Date: August 2020
Subject: Literature List – Red Blood Cells
Issued by: Scientific Customer Services
Number: 200810
Note: Whether references are given in British or American English depends on the original.

New entries are highlighted by this icon.
Table of contents

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>3</td>
</tr>
<tr>
<td>RET/ IRF</td>
<td>9</td>
</tr>
<tr>
<td>RET-$H_e$ / RBC-$H_e$</td>
<td>10</td>
</tr>
<tr>
<td>HYPO-$H_e$ / HYPER-$H_e$ / MicroR / MacroR</td>
<td>18</td>
</tr>
<tr>
<td>NRBC</td>
<td>20</td>
</tr>
<tr>
<td>FRC</td>
<td>24</td>
</tr>
<tr>
<td>Malaria-infected RBC (MI-RBC)</td>
<td>26</td>
</tr>
<tr>
<td>ESR</td>
<td>27</td>
</tr>
</tbody>
</table>
General

**Blanco RA et al. (2019)**
The use of a hematology analyzer with a new generation of software as an alternative to flow cytometry for enumerating residual white blood cells in blood components
Transfusion; 60(1): 155

**What we see as the essence:** In this study, the performance of the XN Blood Bank (BB) mode for residual WBC (rWBC) enumeration in blood components was analysed. In platelet, plasma and RBC components spiked with WBC, the BB mode demonstrated a LOQ of 2 WBC/µL and an excellent concordance with flow cytometry (FC) results. In components obtained from a routine blood bank, the BB mode successfully identified leukodepletion failures and met the guideline criteria of 90% of tested components containing 1 × 10^6 rWBC/unit, which was in agreement with FC results.

**Johnson S et al. (2019)**
A CBC algorithm combined with immature platelet fraction is able to identify JAK2 V617F mutation-positive polycythaemia vera patients
Int J Lab Hematol; 41(2): 271

**What we see as the essence:** The study proposes an algorithm based on CBC and IPF# parameters that allows to identify a cohort of high-likelihood polycythaemia vera (PV) patients and refer them for haematological review. IPF# > 20 × 10^9/L in combination with positive CBC criteria can identify JAK2 V617F mutation-positive PV patients.

**Arbiol-Roca A et al. (2018)**
Reference intervals for a complete blood count on an automated haematology analyser Sysmex XN in healthy adults from the southern metropolitan area of Barcelona
EJIFCC; 29(1): 48
Free online: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5949618/

**What we see as the essence:** The aim of the study was to establish reference intervals for CBC, DIFF and reticulocytes for a Spanish population. Significant gender differences were found for RBC, PLT, HCT and HGB.

**Huisjes R et al. (2018)**
Digital microscopy as a screening tool for the diagnosis of hereditary hemolytic anemia
Int J Lab Hematol; 40(2): 159

**What we see as the essence:** Advanced RBC Morphology from CellaVision was used to characterise hereditary haemolytic anaemia. Cutoffs were reported for several RBC abnormalities and showed a high sensitivity and specificity for detection of different conditions.
Cao J et al. (2017)
Establishing a Stand-Alone Laboratory Dedicated to the Care of Patients With Ebola Virus Disease
Lab Med; 48(2): 188
https://doi.org/10.1093/labmed/lmw072

What we see as the essence: The pocH-100i was used in a laboratory dedicated to detection of Ebola virus disease. Its accuracy was verified by comparison with the XE-2100 in the main laboratory, and its precision and reportable range were also consistent with Sysmex’s claims.

Jo S et al. (2017)
Performance evaluation of recently launched Sysmex XN-550 Automatic Hematology Analyzer
Int J Lab Hematol; 39(1): e4

What we see as the essence: The XN-550 showed a good analytical performance and strong correlation with XE-2100 and XN-3000 analysers for routine CBC parameters.

Berda-Haddad Y et al. (2017)
Increased mean corpuscular haemoglobin concentration: artefact or pathological condition?
Int J Lab Hematol; 39(1): 32

What we see as the essence: The use of the optical RBC parameters from the XN-Series can save time and help in the determination of the cause of increased MCHC.

Bruegel M et al. (2015)
Comparison of five automated hematology analyzers in a university hospital setting: Abbott Cell-Dyn Sapphire, Beckman Coulter DxH 800, Siemens Advia 2120i, Sysmex XE-5000, and Sysmex XN-2000
Clin Chem Lab Med; 53(7): 1057
https://www.degruyter.com/view/journals/cclm/53/7/article-p1057.xml

What we see as the essence: A comparison of Abbott, Beckman Coulter, Siemens and Sysmex analysers found superior flagging performance of the XN-2000, especially for blasts and variant lymphocytes. Otherwise, the analysers were comparable.
**Tabe Y et al. (2015)**
Performance evaluation of the digital cell imaging analyzer DI-60 integrated into the fully automated Sysmex XN hematology analyzer system

https://www.degruyter.com/view/journals/cclm/53/2/article-p281.xml

**What we see as the essence:** This performance evaluation of the digital imaging analyser DI-60 showed a good agreement between results from the DI-60 and manual microscopy. In addition, blasts were correctly classified with 95% sensitivity and 99% specificity.

---

**Egele A et al. (2016)**
Classification of several morphological red blood cell abnormalities by DM96 digital imaging
Int J Lab Hematol; 38(5): e98


**What we see as the essence:** The authors report the cutoff values for most of the RBC abnormalities that can be detected by the Advanced RBC Morphology software.

---

**Mazumdar R et al. (2013)**
The automated monocyte count is independently predictive of overall survival from diagnosis in chronic lymphocytic leukaemia and of survival following first-line chemotherapy
Leuk Res; 37(6): 614


**What we see as the essence:** A monocyte count $>0.91 \times 10^9/L$ at the time of diagnosis was associated with a shortened overall and treatment-free survival in CLL patients.

---

**Briggs C et al. (2012)**
Performance evaluation of the Sysmex haematology XN modular system
J Clin Pathol; 65: 1024

https://jcp.bmj.com/content/65/11/1024.long

**What we see as the essence:** The XN showed reduced sample turnaround time and reduced number of blood film reviews than the XE-2100 without loss of sensitivity and with more precise and accurate results for both platelets and low WBC counts.
Van Dievoet MA et al. (2016)
Performance evaluation of the Sysmex® XP-300 in an oncology setting: evaluation and comparison of hematological parameters with the Sysmex® XN-3000
Int J Lab Hematol; 38(5): 490

What we see as the essence: The XP-300 showed very good precision and linearity results, comparable with the XN-3000 analyser.

Cornet E et al. (2016)
Evaluation and optimization of the extended information process unit (E-IPU) validation module integrating the sysmex flag systems and the recommendations of the French-speaking cellular hematology group (GFHC)
Scand J Clin Lab Invest; 76(6): 465

What we see as the essence: Using the biomedical validation criteria, 21.3% of samples triggered a smear review. Modification of four criteria reduced the number of smears from 21.3% to 15.0% without loss of clinical value.

Egele A et al. (2015)
Automated detection and classification of teardrop cells by a novel RBC module using digital imaging/microscopy
Int J Lab Hematol; 37(6):e153

What we see as the essence: The authors report excellent detection of teardrop cells in samples from patients with myelofibrosis and MDS, using the Advanced RBC Morphology software.

Ferrero-Vacher C et al. (2015)
Utilisation des paramètres érythrocytaires Sysmex dans un cas d’hémolyse sévère (Erythrocytic parameters Sysmex in a case of severe haemolyisis)
Annales de Biologie Clinique; 73(6): 729

Article in French: http://www.jle.com/fr/revues/abc/e-docs/utilisation_des_parametres_erythrocytaires_systmex_dans_un_cas_dhemolyse_severeparametres_erythrocytaires_systmex_et_hemolyse_305923/article.phtml

What we see as the essence: Case report of severe haemolytic anaemia with cold agglutinins, identified by increased MCHC and qualitative alarms. The RBC-O and HGB-O parameters from the RET channel, and the RBC most frequent volume (R-MFV) allowed to report the correct results.
Arneth B et al. (2015)
Technology and New Fluorescence Flow Cytometry Parameters in Hematological Analyzers
J Clin Lab Anal; 29(3): 175
Free online: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6807107/

What we see as the essence: This paper gives a good overview of the technology behind the XE-Series and the benefits of flow cytometry and automatic cell counting. It shows that the XE-5000 delivers faster accurate results than older analysers.

JO SY et al. (2015)
Performance evaluation of the new hematology analyzer Sysmex XN-series
Int J Lab Hematol; 37(2):155

What we see as the essence: A good correlation was found between the XN- and XE-Series for all parameters. The XN-Series dramatically reduced the smear rate (by 58%). Even at counts below 500/µL the XN provided an accurate WBC count using the Low WBC mode.

Genevieve F et al. (2014)
Smear microscopy revision: propositions by the GFHC
feuillets de Biologie; VOL LVI N° 317
Free online: https://www.sysmex.fr/fileadmin/media/f107/Documents/Haematology_Smear_microscopy_revision.pdf

What we see as the essence: The GFHC reviewed in detail the criteria used within the CBC to generate blood smears and has decided on a number of minimum recommendations, defining threshold values and various situations in which the blood smear review is desirable.

Hotton J et al. (2013)
Performance and Abnormal Cell Flagging Comparisons of Three Automated Blood Cell Counters: Cell-Dyn Sapphire, DxH-800, and XN-2000
Am J Clin Pathol; 140(6): 845
https://academic.oup.com/ajcp/article/140/6/845/1761105

What we see as the essence: Repeatability, linearity and carryover was good for all tested analysers, and correlation between the analysers was good for HGB, MCV, PLT and WBC.
Quotes: "The XN showed a higher sensitivity than the SAPH and DxH for all flags of interest." "For the first time, we have decreased the slide review for our laboratory from 20% with the SAPH to 9.3% with the XN."
Wang H et al. (2013)
Use of RBC-O and S-MCV Parameters of Sysmex XE-2100 in a Patient with RBC Cold Agglutination
Clin Lab; 59: 217
https://www.clin-lab-publications.com/article/1068

**What we see as the essence:** A combination of sample dilution and the use of RBC parameters from the RET channel on the XE-2100 is described to obtain accurate RBC parameters from samples with RBC cold agglutination without heating of the sample.

Godon A et al. (2012)
Anomalies et erreurs de détermination de l’hémogramme avec les automates d’hématologie cellulaire Partie 3. Hémoglobine, hématies, indices érythrocytaires, réticulocytes*
Ann Biol Clin 2012; 70(2): 155
Article in French - Free online: http://www.jle.com/fr/revues/abc/e-docs/anomalies_et_erreurs_de_determination_de_lhemogramme_avec_les_automates_dhematologie_cellulaire_partie_3_hemoglobine_hematies_indices_erythrocytaires_reticulocytes_292317/article.phtml

**What we see as the essence:** A summary report about potential interferences of CBC parameters with focus on situations leading to abnormal HGB, RBC and MCV, resulting in abnormal calculated RBC indices, e.g. MCHC. Alternative strategies may support management of interferences.

Urrechaga E et al. (2011)
Erythrocyte and reticulocyte parameters in iron deficiency and thalassemia
J Clin Lab Anal; 25: 223
Free online: https://onlinelibrary.wiley.com/doi/full/10.1002/jcla.20462

**What we see as the essence:** Beta-thalassaemia can be recognised through high RBC, small MCV, high %MicroR and moderately increased IRF, whereas iron deficiency shows high RDW and %HYPO-He.
RET/IRF

Tiwari A et al. (2018)
Applying newer parameter Ret-He (reticulocyte haemoglobin equivalent) to assess latent iron deficiency (LID) in blood donors-study at a tertiary care hospital in India
Vox Sang 2018; 113(7): 639

What we see as the essence: RET-Hₑ can be used as a routine screening test to detect latent iron deficiency in blood donors. This could provide an opportunity to make appropriate and timely interventions like dietary changes or drug supplementation.

Morkis IVC et al. (2015)
Assessment of immature platelet fraction and immature reticulocyte fraction as predictors of engraftment after hematopoietic stem cell transplantation
Int J Lab Hematol; 37(2): 259

What we see as the essence: Both IRF% and IPF% can be used to predict neutrophil and platelet recovery, respectively. Work was done on XE-5000.

Yesmin S et al. (2011)
Immature reticulocyte fraction as a predictor of bone marrow recovery in children with acute lymphoblastic leukaemia on remission induction phase
Bangladesh Med Res Council Bull; 37(2): 57

What we see as the essence: In 52% of paediatric ALL patients, IRF% values rose before NEUT# values during recovery after chemotherapy. Therefore, monitoring of both parameters may be beneficial.

Gonçalo AP et al. (2011)
Predictive value of immature reticulocyte and platelet fractions in hematopoietic recovery of allograft patients
Transplant Proc; 43: 24
http://www.transplantation-proceedings.org/article/S0041-1345(10)01945-7/abstract

What we see as the essence: The immaturity fractions IRF and IPF offer an easy and early evaluation method of posttransplantational recovery of the bone marrow.
**RET-Hₑ / RBC-Hₑ**

**Morton SU et al. (2020)**
Screening With Reticulocyte Hemoglobin Increased Iron Sufficiency Among NICU Patients
*Pediatr Qual Saf*; 5(2): e258

*Free online: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7190262/*

**What we see as the essence:** The authors found that implementation of an iron supplementation guideline utilizing RET-Hₑ values can improve iron sufficiency even for heterogeneous out-born neonatal intensive care unit patient populations. Normal RET-Hₑ range was defined as 27–38 pg based on published literature and expert consensus.

**Chinudomwong P et al. (2020)**
Diagnostic performance of reticulocyte hemoglobin equivalent in assessing the iron status
*J Clin Lab Anal*; 34(6): e23225

*Free online: https://onlinelibrary.wiley.com/doi/full/10.1002/jcla.23225*

**What we see as the essence:** RET-Hₑ (n = 953) was investigated in a variety of conditions, involving inflammation, and its diagnostic performance was evaluated in assessing the iron status. Iron deficiency anaemia (IDA) can be ruled out at a cut-off ≥30 pg. For RET-Hₑ <30 pg the study proposed a diagnostic algorithm to identify/distinguish between IDA and non-ID anaemia.

**Tantawy AA et al. (2019)**
Reticulocyte Hemoglobin Content (Ret He): A Simple Tool for Evaluation of Iron Status in Childhood Cancer
*J Pediatr Hematol Oncol*; 42(3): e147

*https://journals.lww.com/jpho-online/Abstract/2020/04000/Reticulocyte_Hemoglobin_Content__Ret_He___A_Simple.23.aspx*

**What we see as the essence:** RET-Hₑ is considered an easy and affordable tool for assessment of iron deficiency anaemia (IDA) in children with cancer during chemotherapy. Due to the influence of underlying inflammatory conditions it is judged to be a more reasonable test than conventional iron parameters.
Levy S et al. (2018)
The clinical utility of new reticulocyte and erythrocyte parameters on the Sysmex XN 9000 for iron deficiency in pregnant patients
Int J Lab Hematol; 40(6): 683


What we see as the essence: This study demonstrates the clinical efficacy of RET-He, %Hypo-He and %Micro-R for detecting ID in nonanemic pregnant patients. They are as well a cost effective alternative.

Jarc E et al. (2017)
Comparison of erythrocyte and reticulocyte indices for the diagnosis of iron deficiency
Zdrav Vestn (Slovenian Med J); 86(1-2): 19

Free online: https://www.researchgate.net/publication/319877155

What we see as the essence: Reticulocyte indices (Sysmex RET-He and Siemens CHr) are directly comparable. RET-He showed a slightly better predictive power for iron deficiency identification in IDA. Hypo-He (Sysmex) and %HYPO (Siemens) are not exchangeable, both can be used for long-term iron deficiency evaluation.

Wirawan R et al. (2017)
Concordance between Reticulocyte Hemoglobin Equivalent and Reticulocyte Hemoglobin Content in CKD Patients Undergoing Hemodialysis
Acta Med Indones; 49(1): 34

Free online: http://www.actamedindones.org/index.php/ijim/article/view/316/pdf

What we see as the essence: A very strong correlation (r=0.91) and a good concordance was found between RET-He and CHr with a mean bias of 0.5 pg in chronic kidney disease patients undergoing haemodialysis. It indicates that RET-He and CHr can both be used for assessing iron status.

Toki Y et al. (2017)
Evaluation of the hypochromic erythrocyte and reticulocyte hemoglobin content provided by the Sysmex XE-5000 analyzer in diagnosis of iron deficiency erythropoiesis
Int J Hematol; 106(1): 116

http://rd.springer.com/article/10.1007/s12185-017-2212-6

What we see as the essence: RET-He was shown to be a clinically useful marker for determining iron deficiency in the general population and can also be used for the evaluation of the efficacy of iron administration.
Buttarello M et al. (2016)
Evaluation of the hypochromic erythrocyte and reticulocyte hemoglobin content provided by the Sysmex XE-5000 analyzer in diagnosis of iron deficiency erythropoiesis
Clin Chem Lab Med; 54(12): 1939

What we see as the essence: RET-Hₚ and %Hypo- Hₑ, measured on the XE-5000, allowed identification of patients with iron deficiency, especially those who had already developed anaemia. RET-Hₑ had a better sensitivity, presumably because it is more responsive to iron deficiency.

Mehta S et al. (2016)
Reticulocyte Hemoglobin vis-a-vis Serum Ferritin as a Marker of Bone Marrow Iron Store in Iron Deficiency Anemia
J Assoc Physicians India; 64(11): 38
Free online: https://www.japi.org/n3n5o506k424r4/j3x536k5l434e4w5/v2a4

What we see as the essence: This study showed that RET-Hₑ is a better predictor of bone marrow iron stores in patients with severe anaemia than serum ferritin.

Urrechaga E et al. (2016)
Percentage of hypochromic erythrocytes and reticulocyte hemoglobin equivalent predictors of response to intravenous iron in hemodialysis patients
Int J Lab Hematol; 38(4): 360

What we see as the essence: HYPO-He and RET-Hₑ are reliable parameters for the study of erythropoiesis status in hemodialysis patients.

Al-Ghananim RT et al. (2016)
Reticulocyte Hemoglobin Content During the First Month of Life in Critically Ill Very Low Birth Weight Neonates Differs From Term Infants, Children, and Adults
J Clin Lab Anal; 30(4): 326

What we see as the essence: RET-Hₑ values from the XE-2100 were lower in very low birth weight infants than in term infants, children and adults. RET-Hₑ was 31.8 pg within 24 hr after birth and subsequently declined to a steady-state level of 28.4 pg.
Archer N et al. (2015)
Diagnosis of iron-deficient states
Crit Rev Clin Lab Sci; 52(5): 256
http://www.tandfonline.com/doi/pdf/10.3109/10408363.2015.1038744

What we see as the essence: This review gives an overview of the haematological, biochemical and genetic markers for identifying iron deficiency. RBC-He, RET-He, Delta-He, HYPO-He and MicroR are mentioned besides the standard RBC indices.

Peerschke E et al. (2014)
Using the Hemoglobin Content of Reticulocytes (RET-He) to Evaluate Anemia in Patients With Cancer
Am J Clin Pathol; 142(4): 506
Free online: https://academic.oup.com/ajcp/article/142/4/506/1766909

What we see as the essence: RET-He values above 31 or 32 pg could be used to rule out iron deficiency in cancer patients. In the present study the use of RET-He would have reduced the number of biochemical iron studies by 66% (from 209 to 70).

Schoorl M et al. (2012)
Effects of iron supplementation on red blood cell hemoglobin content in pregnancy
Hematology Rep; 4(4): e24
Free online: http://www.pagepress.org/journals/index.php/hr/article/view/hr.2012.e24

What we see as the essence: RET-He and RET-He/RBC-He ratio are sensitive markers for screening when a decrease in red blood cell haemoglobin content is observed and for monitoring short-term effects of iron supplementation. The authors recommend integrating these parameters into the protocol for anaemia screening and monitoring during pregnancy.

Schoorl M et al. (2012)
Temporary impairment of reticulocyte haemoglobin content in subjects with community-acquired pneumonia
Int J Lab Hematol; 34(4): 390

What we see as the essence: In patients with community-acquired pneumonia, acute inflammation results in decreased RET-He values at an early stage, reflecting acute erythropoietic dysfunction.
Urrechaga E et al. (2013)
Erythrocyte and reticulocyte indices in the assessment of erythropoiesis activity and iron availability
Int J Lab Hematol; 35(2): 144

What we see as the essence: RET-He and %HYPO-He are helpful in assessing erythropoiesis and iron status.

Fernandez R et al. (2010)
Low Reticulocyte Hemoglobin Content Is Associated with a Higher Blood Transfusion Rate in Critically Ill Patients: A Cohort Study
Anesthesiology 112(5): 1211
Free online: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1932981

What we see as the essence: The authors conclude that low reticulocyte haemoglobin content (RET-He) is common at admission at ICU in nonanaemic patients and it is associated with higher RBC transfusion requirements than in patients with normal RET-He values (39.1% vs. 12.8%, P = 0.02).

Maier-Redelsperger M et al. (2010)
Strong association between a new marker of hemolysis and glomerulopathy in sickle cell anemia
Blood Cell Mol Dis; 45(4): 289

What we see as the essence: A special algorithm combining RBC-He, RET-He and lactate dehydrogenase bears the potential as a marker of haemolysis strongly correlated with albuminuria in sickle cell anaemia patients.

Jonckheere S et al. (2010)
Erythrocyte indices in the assessment of iron status in dialysis-dependent patients with end-stage renal disease on continuous erythropoietin receptor activator versus epoetin beta therapy
Acta Haematol; 124(1): 27
http://www.karger.com/Article/FullText/313785

What we see as the essence: Due to fluctuations of iron status parameters, a fixed time point should be used for iron status monitoring during erythropoietin therapy.
Leers MP et al. (2010)
The value of the Thomas-plot in the diagnostic work up of anemic patients referred by general practitioners
Int J Lab Hematol; 32(6 Pt 2): 572

**What we see as the essence:** The Thomas-plot is helpful in diagnosing patients referred from general practitioners and differentiating functional iron deficiency from classical iron deficiency.

Schoorl M et al. (2010)
Changes in red blood cell hemoglobinization during pregnancy
Free online: https://www.nvkc.nl/sites/default/files/NTKC/2010-3-p206-208.pdf

**What we see as the essence:** RET-H$_e$ is a useful sensitive and early indicator of iron status in the second half of pregnancy and should ideally be measured in combination with zinc protoporphyrin (ZPP) and IRF.

Van Wyck DB et al. (2010)
Analytical and biological variation in measures of anemia and iron status in patients treated with maintenance hemodialysis
Am J Kidney Dis; 56(3): 540
http://www.ajkd.org/article/S0272-6386(10)00918-2/abstract

**What we see as the essence:** RET-H$_e$ could prove superior to transferrin saturation (TSAT) and ferritin in monitoring iron status of haemodialysis patients due to a lower biological variation.

Maconi M et al. (2009)
Erythrocyte and reticulocyte indices in iron deficiency in chronic kidney disease: comparison of two methods
Scand J Clin Lab Invest; 69(3): 365
http://informahealthcare.com/doi/abs/10.1080/00365510802657673

**What we see as the essence:** RET-H$_e$ and CHr correlate and agree well in evaluating CKD patients needing iron support.
Miwa N et al. (2010)
Usefulness of measuring reticulocyte hemoglobin equivalent in the management of haemodialysis patients with iron deficiency
Int J Lab Hematol 32(2): 248

What we see as the essence: RET-Hₑ is equivalent to CHr and useful in managing haemodialysis patients with iron deficiency as it responds more rapidly than HGB.

Mast A et al. (2008)
Reticulocyte hemoglobin content
Am J Hematol; 83(4): 307

What we see as the essence: Reticulocyte haemoglobin can be used to differentiate iron deficiency from other causes of anaemia and as an early marker to monitor the therapy.

Thomas C et al. (2006)
The diagnostic plot: A concept for identifying different states of iron deficiency and monitoring the response to epoetin therapy
Med Oncol; 23(1): 23

What we see as the essence: The Thomas-plot incl. RET-Hₑ can be used for the differential diagnosis of anaemia and also gives therapy options.

Brugnara C et al. (2006)
Reticulocyte hemoglobin equivalent (Ret He) and assessment of iron-deficient states
Clin Lab Haematol; 28(5): 303
Free online: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1618805/pdf/clh0028-0303.pdf

What we see as the essence: RET-Hₑ is a reliable marker of cellular haemoglobin content and can be used to identify iron-deficient states, particularly in dialysis patients. RET-Hₑ and CHr are in good agreement.
**Schoorl M et al. (2006)**
Erythropoiesis activity, iron availability and reticulocyte hemoglobinization during treatment with hemodialysis and in subjects with uremia
Clin Lab; 52(11-12): 621
https://www.clin-lab-publications.com/article/160

*What we see as the essence:* Biochemical parameters reflecting functional iron availability and haematological parameters reflecting haemoglobinisation are interdependent.

**Thomas L et al. (2005)**
Reticulocyte hemoglobin measurement -- comparison of two methods in the diagnosis of iron-restricted erythropoiesis
Clin Chem Lab Med; 43(11): 1193

*What we see as the essence:* RET-H_e can replace CHr in the diagnostic Thomas-plot without loss of sensitivity or specificity.

**Canals C et al. (2005)**
Clinical utility of the new Sysmex XE 2100 parameter - reticulocyte hemoglobin equivalent – in the diagnosis of anemia
Haematologica; 90(8): 1133
Free online: http://www.haematologica.org/content/90/8/1133.long

*What we see as the essence:* RET-H_e is useful for the differential diagnosis of iron deficiency anaemia vs anaemia of chronic disease and could also be helpful in the identification of thalassaemia patients.

**Buttarello M et al. (2004)**
The new reticulocyte parameter (RET-Y) of the Sysmex XE 2100: its use in the diagnosis and monitoring of posttreatment sideropenic anemia
Am J Clin Pathol; 121(4): 489
Free online: https://doi.org/10.1309/W65295DTUWK7U1HH

*What we see as the essence:* RET-Y closely correlates with CHr and can be used for diagnosis and early monitoring after the administration of intravenous iron.
HYPO-He / HYPER-He / MicroR / MacroR

**Schoorl M et al. (2012)**
Efficacy of Advanced Discriminating Algorithms for Screening on Iron-Deficiency Anemia and β-Thalassemia Trait
Am J Clin Pathol; 138(2): 300
Free online: [https://academic.oup.com/ajcp/article/138/2/300/1761358](https://academic.oup.com/ajcp/article/138/2/300/1761358)

*What we see as the essence:* The authors conclude that the advanced algorithms, derived from extended RBC parameters provided by the Sysmex XE-5000 analyzer, are useful as laboratory devices for anaemia screening.

**Persijn L et al. (2012)**
Screening for hereditary spherocytosis in routine practice: evaluation of a diagnostic algorithm with focus on non-splenectomised patients
Ann Hematol; 91(2): 301

*What we see as the essence:* The hereditary spherocytosis diagnostic tool by Mullier *et al.* is useful and works, but needs fine-tuning to the local patient population.

**Mullier F et al. (2011)**
Additional erythrocytic and reticulocytic parameters helpful for diagnosis of hereditary spherocytosis: results of a multicentre study
Ann Hematol; 90(7): 759

*What we see as the essence:* Combining several RBC parameters allows to efficiently screen for hereditary spherocytosis even in mild cases.

**Urrechaga E et al. (2011)**
The role of automated measurement of RBC subpopulations in differential diagnosis of microcytic anemia and β-thalassemia screening
Am J Clin Pathol; 135(3): 374

*What we see as the essence:* Because of high sensitivity and specificity, the new index %MicroR-%HYPO-He was the most reliable index in the differential diagnosis of microcytic anaemias.
Urrechaga E. et al. (2011)
Erythrocyte and reticulocyte parameters in iron deficiency and thalassemia
J Clin Lab Anal; 25(3): 223

What we see as the essence: Beta-thalassaemia can be recognised through high RBC, small MCV, high %MicroR and moderately increased IRF, whereas iron deficiency shows high RDW and %HYPO-Hₑ.

Urrechaga E et al. (2011)
The role of automated measurement of red cell subpopulations on the Sysmex XE-5000 analyzer in the differential diagnosis of microcytic anemia
Int J Lab Hematol; 33(1): 30

What we see as the essence: Because of high sensitivity and specificity, the new index %microcytic-%hypochromic was the most reliable index in the differential diagnosis of microcytic anemia.

Urrechaga E et al. (2009)
Potential utility of the new Sysmex XE 5000 red blood cell extended parameters in the study of disorders of iron metabolism
Clin Chem Lab Med; 47(11): 1411
https://www.degruyter.com/view/journals/cclm/47/11/article-p1411.xml

What we see as the essence: The new parameters %HYPO-Hₑ/%HYPER-Hₑ and %MicroR/%MacroR appear to be sensitive for detecting small changes in the number of red cells with inadequate haemoglobinisation and volume in order to distinguish beta-thalassaemia from iron deficiency anaemia.
NRBC

Monteiro Junior JG et al. (2015)
Nucleated Red Blood Cells as Predictors of All-Cause Mortality in Cardiac Intensive Care Unit Patients: A Prospective Cohort Study
PLoS One; 10(12): e0144259
Free online: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4695082/

What we see as the essence: "The presence of NRBC (XE-2100) was associated with a higher ICU mortality (49.4% vs 21.7%, P<0.001) as well as in-hospital mortality (61.4% vs 33.3%, p = 0.001)."

Cremer M et al. (2015)
Nucleated red blood cells as marker for an increased risk of unfavorable outcome and mortality in very low birth weight infants
Early Hum Dev; 91(10): 559

What we see as the essence: This study of 438 low birth weight infants indicates that an NRBC count obtained 24-120 h after birth can serve as a surrogate marker for later severe morbidity and mortality. The optimal cut-off value was 2x10^9/L with 83% sensitivity and 75% specificity.

Tantanate C et al. (2014)
Performance evaluation of the automated nucleated red blood cell enumeration on Sysmex XN analyser
Int J Lab Hematol; 37(3): 341

What we see as the essence: NRBC counts from the XN-Series could replace manual counts: the precision of the XN-Series was superior and a small bias (manual counts slightly higher than NRBC counts from the XN-Series) was only observed for NRBC counts above 200/100 WBC.

Hotton J et al. (2013)
Performance and Abnormal Cell Flagging Comparisons of Three Automated Blood Cell Counters -Cell-Dyn Sapphire, DxH-800, and XN-2000
Am J Clin Pathol; 140(6): 845
https://academic.oup.com/ajcp/article/140/6/845/1761105

What we see as the essence: Repeatability, linearity and carryover was good for all tested analysers, and correlation between the analysers was good for HGB, MCV, PLT and WBC.
Quotes: "The XN showed a higher sensitivity than the SAPH and DxH for all flags of interest." "For the first time, we have decreased the slide review for our laboratory from 20% with the SAPH to 9.3% with the XN."
Parco S et al. (2013)
Public banking of umbilical cord blood or storage in a private bank: testing social and ethical policy in northeastern Italy
J Blood Med; 4: 23
Free online: http://www.dovepress.com/getfile.php?fileID=15732

What we see as the essence: An excellent correlation was found between manual NRBC counts and NRBC counts from the XE-2100 ($r^2 = 0.94$) in umbilical cord blood. This number may be used to correct the WBC count and thereby guarantee an adequate WBC concentration for blood banking of umbilical cord blood.

Gasparović V et al. (2012)
Nucleated red blood cells count as first prognostic marker for adverse neonatal outcome in severe preeclamptic pregnancies
Coll Antropol; 36(3): 853
Free online: http://hrcak.srce.hr/index.php?show=clanak&id_clanak_jezik=133776

What we see as the essence: An increased count of nucleated red blood cells in preterm newborns born from pregnancies with severe preeclampsia seems to be the first significant marker for detecting adverse neonatal outcome.

Pipitone S et al. (2012)
Evaluation of automated nucleated red blood cells counting on Sysmex XE-5000 and Siemens ADVIA 2120

What we see as the essence: The results show excellent analytical performances for the XE-5000, with high accuracy and precision. In agreement with previous studies, the authors also showed that despite similar performance in terms of analytical imprecision, the overall correlation with microscopy is higher for XE-5000 than for ADVIA 2120, i.e., correlation coefficient 0.97 vs. 0.67 and AUC 0.97 vs. 0.73, respectively.

Kuert S et al. (2011)
Association of nucleated red blood cells in blood and arterial oxygen partial tension
Clin Chem Lab Med; 49(2): 257

What we see as the essence: The NRBC count is an independent risk indicator of poor prognosis and mortality, NRBC-positive patients required a longer stay in the intensive care unit.
Danise P et al. (2011)
Evaluation of nucleated red blood cells in the peripheral blood of hematological diseases
Clin Chem Lab Med; 50(2): 357
https://www.degruyter.com/view/journals/cclm/50/2/article-p357.xml

What we see as the essence: NRBC are found in nearly all onco-haematological diseases at diagnosis and frequently during therapy. They are absent at remission.

Danise P et al. (2009)
Nucleated red blood cells and soluble transferrin receptor in thalassemia syndromes: relationship with global and ineffective erythropoiesis
Clin Chem Lab Med; 47(12): 1539
https://www.degruyter.com/view/journals/cclm/47/12/article-p1539.xml

What we see as the essence: The NRBC count helps defining ineffective erythropoiesis in thalassaemia patients and supporting transfusion management.

Stachon A et al. (2007)
Nucleated red blood cells in the blood of medical intensive care patients indicate increased mortality risk: a prospective cohort study
Crit Care; 11(3): R62
Free online: http://ccforum.com/content/pdf/cc5932.pdf

What we see as the essence: The NRBC count is one indicator of mortality — persistence (observed in daily screenings) and high concentration are both indicators for poor prognosis.

Stachon A et al. (2006)
Poor prognosis indicated by nucleated red blood cells in peripheral blood is not associated with organ failure of the liver or kidney
Clin Chem Lab Med; 44(8): 955
https://www.degruyter.com/view/journals/cclm/44/8/article-p955_8.xml

What we see as the essence: The NRBC count is one indicator of mortality independent of other factors such as kidney or liver failure.

Stachon A et al. (2006)
Daily monitoring of nucleated red blood cells in the blood of surgical intensive care patients
Clin Chim Acta; 366(1-2): 329

What we see as the essence: NRBC count is an early indicator of mortality – daily screening is recommended.
**Wang F-S et al. (2003)**

Development and clinical application of nucleated red blood cell counting and staging on the automated haematology analyser XE-2100

Clin Lab Haematol; 25(1): 17


*What we see as the essence:* The NRBC count correlates well with flow cytometry.

**Stachon A et al. (2002)**

Nucleated red blood cells indicate high risk of in-hospital mortality

J Lab Clin Med; 140(6): 407

https://www.translationalres.com/article/S0022-2143(02)00104-X/fulltext

*What we see as the essence:* NRBC are often an only transient observation, but they indicate a poor prognosis, whether transient or persistent.

**Briggs C et al. (2000)**

New quantitative parameters on a recently introduced automated blood cell counter - the XE 2100

Clin Lab Haematol; 22(6): 345


*What we see as the essence:* The automated NRBC count was highly correlated with the manual reference count (r²=0.97) and thus eliminates the need for manual NRBC counts. The use of the 'optical' platelet count significantly improves the reliability of low platelet counts. The instrument will always report the most accurate platelet count on all samples, whether impedance or ´optical´.
**FRC**

**Hervent AS et al. (2015)**
Evaluation of schistocyte analysis by a novel automated digital cell morphology application
Int J Lab Hematol; 37(5): 588


*What we see as the essence:* This performance evaluation showed that the CELLAVISION Advanced RBC Software Application is easy to use and provides a sensitive and reproducible measurement of schistocytes in peripheral blood.

**Lesesve J-F et al. (2012)**
Fragmented red blood cells automated measurement is a useful parameter to exclude schistocytes on the blood film
Int J Lab Hematol; 34(6): 566


*What we see as the essence:* The automated FRC count offers a better degree of certainty than microscopy to exclude the presence of fragmented RBC.

**Abe Y et al. (2009)**
The effectiveness of measuring for fragmented red cells using an automated hematology analyser in patients with thrombotic microangiopathy

[Free online: http://cat.sagepub.com/content/15/3/257.full.pdf](http://cat.sagepub.com/content/15/3/257.full.pdf)

*What we see as the essence:* In conclusion, the FRC level is a simple and useful marker for thrombotic microangiopathy (TMA), and an FRC level of 1.2% is recommended as the cutoff value for the diagnosis of TMA.

**Imoto S et al. (2005)**
Usefulness of sequential automated analysis of fragmented red blood cells for the differential diagnosis of TTP-hemolytic uremic syndrome following allogeneic hematopoietic cell transplantation
Lab Hematol; 11(2): 131

[Free online: http://europepmc.org/abstract/med/16024337](http://europepmc.org/abstract/med/16024337)

*What we see as the essence:* Sequential monitoring of FRC% may be a reliable marker for a specific type of complication (TTP-HUS; thrombotic thrombocytopenic pupura haemolytic uraemic syndrome) after allogeneic haematopoietic precursor cell transplantation.
**Banno S et al. (2005)**

Quantification of red blood cell fragmentation by the automated hematology analyzer XE-2100 in patients with living donor liver transplantation

*Clin Lab Haematol; 27(5): 292*


**What we see as the essence:** The determination of FRC% by the XE-2100 enables early diagnoses and monitoring of TTP (thrombotic thrombocytopenic purpura) or TMA (thrombotic microangiopathy) and will be useful in the clinical field.
Malaria-infected RBC (MI-RBC)

**Pillay E et al. (2019)**
Evaluation of automated malaria diagnosis using the Sysmex XN-30 analyser in a clinical setting
Malaria J; 18(1): 15

[Free online: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6341646/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6341646/)

**What we see as the essence:** The novel technology of the Sysmex XN-30 provides a robust, rapid, automated and accurate platform for diagnosing malaria. It allows precise recognition and demonstrated a sensitivity and specificity of 100% for malaria parasitaemia detection.

**Post A et al. (2019)**
The XN-30 hematology analyzer for rapid sensitive detection of malaria: a diagnostic accuracy study
BMC Medicine; 17(1): 103

[Free online: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6543632/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6543632/)

**What we see as the essence:** The novel technology of the Sysmex XN-30 provides a robust, rapid, automated and objective platform for diagnosing and quantifying malaria. The XN-30 ensures the prompt initiation of the malaria treatment and the malaria anaemia together with the reliable treatment monitoring.
ESR

Schapkaitz E et al. (2017)
Evaluation of the InteRRliner automated erythrocyte sedimentation rate analyzer for a large academic laboratory
Int J Lab Hematol; 39(3): e66

What we see as the essence: Indicated by the high correlation coefficient of 0.96 the InteRRliner showed an excellent comparability to the HumaSed ESR method.