# 20.

# Integration of Analytical and Diagnostic Concepts by means of Expert Systems – Practical Aplication in the Clinical Laboratory

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## Introduction

The evolutionary events that have taken place within the clinical laboratory during the past two decades are very familiar to everybody. There is the growing complexity and the variety of the tests we are performing. There is the continually increasing workload and the need to shorten turn-around-times, as clinicians want their results more and more rapidly. There are the increasing quality demands that are put on our testing. There are stringent regulatory and accreditation demands. There are also budgetary restrictions and all these things have forced us to automate a lot of our repetitive tasks.

The introduction of artificial intelligence (AI) has gained an important place in this automation process thanks to its key features: (1) the ability to accumulate knowledge; (2) the ability to apply this knowledge in a standardized and reproducible way; and (3) the ability to deal with incomplete and imprecise information. While the first two features can be dealt with by an algorithmic approach, the third cannot and AI is required. AI wants to process knowledge (**figure 1**).

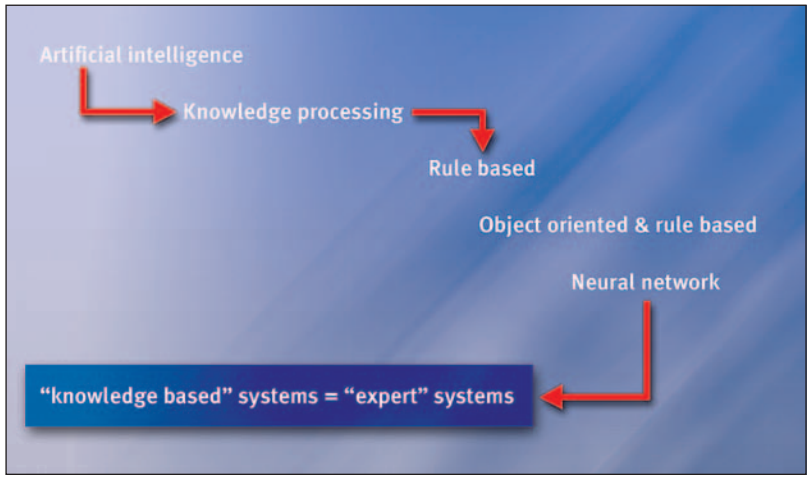


***Figure 1***
*Artificial intelligence; the processing of knowledge.*

Different parts of the clinical laboratory can benefit from implementation of knowledge based systems starting with the guidance and control of test ordering for the clinician and proceeding to workflow analysis, technical validation of test results and interpretation of QC data within the analytical laboratory, and finally medical validation of protocols and clinical interpretation of test results. The first two parts, guidance and control of test ordering and workflow analysis, while very intriguing, fall beyond the scope of this presentation. The remaining parts such as technical validation, interpretation of QC data, medical validation and clinical interpretation very definitely fall within the remit. These are the processes that require to be applied and integrated within the modern laboratory.

A mission statement enunciated by the American Association of Clinical Chemists [**1**] that applies to all specialists in Laboratory Medicine, not just Clinical Chemists states:

'... should become *consultants* and *educators* in the medical community.
They should be advisors in *test selection, test logic* and *test interpretation*.
They should serve as a resource for health professionals in the *appropriate use of laboratory tests* with a focus on *improved patient outcome*.'

The role and responsibility, therefore, goes much deeper than merely producing analytical data.

## Areas for Implementation

*Technical validation:* Technical validation of test results is normally performed by the laboratory technicians while taking into account error flags and other codes produced by the instrument, QC results and previous patient results. But why is it necessary to use AI to achieve this? As the turn-around-time should be kept as short as possible and only technically validated results should be sent to the Laboratory Information System (LIS), technical validation is best performed as soon as the result is generated. When 'manually' performed by technicians, this is a time consuming procedure that is not easily standardised. Technical validation can be automated and standardised by implementing rule-based expertise that takes care of dilutions and reflex testing when certain preset conditions are fulfilled. Most modern instruments now have built-in facilities for automatic dilution, re-testing, reflex testing and specimen routing on the automated transport devices on some of the larger systems.

*Interpretation of QC data:* For most routine parameters in our laboratory we have to run at least two levels of control materials, at least twice a day. Why use artificial intelligence to do this? As evaluation of QC data is an essential part of the process by which patient test results can be validated this evaluation should be performed as soon as QC test results are available. Even with the help of the QC programs installed on individual instruments, a correct interpretation of all QC results and the procedures that have to be followed when appropriate actions are needed, is extremely time consuming. By not using AI solutions, we place a heavy burden on the technician who has to interpret the data particularly when remedial actions require to be taken.

*Medical validation of protocols:* Pathologists perform medical validation of patient test results using their expertise that takes into account previous test results, plausibility, mutual correlation of test results and quality control results. Why use AI? Manual medical validation of thousands of laboratory test results per day, either on paper or on a computer screen, is a very tedious and demanding task and it cannot be guaranteed that this task will be performed as diligently at 6 pm as it had been at 9 am in the morning. There is also a need for standardisation of

medical validation procedures because we do not always validate the protocols of our patients the same way. There also is a need to select only those protocols that warrant special attention. We do not wish to dwell on matters that are logical and do not need our attention.

## Example of Integration

The procedure in our laboratory provides a practical illustration of this integration (**figure 2**). In the laboratory we have a MOLIS laboratory information system. The LIS sends orders to the various analytical instruments and manual work stations which, in turn, return results, including those from point-of-care testing sites for technical validation either by PGP 5 (PGP) or manually. These technically validated data are returned to the LIS from where they are sent to 'VALAB' [**2**] for medical validation. Clinicians have access to patient results as soon as they are sent to the LIS. As long as these results are not medically validated they are put between brackets in the result server (C2M). The acronym 'VALAB' stands for 'Validation Automatique en Laboratoire', (French for Automatic Validation in a Laboratory), a knowledge-based system developed by the company EREMS (Flourens, France) for performing an automatic medical validation (or invalidation) of the medical analyses undertaken in a laboratory. Using VALAB decreases the time between arrival of the samples to be analysed and departure of the validated results. Secondly, it increases the reliability of the biological validation because a smaller workload is imposed on the pathologists, who can consequently focus their work on the validation of difficult cases only. When all patient results are accepted for a particular patient the whole protocol is accepted. When one of the tests does not pass automated medical validation the pathologist has to review and validate it.

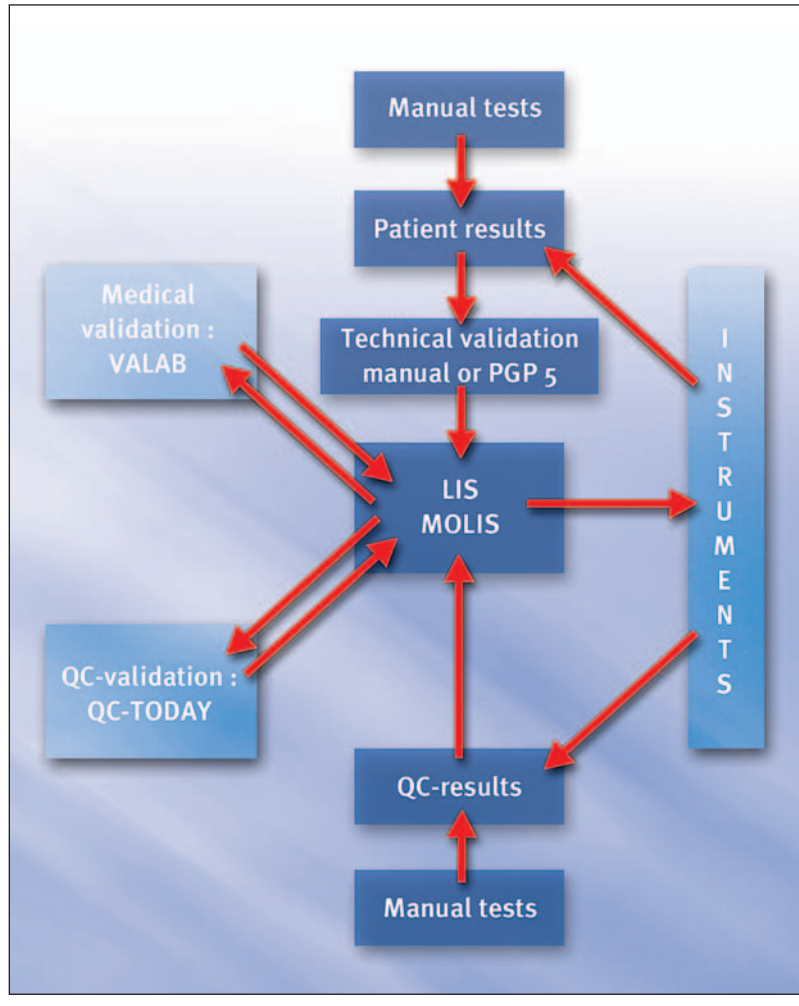


***Figure 2***
*Functional integration in the clinical laboratory.*

QC results are also sent to the LIS and from there to another expert system called QC-TODAY, which is developed by Instrumentation Laboratories This expert system looks at QC data on-line (**figure 3**). When the QC is satisfactory, QC-TODAY sends a message to the LIS and all the patient data that have been performed between two good QC results (the guaranteed period) are automatically accepted and designated by a flag – 'A'. When a patient result for the same parameter is accepted in VALAB, the patient result gets a flag 'V' validated. When a result has both an 'A' and a 'V' flag, it is considered as a medically validated result (brackets in the result server disappear). When a result is not accepted by VALAB, the patient result has to be reviewed by the pathologist who accepts or rejects the result. When the pathologist says 'yes' the result gets a 'V' flag; when the pathologists says 'no' the result is placed on hold ('in control' or 'R'). When the QC results for a certain parameter are not accepted, the technician in the QC-cell can decide, based on predefined criteria, whether this result should be manually accepted (logged by the system) or whether it should be rejected and get a flag 'R'. In **figure 4** it should be noted that there are two periods in which QC is OK and patient

results are accepted, followed by a period when QC is not OK. This is a non-guaranteed period during which patient results can be put 'in control'. In the latter case, the LIS prints a work list of all the patient samples for which the problem parameter was performed on a particular machine during the non-guaranteed period, so that these may be repeated.

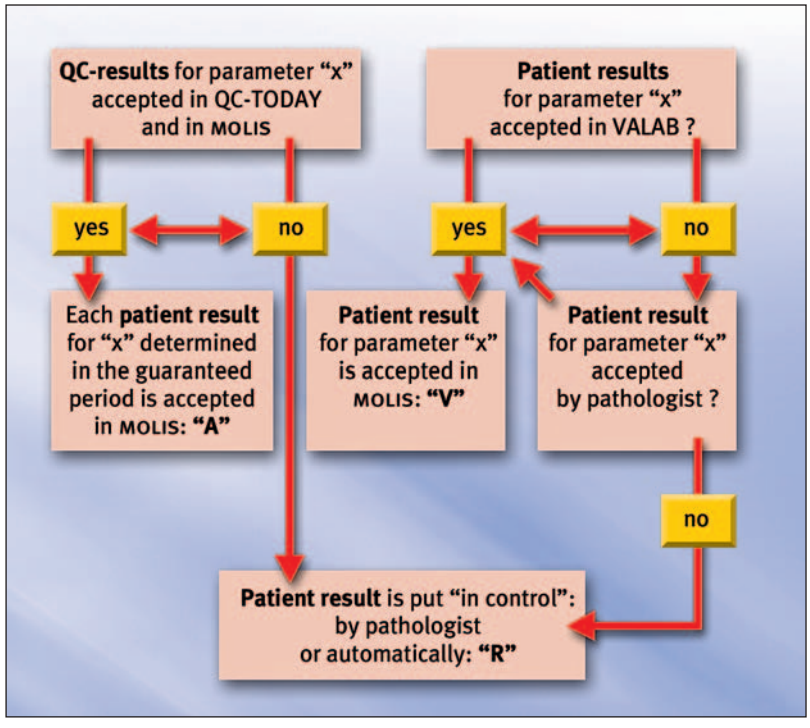


***Figure 3***
*QC and patient result validation*

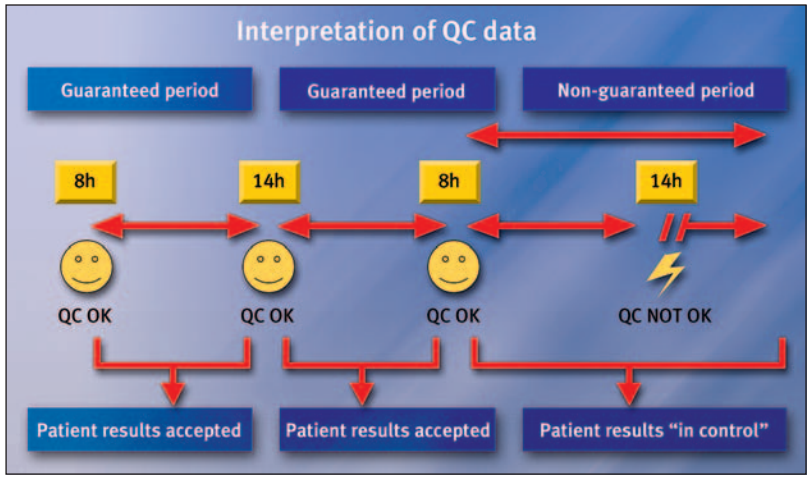


***Figure 4***
*Interpretation of QC data.*

## Clinical Interpretation of Test Result

An important aspect of the pathologist's participation in the patient care process is the opportunity to assist clinicians in the interpretation of laboratory reports. Why use artificial intelligence to do this? There are at least three reasons. First, due to the present variety of tests and rapidly increasing medical knowledge, not every institution can have 'in-house' experts covering all domains in laboratory medicine. Secondly, if an expert leaves the institution, his/her specific knowledge will disappear as well. Finally, even for experts, there is no guarantee that their knowledge will be used to solve medical problems in the same standardized and reproducible way. With increasing interest in evidence-based medicine (defined as a conscious, explicit and judicious use of current best evidence in making decisions about the care of individual patients) I think that expert systems, when they are used well, are ideal tools to implement this philosophy, both in the clinic and in the laboratory. In fact, it seems likely that expert systems can form a direct link between the pathologist and the clinician. However an effective strategy is required to make these systems acceptable in a clinical setting.

An example of a tried and tested rule-based system follows. This is Pro-MD; a rule based expert system shell, originally written in Prolog by Pohl and Trendelenburg [**3**]. Pro-MD has been used in my laboratory to develop two decision support systems: (1) the clinical interpretation of alkaline phosphatase isoenzymes patterns written using the DOS version of Pro-MD [**4**] and unilaterally linked to the LIS and (2) clinical interpretation of amylase isoenzymes patterns written using the Windows version of Pro-MD in a stand-alone system.

Stand-alone systems have drawbacks. When attempting to introduce these systems into the laboratories of colleagues, they were assessed as being too time-consuming and error prone as all the data had to be introduced by hand. A further drawback is that the interpretation of the protocol has to be attached to the original laboratory protocol. Unilaterally coupled systems, on the other hand, are capable of downloading data, but interpretation still has to be attached to the laboratory protocol.

There is a need for bilateral communication between the expert system and the LIS. We really wanted such a system to replace our Prolog. The solution was found with the development of j.MD, a system developed in a Java environment by Trendelenburg and Wormek. The β-version has been used to reprogram the expert systems for the interpretation of alkaline phosphatase and amylase isoenzymes patterns in my laboratory. So, a third layer has been added to the system as illustrated in **figure 5**, namely clinical interpretation by j.MD.

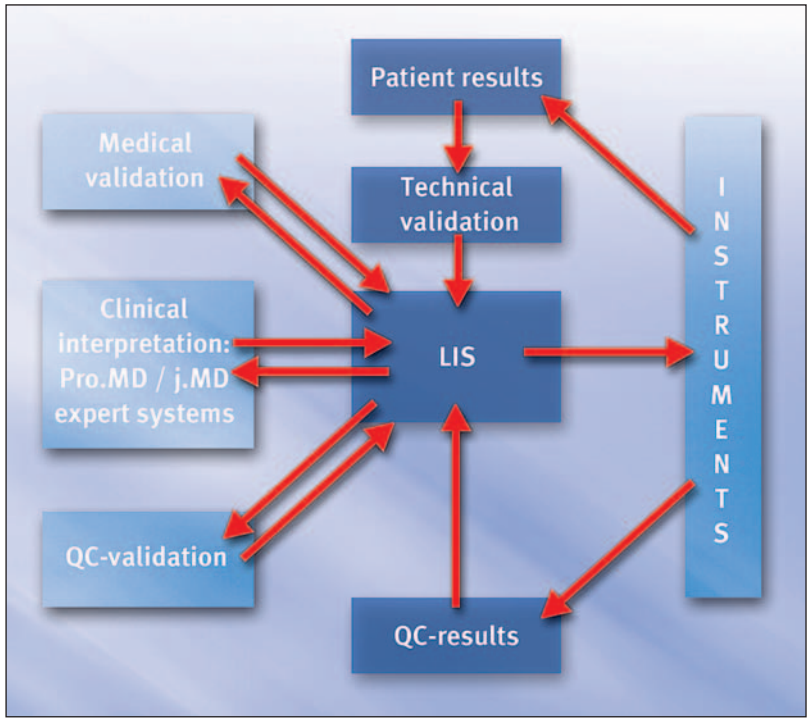


***Figure 5***
*The addition of j.MD clinical interpretation into the functional integration.*

## j.MD

j.MD is a Java-based expert system shell. A shell is the environment on to which an expert system can be developed. It has a TCP/IP client server architecture and data and results are transmitted as extensible mark-up language (XML) documents. Test results are identified by their LOINC (Logical Observation Identifier and Naming Convention) codes. The knowledge base and objects are created through wizards and reports are generated from author-defined text patterns. The knowledge base is defined through rules, concepts and parameters (**figure 6**). Parameters can be either measured or calculated. Measured parameters have properties and one of these properties is the LOINC code. LOINC codes are unique identifiers of clinical laboratory tests and were originally published by the Regenstrief Institute, Idianapolis (www.loinc.org). These codes are integrated into the j.MD software by means of a database viewer. **Figure 7** provides an example of the database viewer for haemoglobin methods; the arrow indicates the method selected; the subsequent screen shots (**figures 8–11**) illustrate the sectional construction of the expert system.

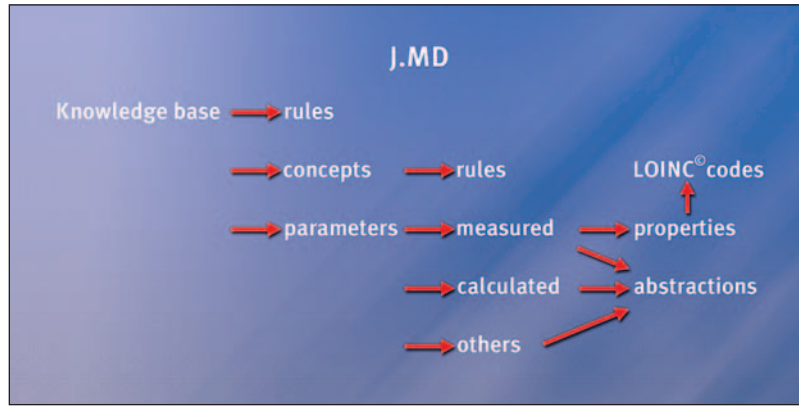


***Figure 6***
*j.md. The knowledge base is defined through rules, concepts and parameters.*

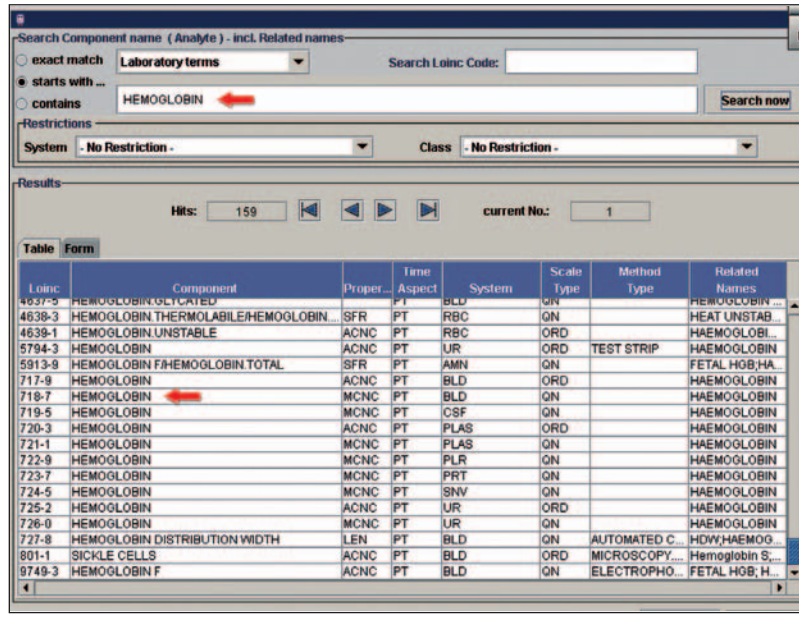


***Figure 7***
*Database viewer for haemoglobin methods, the arrow indicating the method selected.*

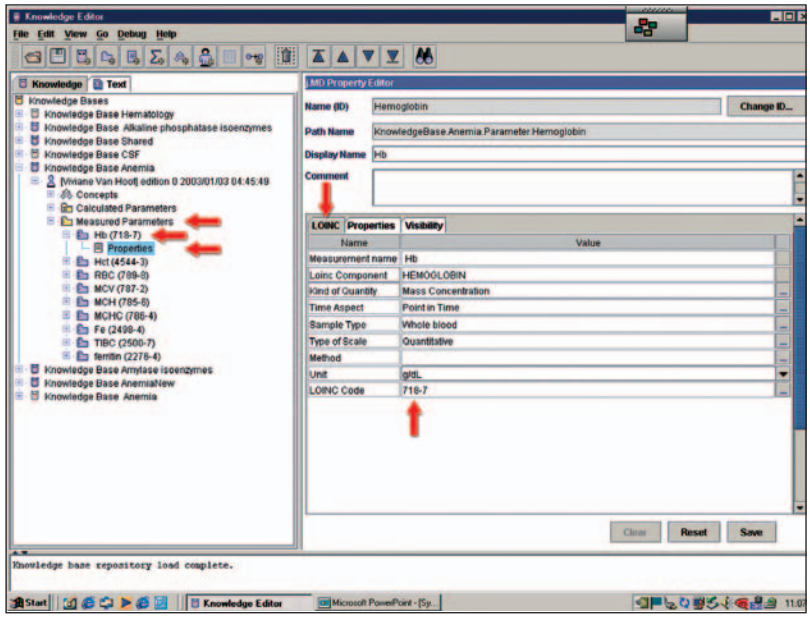


***Figure 8***
*j.MD Property Editor.*

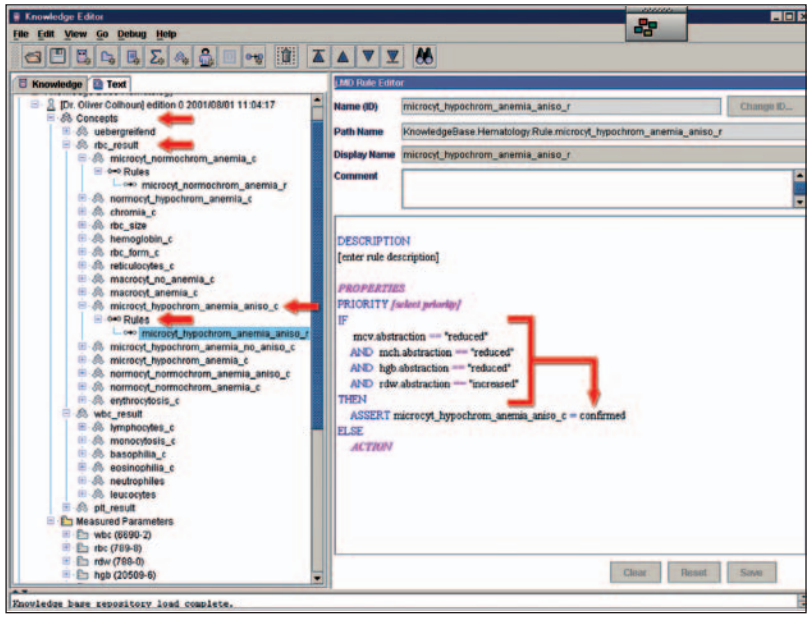


***Figure 9***
*j.MD Rule Editor.*

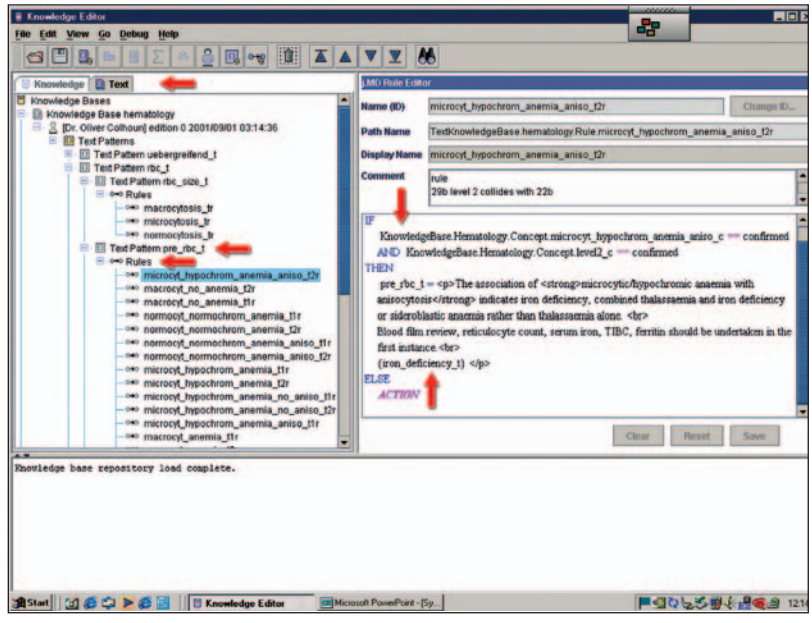


***Figure 10***
*j.MD Rule Editor. Example of rule with interpretation and recommendations.*

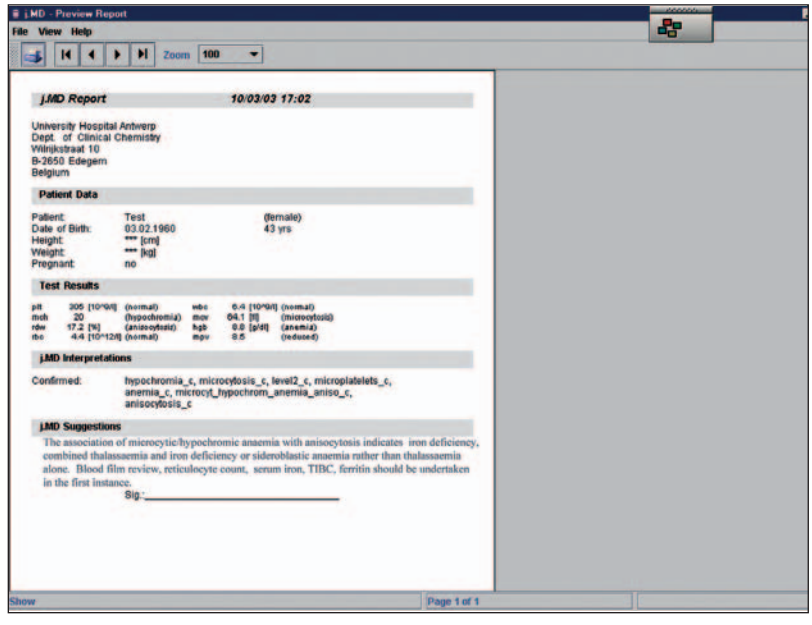


***Figure 11***
*j.MD example of report which includes demographics, test results, j.MD interpretations and suggestions for further actions.*

It is, of course, necessary to have the system accepted in a clinical setting. How can this be achieved? In the first place the expert system must be developed in close association with the clinicians who will be using it. There are three different stages at which the clinicians must be involved, namely (1) during the implementation of the knowledge, (2) when testing the system which can be a very tedious process and (3) when updating the system. It is also necessary to counteract an intuitive mistrust of black box technologies. This can be achieved by incorporating an easily accessible explanation module within the expert system shell that explains the reasoning behind the development of the rules. Not only does this serve to convince the user but it also provides an excellent educational tool.

## Managing and controlling the expertise

Edwards *et al* [**5**] make a very important point when identifying a fundamental difference between human error and computer error that make the latter infinitely more dangerous. When confronted with unfamiliar data, humans will modify their behaviour accordingly and will be prudent. The expert system, on the other hand, when confronted with unfamiliar data will ignore anything not explicitly represented in its rules. The result will be a misclassification error. For this reason every report produced by an expert system should be read by the pathologist.

Data on 'overall' performance of these systems, and statements such as 'good experimental agreement with experts' offer little reassurance to clinicians who have to make decisions for individual patients. There are tools available, however, to design effective monitoring schemes that result in a quantifiable level of confidence in an expert system's current level of performance [**6,7**].

## Legal Liability

Legal liability is another important issue. In this context it is important to appreciate that there is a fundamental difference between types of expert systems. The 'problem solving' expert system reaches a conclusion upon which the user is required to act. An example of this type of expert system would be one that calculates fluid and electrolyte balances required for continuous haemofiltration with haemodialysis and makes use of information received from the patient. On this basis, the system decides if the filtrate should be increased or decreased. This system has taken the responsibility for making a decision by providing a definite answer. The decision could be carried out either automatically or by a non-expert, who just follows the instructions. A second type is the 'problem formulating' or 'decision support' expert system which presents a range of options or probable diagnoses from which the user has to select the one which is most appropriate under the circumstances. The final decision is left with the user albeit that the choice is made from a selection provided by the system. The user, of course, must be a suitably qualified person to interpret the conclusion or select the most appropriate option.

There are also many parties involved here including the creator or developer, the knowledge engineer, the system designer, the expert who provides the knowledge, the supplier or vendor, the purchaser and the end-user. Each has his/her responsibility. The patient, too, may have a responsibility when an expert system becomes available through a website. This last will increase as more and more patients make use of such freely accessible systems.

Day [**8**] has made helpful suggestions in his publication as follows:
'The expert system of the type which is not designed to produce a definite answer, is a true decision support device equivalent to an interactive text book.'
'The persons under whose care and control the patient has been placed have the ability to accept or reject the expert system's conclusions as either being in accordance with their own assessment or not.'
'This means that the responsibility and therefore accountability, and potential liability of making the decision rests with the decision-maker, namely the doctor, or some other suitably qualified user of the system.'

When offering interpretation by expert system it is advisable to include a disclaimer. The 'disclaimer' which accompanies interpretation by the decision support systems for the clinical interpretation of alkaline phosphatase and amylase isoenzyme patterns is: 'The purpose of this expert system is to assist the clinicians in the exercise of their independent professional judgement, in view of the clinical information available for their patients. Although the knowledge contained in this expert system has been obtained from highly reputable sources and is believed to be accurate in accordance with the currently available information, the author assumes no liability in connection with the use of any specific information contained herein.'

## Conclusions

Expert systems have a great potential for benefit in the routine clinical laboratory, whether by automating and standardizing routine and repetitive tasks and procedures, or by assisting in the practical application and dissemination of specialized knowledge. To enhance user friendliness and efficiency, stand-alone expert systems are gradually abandoned, as they become uni- and bidirectionally connected to, and eventually embedded within, the existing laboratory information systems. Failure or success of these systems depends heavily on their continuous management and control and on the communication between end users, domain experts, knowledge engineers and LIS providers.

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