XE-5000 Case Manager – combining laboratory information with clinical knowledge

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The XE-5000 Case Manager embodies a new concept in diagnostics – one that combines proven Sysmex fluorescence flow cytometry with case-related clinical data. The clinical value of the large number of new analytical parameters has been demonstrated convincingly in recent years in a wide variety of publications. However, a great deal of clinical and laboratory-based haematological background knowledge and considerable time investment is required in order to interpret these parameters appropriately, and thus to be of real utility in diagnostics and treatment monitoring.

In daily clinical practice, the treating physician is flooded by the vast amount of available lab parameters and data from which the results relevant to each particular medical case need to be selected. A compounding factor is that the diagnostic significance of new analytical parameters, as well as their value in monitoring response to treatment, is not widely known.

**The benefits of the Case Manager**

The core function of the XE-5000 Case Manager is rapid recognition of parameter combinations that are characteristic of certain diseases and disease entities, in order to reduce the growing complexity involved in diagnostics. Individual values are not considered in isolation, but instead are processed through a diagnostic rule set together with other haematology parameters. Whenever all the conditions of one of the rules should be satisfied, the Case Manager will trigger an alert (see Fig. 2) indicating that the pattern of results of the patient sample matches that known to be specific for a particular disease entity. The Case Manager will then display a clinical example of a known case (see Fig. 3) thereby offering assistance in the diagnostic process. The Case Manager is not a program designed to generate diagnoses autonomously, but rather serves to facilitate and speed up diagnostics.
The diagnostic set of rules used by the Case Manager focuses on specificity, showing values of 95% or higher. This means that the incidence of false positive alerts will be very low, positively affecting the positive predictive value, a measure for the probability with which a certain disease entity is actually present. In this way the laboratory can provide targeted information and speed up the diagnosis without inundating the clinician with data.

In routine operation, the Case Manager runs in the background, without interfering with the laboratory workflow. Using the ‘Case Manager Client’ function, identified cases can be used to facilitate rapid diagnosis on any chosen computer and at any convenient time.

Fig. 2 XE-5000 result screen displaying the Case Manager alert.

Fig. 3 Case Manager screen displaying the initial page of the example case which was triggered by the result constellation of a particular sample.

Fig. 4 Besides providing parameter results, the XE-5000 Case Manager may also point to specific clinical findings. Together with the patient results they could potentially speed up diagnosis.
What does the Case Manager offer to the patient?

The Case Manager supports rapid diagnosis and therefore early initiation of treatment. Sometimes seemingly ‘minor’ abnormalities found in lab results can be of crucial significance for the patient’s treatment. For example, in a patient who arrives at the clinic as an emergency case with extreme thrombocytopenia, a cluster of symptoms that includes reticulocytosis, elevated immature platelet fraction (IPF), the presence of fragments and other blood count parameters, may be recognised by the Case Manager as typical for thrombotic thrombocytopenic purpura (TTP). The laboratory can then inform the treating physician of this suspicion, thereby saving valuable time as TTP is a life threatening condition with a high mortality rate.

What does the Case Manager offer to the clinician?

Suspected diagnoses can be confirmed promptly, since automatically recognised clusters of symptoms make it possible to indicate specific clinical pictures. The clinician can learn about new parameters in a clinical context and is able to interpret them rapidly. At the same time, new scientific findings enter continually into the Case Manager’s set of rules. Based on clear case examples, the clinician can become familiar with the entire range of analytical possibilities offered by automated haematology. This happens in a way that is not only comprehensible, but equally importantly is relevant to daily practice.

What does the Case Manager offer to the laboratory physician?

Just for anaemia diagnosis alone, in addition to the classic blood count, new parameters such as e.g. RET-H, Delta-H, RPI, fragmented red cells, %MicroR and %MacroR, %HYPO-H and %HYPER-H, are available. The Case Manager links these data together, analyses them and indicates the clinical value of the new parameters based on concrete case examples.
What does the Case Manager offer to laboratory staff?

The clinical value of the ‘extended’ parameters and the clinical pictures associated with them are explained in context and can be used for continuing professional development. Each case is subdivided into the sections Summary, Example case, Differential diagnosis, Laboratory results, Underlying disease, Explanation and Literature. In all chapters the focus is on the clinical value of the information provided. As a result, the diagnostic process becomes more comprehensible, and technical expertise is continually expanded.

The case studies for the Case Manager

The latest generation of the Case Manager encompasses several important clinical pictures involving leukopoiesis, erythropoiesis and thrombopoiesis. In particular, it also takes into account clinical pictures that sometimes are difficult to separate in practice. This applies, for example, to cases of iron deficiency anaemia in comparison with thalassaemia or a myelodysplastic syndrome. The Case Manager offers 27 well-documented case descriptions including several which, despite apparently similar laboratory results, lead to completely different diagnoses. Inter alia these case descriptions help especially in these difficult-to-differentiate cases, to achieve faster assignment of the case to the right differential diagnostic track. Several examples may be useful as illustrations:
Hereditary spherocytosis (HS)
In some cases, like in hereditary spherocytosis, specific aspects of the automated measurement facilitate the diagnosis: A specific feature lies in the staining characteristics of reticulocytes. Although the HGB may be normal, red blood cells with a membrane defect may appear microcytic and are measured as such. Patients with differing levels of severity of hereditary spherocytosis exhibit varying degrees of microcytic red cells that are, however, not hypochromic. In many cases, this can be detected by the Case Manager, which differentiates HS from other microcytic conditions such as iron deficiency anaemia, functional iron deficiency or thalassaemia with the help of a specific index (%MicroR/%HYPO-H) in combination with information about the reticulocytes and their various maturity grades.

Disseminated intravascular coagulopathy (DIC) in malaria infections
The reticulocyte maturity information is additionally helpful in the identification of Plasmodium falciparum malaria infection and its sequelae (e.g. disseminated intravascular coagulopathy (DIC)). In the Case Manager, identification of both HS and malaria is based on the experience that a greatly elevated reticulocyte count in combination with a decreased immature reticulocyte fraction (IRF) is physiologically implausible. The presence of intracellular malaria parasites will manifest as an elevated reticulocyte level. The parasitic nucleic acids of Plasmodium falciparum are stained, thus allowing red blood cells to appear in the scattergram as ‘more mature’ reticulocytes. The total reticulocyte number and the low-fluorescence reticulocyte (LFR) value are elevated, whereas the immature reticulocyte fraction is not elevated. The additional parameters described above permit further diagnostic differentiation of this phenomenon.

Myelodysplastic syndromes
No matter how different the various subtypes of myelodysplastic syndrome may be, cases of dysplasia share one common thing: reduced neutrophil granularity, which the XE-5000 can detect (the parameter NEUT-X). When this information is linked with other sets of haematological parameters, more detailed classification of the MDS subtype may be possible in some cases. True, not every MDS that occurs in a hospital over the course of time will be identifiable with haematological parameters alone. Even so, the Case Manager’s example cases provide suggestions pointing to e.g. chronic myelomonocytic leukaemias (CMML), an atypical chronic myeloid leukaemia (aCML) or an acute erythroid leukaemia with a very high specificity of over 95%. Such an indication can speed up the initiation of more directed investigations, and thus contribute to speedy diagnosis of these conditions.
Haemolytic anaemias
Certain clinical conditions are extremely time-critical for the patient and must be diagnosed promptly, in order to begin life-saving treatment without delay. This includes several of the haemolytic anaemias, for example microangiopathic haemolytic anaemia (MAHA). One relevant example one can mention here is TTP, which, just like acute immune thrombocytopenic purpura (AITP), can present with marked thrombocytopenia. Whereas TTP often requires immediate plasma replacement, in AITP immediate treatment is not always necessary. The presence of fragments, which may occur in MAHA, for example in TTP, is a critical diagnostic indication which is utilised by the Case Manager.

Summary
The Case Manager can help pave the way for seamless communication in the clinical domain and for engaging the laboratory as an active partner in serving the patient.

- The Case Manager can support faster diagnosis, and initiation of appropriate treatment, where relevant.
- Evidence in support of suspected diagnoses can be provided more promptly, since automatically recognised clusters of symptoms make it possible to indicate specific clinical pictures.
- The laboratory can support the diagnosis rapidly and specifically in difficult cases without additional costs and reduce the flood of data for the clinician.
- The clinical value of the extended parameters and the clinical pictures implied by them are explained in context and can be used for continuing professional development.
Literature


