Quantitative and qualitative monitoring of erythropoiesis with RET-H_e – even on XE-2100 and XT-2000i

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Quantitative and qualitative monitoring of erythropoiesis – the basis for clinical diagnostics and decision making

Detection of functional iron deficiency is a challenging task. Iron deficiency is a major but highly underestimated health problem worldwide, which in the long run can lead to iron deficiency anaemia and impaired erythropoiesis. Assessment of erythropoietic activity is therefore of prime importance in anaemia diagnostics.

Conventional biochemical markers of iron status, such as ferritin or transferrin, are influenced by an acute phase response or by clinical conditions like chronic inflammation, cancer, or endstage renal failure. It is in exactly these cases that functional iron deficiency may occur when sufficient iron is in the body stores but cannot be made available for erythropoiesis.

The classical haematological parameters derived from the CBC give no information about newly produced red cells, the reticulocytes. Since red blood cells (RBC) have a lifespan of about 120 days, RBC parameters referring to all RBC (mature RBC and reticulocytes) represent a time averaged value only. Consequently, parameters like MCV and MCH, or percentage of hypochromic RBC will only indicate a change in erythropoietic activity at an advanced stage of iron deficiency. Likewise under therapy, the same RBC parameters are the last to display erythropoietic recovery. This may become particularly critical when a quick detection of successful or unsuccessful treatment is needed. Looking at reticulocyte parameters rather than total RBC is therefore highly advisable in efficient anaemia diagnosis and therapy monitoring.

Quantitative and qualitative reticulocyte information on XT-2000i and XE-2100

The XT-2000i and XE-2100 determine the absolute reticulocyte count by means of fluorescence flow cytometry. Additionally, they provide the parameter ‘IRF’, the immature reticulocyte fraction, reflecting the proportion of the youngest reticulocyte populations. Thus, IRF gives an excellent view of the erythropoietic activity of the bone marrow as a quantitative parameter. However, it gives no information on the haemoglobinisation, i. e. the ‘quality’ of newly formed red blood cells. This is done now by the parameter RET-H_e with the XE/XT-Series instruments if these are equipped with the (optional) RET Master software. RET-H_e represents the mean haemoglobin content of the reticulocytes.

For many years RET-H_e has been shown to be highly useful in monitoring intravenous iron therapy and administration of erythropoietin. In classical as well as in functional iron deficiency RET-H_e values are low. Under successful therapy RET-H_e values are expected to rise after only a few days; and this parameter is not influenced by the presence or absence of inflammation. Likewise, prognosis of the onset of anaemia or worsening anaemic conditions is possible with RET-H_e being among the first indicators (see References).

It may also serve as an inexpensive screening parameter with a high predictive value for iron deficiency, e. g. in infants. The information on haemoglobinisation is provided quickly, easily and at low cost simply by selecting the RET profile of the instrument.

With the introduction of XT-2000i and XE-RET Master Sysmex once again follows its successful and well-established X-Class concept to provide clinically useful parameters on analysers designed for smaller workloads, such as the XT-series, as well as the larger XE-series. Since the introduction, the clinical usefulness of the extended reticulocyte parameters have been widely appreciated by its many users.

Sysmex XT-2000i and XE-RET Master

RET-H_e derives from forward scattered light signals measured in the reticulocyte channel. Since these signals correlate strongly with the haemoglobin content of the reticulocytes, they are used to determine the average 'reticulocyte haemoglobin equivalent' (RET-H_e) reported in pg.

The XT-2000i and XE-RET Master software completely integrates itself into the existing data management software of the XT-2000i and XE-2100. For every test order for the measurement of any RET parameter, the RET-H_e value is displayed automatically together with other reticulocyte parameters. The cumulative data display in particular is of assistance in patient monitoring. User customisation of displays is also possible. The RET-H_e results can also be transmitted to the Host computer and/or a printer.

When using the XT-2000i and XE-RET Master, the RET-H_e parameter will be included in the comprehensive quality control system based on Sysmex's QC material *e*-Check (XE). The quality control spectrum for RET-H_e is complemented by the 'XbarM' moving calculation program based on fresh patient blood.

The RET Master additionally provides several research parameters: RBC-H_e, Delta-H_e, RET-Y, RBC-Y, IRF-Y, FRC#, FRC% (fragmented red cells) and RPI. First studies on RBC-H_e (derived from the numerical parameter RBC-Y) suggest its usefulness in the differential diagnosis between iron deficiency anaemia and anaemia of chronic disease (References 1+2).

Delta-H_e (D-H_e) is the difference between the average haemoglobin equivalents for red blood cells and reticulocytes. It is a sensitive indicator for changes in the haemoglobinisation of reticulocytes and likely to be of even more prognostic value than RET-H_e.

Another useful haematological parameter known from the literature is RPI (reticulocyte production index), which is also available with the XT-2000i and XE-RET Master. It is a calculated value which considers reticulocyte as well as haematocrit values and can serve as an indicator for any change in red cell production. It may therefore permit early detection for example of an aplastic crisis.

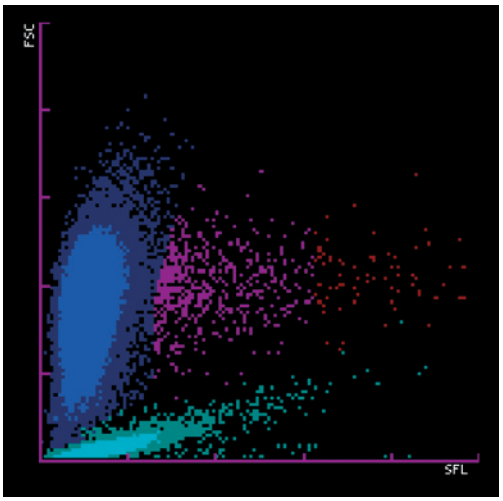

Fig. 1 *View of the RET scattergram of XT-2000i in a case of severe hypochromic anaemia. The reticulocyte haemoglobin equivalent (RET-H_e) which gives information on haemoglobinisation during erythropoiesis in real time shows decreased values. This parameter is a sensitive, early indicator if and when adequate haemoglobinisation of the erythrocytes restarts. It increases as haemoglobinisation improves.*

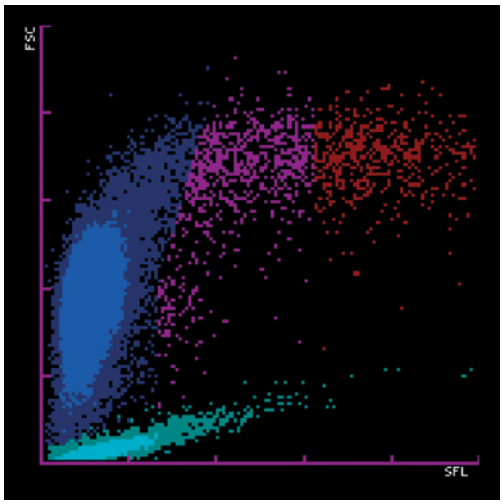

Fig. 2 *Three days after i.v. iron and erythropoietin substitution. Not only the concentration of reticulocytes, but also the average reticulocyte haemoglobin content has increased, as can be seen in the RET scattergram from the upward shift of the reticulocyte clusters, whereas the erythrocyte cluster has not changed substantially. Significant changes in erythrocyte count and haemoglobin value in this patient were only detected 6 days after start of therapy, demonstrating that RET-H_e can detect the start of the bone marrow response much earlier.*

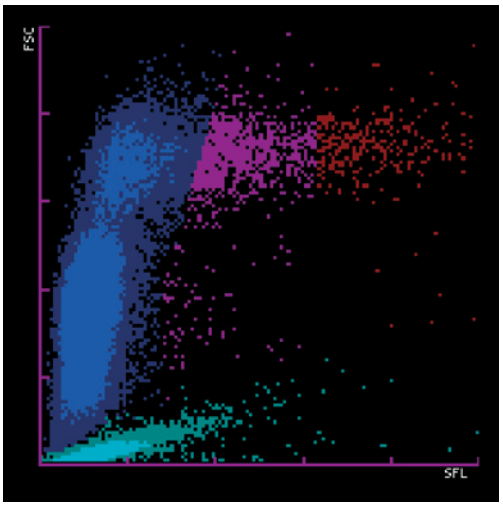

Fig. 3 *Already after three days therapy, recovery from anaemia to normal had been prognosed. As therapy went on this was confirmed after 6 days also by standard red cell parameters and can be seen here from a second red cell population in the RET scattergram revealing RBC of sufficient haemoglobinisation.*

The determination of red blood cell fragmentation in peripheral blood is useful for accurate diagnosis and follow-up of thrombotic microangiopathies. The XT-2000i and XE-RET Master display the research parameter FRC as an absolute count (#) and as percentage (%) of the RBC count and provide sensitive determination of fragmented red cells with increased precision compared to the manual method (Reference 5).

The flexibility of the XT- and XE-PRO software in conjunction with the capabilities of XT-and XE-series' core technology, fluorescence flow cytometry, allow development and addition of new reportable parameters continuously during the lifetime of the analyser. Because the XT-2000i and XE-RET Master is available as a separate, optional software module, all XT-2000i and XE-2100 users of today can benefit from its clinical utility simply by having the software installed.

References

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Sysmex Europe GmbH
Bornbarch 1, 22848 Norderstedt, Germany, Phone +49 40 52726-0 · Fax +49 40 52726-100 · info@sysmex-europe.com · **www.sysmex-europe.com**
Please find your local Sysmex representative address under www.sysmex-europe.com