial and viral meningitis based on dominance-based rough set approach analysis

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Abstract

Differential Diagnosis of bacterial and viral meningitis remains an important clinical problem. A number of methods to assist in the diagnoses of meningitis have been developed, but none of them have been found to have high specificity with 100% sensitivity.

We conducted a retrospective analysis of the medical records of 148 children hospitalized in St. Joseph Children's Hospital in Poznań. In this study, we applied for the first time the original methodology of dominance-based rough set approach (DRSA) to diagnostic patterns of meningitis data and represented them by decision rules useful in discriminating between bacterial and viral meningitis. The induction algorithm is called VC-DomLEM; it has been implemented as software package called jMAF (http://www.cs.put.poznan.pl/jblaszczynski/Site/jRS.html), based on java Rough Set (jRS) library.

In the studied group, there were 148 patients (78 boys and 70 girls), and the mean age was 85 months. We analyzed 14 attributes, of which only 4 were used to generate the 6 rules, with C-reactive protein (CRP) being the most valuable.

Factors associated with bacterial meningitis were: CRP level ≥ 86 mg/L, number of leukocytes in cerebrospinal fluid (CSF) ≥ 4481 μL^{-1}, symptoms duration no longer than 2 days, or age less than 1 month. Factors associated with viral meningitis were CRP level not higher than 19 mg/L, or CRP level not higher than 84 mg/L in a patient older than 11 months with no more than 1100 μL^{-1} leukocytes in CSF.

We established the minimum set of attributes significant for classification of patients with meningitis. This is new set of rules, which, although intuitively anticipated by some clinicians, has not been formally demonstrated until now.

Abbreviations: ANC = absolute neutrophil count, AUC = area under the ROC curve, BMS = Bacterial Meningitis Score, CRP = C-reactive protein, CSF = cerebrospinal fluid, DRSA = dominance-based rough set approach, PCR = polymerase chain reaction, ROC = receiver operating characteristics.

Keywords: bacterial meningitis, decision rules, viral meningitis

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1. Introduction

In countries with high rates of compliance using vaccinations against the main bacterial pathogens, bacterial meningitis is rare, but aseptic meningitis is becoming increasingly common.[1–3] Differential diagnosis of bacterial and viral meningitis remains an important clinical problem, particularly in the initial hours of hospitalization. Management of these 2 entities, however, is completely different. Children with bacterial meningitis need to be treated with antibiotics immediately, while those with a viral infection can be discharged without treatment.[4] There is no single parameter useful for quickly establishing the etiology of meningitis. An optimal marker for diagnosis must be accessible, and the method of identifying it cheap and rapid. However, relying solely on 1 marker increases the risk of diagnostic error. Several analyses have compared sensitivity and specificity of common symptoms of meningitis and been found to have limitations.[5–8] However, combination of several different parameters may decrease the risk of diagnostic error. A number of methods to assist in the diagnoses of meningitis have been developed, but none of them have been found to have high specificity with 100% sensitivity.[5–7] The Bacterial Meningitis Score (BMS) designed by Nigrovic et al is one of the best so far, reaching 95% sensitivity.[9] As the BMS relies heavily on the cerebrospinal fluid (CSF) Gram stain results, its usefulness is limited; however, bacterial meningitis is very unlikely when patient scores a 0 on the 6-points scale.[9] This method's scale is based on a child with pleocytosis in CSF without any additional

Table 1

Explanation of the study.

How the study was done?

To express "condition-decision" relationships hidden in the data, we used the concept known as DRSA

1. We let the system learn from our cases to distinguish between bacterial and viral meningitis.
- Preparation of the data for analysis (see table in suppl. file, http://links.lww.com/MD/B817).
- Introduction of the data to the system.
2. Data analysis by the system: the induction algorithm VC-DomLEM; implemented as software package called jMAF (http://www.cs.put.poznan.pl/jblaszczynski/Site/jRS.html), based on java Rough Set (jRS) library.
3. Generation of the decision rules: structured using the concept of relation "if E, then H," where E denotes rule premise, and H rule conclusion. A set of 6 rules covered all patients.

Rules are characterized by their strength, defined as a ratio of the number of patients matching the condition and the number of all patients in the sample, and by their coverage, defined as a ratio of the number of patients matching the condition part of a rule and the number of all patients in the class.

4. Establishing a diagnosis of viral versus bacterial meningitis based on previously obtained rules.

Patients meeting all conditions from any of the rule 1 to 4 were diagnosed with bacterial meningitis.

Patients meeting all conditions from rule 5 or 6 were diagnosed with viral meningitis.

DRSA = dominance-based rough set approach.

symptoms, such as seizures, absolute neutrophil count (ANC) $>10 \times 10^9$ L^{-1}, positive direct CSF examination, CSF protein >80 mg/dL, or ANC in CSF $>1 \times 10^9$ L^{-1}.[9] The BMS was the first validated model derived from a pediatric population in the postconjugate vaccination era and has been applied to a number of pediatric patients worldwide. A number of other scales exist. The meningitis scale proposed by Oostenbrink et al is useful in determining which patients need lumbar puncture due to the high probability of bacterial etiology.[10] The parameters analyzed are a combination of clinical symptoms and laboratory test results with a maximum score of 44 points, but patients who score less than 8.5 points are not considered to be cases of bacterial meningitis.[10] Thus, the risk of bacterial etiology increases with the increasing points in the scale; however the limit below in which one can exclude a diagnosis of bacterial meningitis has not been established. Another model, designed by Spanos et al, relies heavily on CSF analysis.[11] Bacterial etiology is considered to be probable when 1 or more from the following is detected: CSF glucose <1.9 mmol/L, CSF/blood glucose ratio <0.23, CSF protein >2.2 g/L, CSF leukocytes >2000 μL^{-1}, CSF neutrophils >1180 μL^{-1}.[11] The model proposed by Bonsu and Harper can be used without CSF results, but requires complicated mathematic analysis to be performed by a computer and takes into account procalcitonin level.[12] Moreover, due to the cost constraints, procalcitonin is not routinely monitored, and in patients with high C-reactive protein (CRP) it does not offer additional data.

Currently, there are numerous new inflammatory markers that can help predict bacterial etiology of infection. Analysis of C3 concentration in CSF has 100% sensitivity and specificity,[13] and a similar result can be obtained for Heparin-binding protein.[14] Unfortunately, these tests are not routinely performed, which limits their usefulness in the clinical decision-making process.

The weak points in the aforementioned scales highlight the need for another tool. Knowledge discovery from data is a field of computer science that concerns the process of automatically searching the data for patterns that can be observed as knowledge about the world. The patterns reveal evidence by "condition-decision" relationships hidden in the data. The most natural representation of these relationships is by "if..., then..." decision rules relating some conditions of independent variables (called condition attributes) with some decisions dependent on a variable (called decision attribute). In case of diagnostic data, condition attributes correspond to anamnesis and the results of the clinical

examination of the patient, and the decision attribute indicates the disease. In our case, the disease is childhood meningitis, and the patterns discovered from data are intended to discriminate between 2 classes of disease: bacterial and viral.

In this study, we applied for the first time the original methodology of dominance-based rough set approach (DRSA) to diagnostic patterns of meningitis data and represented them by so-called monotonic decision rules useful in discriminating between bacterial and viral meningitis.[15] Explanation of the study is presented in Table 1.

2. Materials and methods

We conducted a retrospective analysis of the medical records of 148 children hospitalized with meningitis in the Infectious Diseases Department at St. Joseph Children's Hospital in Poznań, Poland. In the group analyzed, there were 64 (43%) patients with viral and 84 (57%) with bacterial meningitis. The following parameters were analyzed: CRP concentration in serum, ANC in peripheral blood, serum glucose and CSF glucose level, cell count, and protein concentration. Symptoms present on admission such as fever, seizures, rash, headache, and vomiting, and duration of symptoms were also analyzed.

Bacterial meningitis was diagnosed based on positive CSF culture (or detection of bacterial genetic material by polymerase chain reaction [PCR]) along with typical clinical symptoms: fever, headache, and existing meningeal signs. The gold standard for bacterial meningitis was positive culture. For rapid diagnosis, fast latex tests and direct examination of Gram stain were performed. Samples with negative culture were sent to National Reference Centre for Diagnostic of Invasive Bacterial Neuroinfections in Warsaw (KOROUN) in order to screen for the genetic material of potential pathogens by PCR. Viral etiology was confirmed by serum serology or based on clinical symptoms in patients with mumps. The study was performed with approval of the Poznań Medical University Ethical Committee.

2.1. Dominance-based rough set approach

To discover cause-effect relationships existing in the data, we used the concept of rough set,[15] and its particular extension, known as DRSA.[16–20] In our application, inconsistency meant that 2 patients have similar data from anamnesis and clinical examinations, while 1 is classified as bacterial meningitis, and

another as aseptic meningitis. The rough sets of patients, corresponding to bacterial and viral cases, are composed of 2 classical sets each, called lower approximation (composed of consistent patients from bacterial or viral group), and upper approximation (composed of both consistent and inconsistent patients from bacterial or viral group). Then, "if . . . , then . . . " decision rules are induced from these approximations. Rules induced from lower approximations are called certain, and those induced from upper approximations, possible. DRSA was designed for reasoning about ordered data, that is, such that the value sets of condition attributes are monotonically dependent on the order of the decision classes. Consequently, the rules induced from dominance-based rough approximations are monotonic, and their syntax is the following:

"if atr_i (patient)>v_i & atr_j (patient)>v_j & . . . & atr_p (patient)>v_p, then the patient has bacterial meningitis," "if atr_k (patient)<v_k & atr_l (patient)<v_l & . . . & atr_s (patient)<v_s, then the patient has viral meningitis," where atr_h is an h-th condition attribute and v_h is a specific value of this attribute discovered from data, that sets an elementary condition atr_h (patient) > v_h or atr_h (patient) < v_h belonging to the condition part of a rule assigning a patient to either bacterial class or viral class, respectively. The aforementioned syntax of the rules assumes that value sets of all condition attributes are numerical and that the greater the value, the more probable is that the patient develops bacterial meningitis; analogously, this syntax assumes that the smaller the value, the more probable that the patient develops viral meningitis. Numerical attributes with value sets ordered in this way are called gain-type. Value sets of cost-type attributes are ordered in the opposite way; consequently, elementary conditions on cost-type attributes have opposite relation signs. In the case of meningitis data, it is impossible to know a priori if attributes corresponding to anamnesis and clinical examination are gain- or cost-type. For this reason, we adopted the approach described previously,[21] that is, we doubled each original attribute and for the first one we assumed it is of gain-type, while for the second one we assumed it is of cost-type. Such a transformation of data does not affect the truth of discovered cause-effect relationships. Then, the induction algorithm takes decision for rules elementary conditions defined using one or both copies of given attributes. For instance, in a rule suggesting the assignment of a patient to the bacterial class, there may appear the following elementary conditions concerning attribute, atr_i:

↑atr_i(patient)>v_{i1} or ↓atr_i(patient)<v_{i2},

↑atr_i(patient)>v_{i1} and ↓atr_i(patient)<v_{i2}, which can be summarized as atr_i(patient)∈[v_{i1}, v_{i2}]

when v_{i1} < v_{i2},

where ↑atr_i and ↓atr_i are gain-type and cost-type copies of attribute atr_i, respectively.

The applied transformation of attributes permits discovering global and local monotonic relationships between anamnesis, clinical examination and class assignment.

For each rule one can calculate its strength, being a ratio of the number of patients matching the condition part of the rule and the number of all patients in the data set, as well as its coverage, being a ratio of the number of patients matching the condition part of the rule and the number of all patients in the suggested class.

In case of our application of DRSA, the rules were induced from the meningitis data transformed in the way described earlier, and structured into lower and upper approximations of bacterial and viral classes of patients. VC-DomLEM induction algorithm was employed,[22] implemented as a software package called jMAF using java Rough Set (jRS) library, and available at http://www.cs.put.poznan.pl/jblaszczynski/Site/jRS.html.

The sets of rules obtained by VC-DomLEM were used to construct basic classifiers in variable consistency bagging.[23–25] Variable consistency bagging (VC-bagging) was applied to improve the accuracy of prediction of the resulting ensemble of basic classifiers. Estimation of both rule and attribute relevance was performed by measuring Bayesian confirmation, as described previously.[11] Decision rules were induced repetitively on bootstrap samples and then tested on patients who were not included in the samples. Reported results were obtained in a 5-fold cross validation experiment that was repeated 10 (for a single basic classier) or 100 times.

Let us observe that a rule can be seen as a consequence relation "if P, then C," where P is rule premise, and C rule conclusion. The relevance of a rule is assessed by the Bayesian confirmation measure which quantifies the contribution of rule premise P to correct classification decision of unseen patients. For some reasons described previously,[11] we chose confirmation measure denoted by s(C,P), for its easy interpretation as difference of conditional probabilities involving C and P in the following way: s(C,P)=Pr(C|P)−Pr(C|¬P), where probability Pr(×) is estimated on the testing samples of patients. The relevance of each single attribute is also assessed by the Bayesian confirmation measure, but in this case, it quantifies the degree to which the presence of attribute atr_i in premise P, denoted by atr_i▷ P, provides evidence for or against rule conclusion C. Here, we use again confirmation measure s(C,atr_i▷ P), but now it is defined as follows: s(C,at_i▷ P)=Pr(C|atr_i▷ P)−Pr(C|atr_i▷¬P). In consequence, the attributes being present in the premise of rules that make correct decisions, or attributes absent in the premise of rules that make incorrect decisions, become more relevant.

2.2. Statistical analysis

The Shapiro-Wilk test was used for normality analysis. For comparison between bacterial and viral meningitis of normally distributed data Student t test was used. The Mann-Whitney test was used for data not following a normal distribution. The comparison between normal and abnormal ranges of analyzed parameters and types of meningitis was performed using the chi-square test of independence. The odds ratios were denoted as well as 95% CI. Receiver operating characteristics (ROC) curves were calculated to determine the potential of parameters to discriminate between different samples. An optimal cut-off point was calculated according to the highest accuracy (minimal false negative and false positive results). The area under the ROC curve (AUC) was used to check the prognostic value of particular parameters. All tests were performed 2-tailed and were considered as significant at $P < .05$. Calculations were performed by Statistica 10 (StatSoft) and MedCalc v.15.2.2 (MedCalc Software bvba).

3. Results

In the studied group, there were 148 patients (78 boys and 70 girls), and the mean age was 85 months. Selected symptoms and mean values of biochemical and hematological parameters in patients with bacterial and viral meningitis are presented in Table 2. The set of decision rules are presented in Table 3. Figure 1 presents a comparison of different parameters discriminating between bacterial and aseptic meningitis. A comparison between patients with bacterial and viral meningitis

Table 2

Characteristics of patients with meningitis.

Attribute name	Bacterial meningitis (n=84)		Viral meningitis (n=64)		P value
	Mean	**SD**	**Mean**	**SD**	
Age (months)	61.61	64.91	117.73	57.23	<.0001
Duration of symptoms (days)	1.98	0.73	4.41	2.71	<.0001
Serum CRP (mg/L)	219.02	94.32	6.88	12.24	<.0001
Serum ANC (1000 μL^{-1})	19.99	9.32	10.36	6.07	<.0001
Serum glucose (mg/dL)	118.90	54.29	95.61	25.63	.0013
CSF protein (g/L)	2.45	2.05	0.67	0.46	<.0001
CSF glucose (mg/dL)	35.32	24.91	56.73	16.44	<.0001
CSF leukocytes (n/μL)	5791.18	13072.70	439.27	664.09	<.0001
Symptom	**Bacterial meningitis n %**		**Viral meningitis n %**		
Headache	38	45.24	56	87.5	.0001
Rash[†]	33	39.29	4	6.25	.0001
Vomiting[‡]	6	7.14	49	76.56	.0001
Seizures	17	20.24	6	9.37	.1076

ANC = absolute neutrophil count, CRP = C-reactive protein, CSF = cerebrospinal fluid, SD = standard deviation.

[*] Higher risk in viral meningitis OR=8.474.

[†] Higher risk in bacterial meningitis OR=9.706.

[‡] Higher risk in viral meningitis OR=2.541.

Table 3

Description of rules generated by DRSA.

Rule no	1	2	3	4	5	6
Confidence	1	1	1	1	1	1
No of supporting cases	80	30	69	2	61	57
Strength	0.54	0.20	0.47	0.01	0.41	0.38
Coverage factor (%)	95	36	82	2	95	89
Negative coverage	0	0	0	0	0	0
Inconsistency measure	0	0	0	0	0	0
Confirmation measure	1	1	1	1	1	1
s-Confirmation measure	0.94	0.54	0.81	0.4	0.96	0.92

shows the statistically significant differences between groups. Details are presented in Table 3.

Usefulness of chosen parameters in predicting bacterial etiology of meningitis is presented in Table 4.
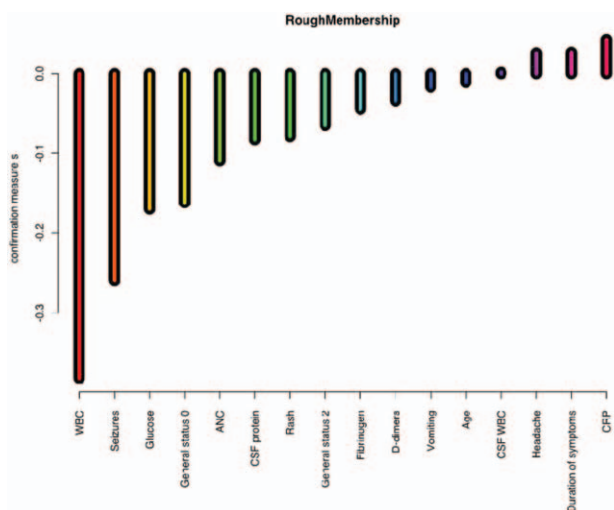

Figure 1. A comparison of different parameters discriminating between bacterial and aseptic meningitis.

Decision rules generated from the data set of our patients suspected of having meningitis (with fever and positive meningeal signs) are as follows:

1. If CRP level is ≥86 mg/L, then the patient has bacterial meningitis (coverage factor 95%).
2. If the number of leukocytes in CSF is ≥4481 μL^{-1}, then the patient has bacterial meningitis (coverage factor 36%).
3. If the patient is in first month of life, then it is bacterial meningitis (coverage factor 82%).
4. If the symptoms last 2 days or less and CRP level is ≥76 mg/L, then the patient has bacterial meningitis (coverage factor 2%).
5. If CRP level is ≤19 mg/L, then the patient has viral meningitis (coverage factor 95%).
6. If CRP level is ≤84 mg/L and patient is 11 months old or above and leukocytes in CSF is ≤1100 μL^{-1}, then the patient has viral meningitis (coverage factor 89%).

3.1. Description of the rules

3.1.1. Rule number 1.
Patients suspected of having meningitis based on clinical symptoms (fever, meningeal signs) with CRP ≥86 mg/L had bacterial meningitis. This rule identified 80 out of 84 patients with bacterial meningitis (95%). The 4 patients not covered had CRP ≤86 mg/L. All patients with CRP of 86 mg/L or higher had bacterial meningitis.

There were no patients with viral meningitis who met these criteria.

Table 4

Usefulness of chosen parameters in predicting bacterial etiology of meningitis.

Parameter	Criterion	Sensitivity	Specificity	+LR	−LR
Serum CRP (mg/L)	>45	98.81	98.44	63.24	0.01
Serum CRP (mg/L)	>80	95.24	98.44	60.95	0.05
Serum CRP (mg/L)	>84	95.24	100.00		0.05
CSF protein (g/L)	>0.96	85.71	90.62	9.14	0.16
CSF glucose (mg/dL)	≤40	61.90	93.75	9.90	0.41
CSF leukocytes (n/μL)	>992	72.62	90.62	7.75	0.30
ANC (1000 μL^{-1})	>6	82.14	87.50	6.57	0.20
Age (in months)	≤74	70.24	79.69	3.46	0.37
Duration of symptoms (days)	≤3	97.62	53.13	2.08	0.04

ANC = absolute neutrophil count, CRP = C-reactive protein, CSF = cerebrospinal fluid, +LR = positive likelihood ratio, −LR = negative likelihood ratio.

3.1.2. Rule number 2. If the number of leukocytes in the CSF is ≥4481 μL^{-1}, the patient with clinical symptoms of meningitis has bacterial meningitis. It covered 30 cases (35.7%) of bacterial meningitis and did not cover any patients with viral meningitis. The additional value of this rule was that it covered 2 cases (out of 4) not covered by rule number 1.

3.1.3. Rule number 3. Suspicion of meningitis in a child within the first month of life, the etiology is assumed to be bacterial. Rule number 3 is based only on the patient's age. In a clinical setting this is reasonable approach: a newborn suspected of a generalized infection, the risk of bacterial etiology is very high, and antibiotics are started immediately. Rule number 3 covered 2 cases of bacterial meningitis (1 of which was not covered by rule number 1 or rule number 2) (2.38%). There were no patients with aseptic meningitis who met these criteria.

3.1.4. Rule number 4. If the symptoms last 2 days or less, and CRP level is ≥76 mg/L, then the patient with clinical signs of meningitis has bacterial meningitis. In other words, when the level of CRP is ≥76 mg/L and the symptoms last no longer than 2 days, the patient is diagnosed as having bacterial meningitis. This rule covered 1 case of bacterial meningitis not covered by rules number 1, 2, or 3. Using all 4 of the aforementioned rules together all patients with bacterial meningitis were identified. There were no patients with viral meningitis who met any of these criteria.

3.1.5. Rule number 5. Patients suspected of having meningitis (fever, meningeal signs) with CRP ≤19 mg/L can be diagnosed with viral meningitis. This rule covered 61 (95%) patients with viral meningitis. There were no patients with bacterial meningitis who met that criterion.

3.1.6. Rule number 6. Patients suspected of having meningitis (fever, meningeal signs) with CRP ≤84 mg/L, with their number of leukocytes in CSF ≤1100, and being no younger than 11 months old can be diagnosed with viral meningitis. This rule covered 57 (89%) patients with viral meningitis. There were no patients with bacterial meningitis who met those criteria. This rule covered 3 patients not covered by rule number 5.

We analyzed 14 attributes, of which only 4 were used to generate these 6 rules, with CRP being the most valuable. Figure 1 shows the classification of the attributes according to their relevance in generating the rules. CRP was shown to be the most effective parameter in distinguishing between viral and bacterial meningitis and was used in 4 of the rules. Symptoms duration was the next most important factor, followed by the number of leukocytes in the CSF. Other parameters proved weaker.

4. Discussion

DRSA analysis was performed on the data set of our patients to generate 6 rules helpful in distinguishing between bacterial and viral meningitis. Four rules (1–4), when applied together, were able to identify all patients with bacterial meningitis, whereas only 2 rules (5–6) were capable of describing all patients with viral meningitis.

Using rules number 1, 3, and 4, disease etiology could be accurately diagnosed before CSF was taken in 83 of the 84 with bacterial meningitis. Before lumbar puncture, using rule number 5 alone, etiology could be established in 95% patients with viral meningitis. The formulated rules cannot be interpreted further. They must keep their original form and cannot be interpreted in the opposite way. They are true only in a full meaning. For example, rule number 1 does not mean: if CRP is <86 mg/L, the patient does not have bacterial meningitis. It can only be applied to a patient meeting all the stated conditions. Only a patient with fever, existing meningeal signs—clinical suspicion of bacterial meningitis and CRP ≥86 mg/L—can be diagnosed with bacterial meningitis using rule number 1. We can diagnose viral meningitis in a patient with fever and positive meningeal signs—clinical suspicion of meningitis and CRP ≤19 mg/L (rule number 4). For patients with CRP between 20 and 85 mg/L, the system generated rules containing more restrictions. We chose parameters traditionally known as capable of discriminating between bacterial and viral meningitis, which are commonly used in many scales.

Positioning the attributes with DRSA methodology helped to show which of them should guide the decision-making process. Attributes having the greatest impact provided satisfactory accuracy for diagnosis, whereas the others could be omitted in constructing decision rules.

We showed in our analysis the important predictive role of CRP, which were greater than results for the CSF analysis. CRP has also been demonstrated in other studies.[26,27] Nigrovic et al reported that a CRP concentration >100 mg/L is a sensitive marker for bacterial meningitis, but lacks specificity.[26,27] Oostenbrink et al proposed a clinical score in which 1 criterion that suggested bacterial infection was a CRP level higher than 50 mg/L.[10] In this study sensitivity for elevated CRP was 86% and specificity 67%. The rules based on CRP are very useful in clinical practice because they enable diagnosis before a lumbar puncture is performed. In a patient suspected of having meningitis with CRP <19 mg/L, according to rule number 5, antibiotic treatment can be postponed until CSF collection in order to increase the validity of a negative CSF culture. This can help in antibiotic stewardship. The decision to not give antibiotics to a child with

meningitis of probable viral etiology, before the culture comes back negative, is very difficult. Many doctors start treatment even if the child is in good condition and viral etiology is highly probable based on the results of general analysis of CSF. Relying only on one's gut feeling is not acceptable currently. Having a reliable tool to support the decision-making process provides a large advantage. We know from the literature that the level of leukocytes in the CSF is also important in diagnosing bacterial meningitis.[28–30] Based on our data to use this as a sole parameter in a patient with suspected bacterial meningitis, the level of leukocytes in the CSF must be $\geq 4481 \ \mu L^{-1}$. Beek et al detected in approximately 90% of bacterial meningitis pleocytosis in the CSF of 100 cells per μL^{-1}.[31] It should be noted that in immunosuppressed patients the pleocytosis in the CSF can be lower, and in almost 5% of immunocompetent children bacterial meningitis can occur without CSF pleocytosis.[30]

We have shown statistically significant differences between patients with bacterial and aseptic meningitis regarding the evaluated parameters. It was confirmed in a conventional way, what is already known from the literature, but any of the single parameters used here can distinguish between bacterial and viral meningitis. Statistical analysis of the existing cases indicates differences between patients. Conclusions drawn in this study cannot be easily translated to future cases.

The disadvantage of classical scaling discussed at the beginning of this paper demonstrates how the conversion of clinical data into numeric values risks losing the primary character of the data. Different parameters are added together as if they were equal, such that the sum of completely different parameters can yield the same results. The obtained results are noninformative, in that they do not show how the diagnosis was made. It discourages the application of this system in therapeutic decisions because it does not give decision-makers the chance to evaluate the independent results. For example, 2 points on the BMS score can be given to a patient with seizure and ANC in peripheral blood higher than $10 \times 10^9 \ L^{-1}$ and in a patient positive upon direct examination of their CSF. While in the first patient an alternative diagnosis can be taken into account, the second patient's diagnosis of bacterial meningitis is more certain.

In this study, we described 148 patients treated as teaching examples for induction algorithm, which differentiates between the etiology of viral and bacterial meningitis and their associations with patient characteristics. Those relations are represented by logical rules, termed decision rules. Representations should be minimized to the number of rules required to cover all cases, and the number of attributes used in each rule should also be minimized. We detected 6 rules in our population that should be useful in the decision-making process of future cases. DRSA supports routine diagnostic process performed by clinicians and its application does not require data conversion. Thus, it preserves its primary character and enables combination of parametric and nonparametric data.

Classification of attributes helps in choosing the most valuable parameters for decision making. Final decision is to be made by doctors, not computers; however, this algorithm helps doctors to make sense of discrepant data and differentiate between similar diseases. By generating rules based on past cases reliable disease attributes are considered and plugged into the algorithm. Rules can also be used in a patient with incomplete data. For such a patient, you would apply a rule where you have all of the remaining data. Rules are characterized by a high degree of certainty. All results were obtained in a 5-fold cross validation experiment that was repeated 10 to 100 times.

Knowing that DRSA is a valuable diagnostic tool one could ask why it is not use more widely. The answer is simple: it is technically complicated. Before you generate the set of rules and use them in clinical practice, you must teach the system. To prepare the data set for analysis, doctors must be aware of the nature of this analysis, which is completely different from conventional statistics. Thus, the first problem is choosing right medical problem to apply this tool. DRSA is useful when the diagnosis is based on several parameters such as bacterial versus viral pneumonia or gastroenteritis.[17,20] It helps to detect the most useful attributes, which in turn limits costs of studies to be performed. This method can also evaluate the prognostic value of given factors. No previous analyses of meningitis cases have been performed with this method. However, we are ready to cooperate with other centers to increase our database of patients with meningitis.

Due to the decreasing number of bacterial meningitis cases, it will be difficult to build the clinical experience among doctors. Intelligent Systems Supporting Clinical Decisions help by using experience based on previous patients supported in the literature. Such tools offer a complex analysis of many clinical data—sustaining their individual character.

Decision rules generated by DRSA methodology constitute a novel tool to support clinical reasoning.[21] We let the system learn from our cases to distinguish between bacterial and viral meningitis in order to help making decisions on unseen cases. The rules induced by DRSA are nonredundant summarization of the data.[22] Strong decision rules with large values of Bayesian confirmation provide useful information about relevant cause-effect relationships discovered in the analyzed meningitis data.

Using the theory of rough classification, we established the minimum set of attributes significant for high-quality classification of patients and consequently observed indications for starting or withholding treatment in a patient with meningitis in terms of these attributes. This is new set of rules, which, although intuitively anticipated by some clinicians, has not been formally demonstrated until now.

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