Literature list – red blood cells
Customer information

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Reticulocytes (RET/ IRF)

Equey T et al. (2022)
Standardization of reticulocyte counts in the athlete biological passport: A practical update.
Int J Lab Hematol; 44(1): 112

Free online: https://onlinelibrary.wiley.com/doi/epdf/10.1111/ijlh.13732

Summary: The study confirms the tendency of a small positive bias for the RET% value determination when switching from XT/XE to XN technology. The proposal of a model allows a suitable comparison of data in the Athletic Biological Passport for the range of RET% encountered in anti-doping.

Feugray G et al. (2022)
Assessment of Reticulocyte and Erythrocyte Parameters From Automated Blood Counts in Vaso-Occlusive Crisis on Sickle Cell Disease.
Front Med; 9: 858911

Free online: https://www.frontiersin.org/articles/10.3389/fmed.2022.858911/full

Summary: The authors developed an algorithm to predict the probability of a vaso-occlusive crisis (VOC) on sickle cell disease (SCD) patients within the following year. A reticulocyte count (RET) of >189.4 x10^9/L and a medium fluorescence reticulocytes (MFR) of > 19.75% presented a sensitivity of 81.8% and a specificity of 88% to predict VOC in patients with SCD at steady state.

Jeppesen JS et al. (2021)
Immature reticulocytes are sensitive and specific to low-dose erythropoietin treatment at sea level and altitude.
Drug Test Anal; 13(7): 1331


Summary: IRF and IRF/RBC ratio changes identified 90% of study participants treated with a micro-dose of recombinant human erythropoietin at sea level during and after the exposure period with a specificity of >99%.

Jiang H et al. (2019)
Interferents of Automated Reticulocyte Analysis Integrated with Relevant Clinical Cases.
Clin Chem; 65(7): 1251

https://www.clin-lab-publications.com/article/3060

Summary: XN-9000 showed high agreement with the manual counting method (r = 0.956) in a cohort of 510 samples. The analyser was able to correctly count RET% and RET# in presence of most interferences or indicate result unreliability in severe cases.
**La Gioia A et al. (2018)**
Short preheating at 41°C leads to a red blood cells count comparable to that in RET channel of Sysmex analysers in samples showing cold agglutination.
J Clin Pathol; 71(8): 729
https://jcp.bmj.com/content/71/8/729.long

**Summary:** Detailed evaluation of the RET channel in terms of resolving cold-agglutinins. It provides comparable results like traditional manual 37°C/2h pre-treatment and therefore, the authors recommended it to shorten the TAT.

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**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

**Summary:** Both IRF% and IPF% can be used to predict neutrophil and platelet recovery, respectively. Work was done on XE-5000.

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**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

**Summary:** In 52% of paediatric ALL patients, IRF% values rose before NEUT# values during recovery after chemotherapy. Therefore, the authors concluded that monitoring of both parameters may be beneficial.

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**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

**Summary:** In this study, immature platelet (IPF) and immature reticulocyte fraction (IRF) were presented as early and readily available assessment methods for post-transplant bone marrow recovery.
Reticulocyte haemoglobin equivalent (RET-He / RBC-He)

De Leur K et al. (2022)
The alternative Thomas-plot: A new tool for effective anemia diagnostics.
Int J Lab Hematol; 45(1):96

**Summary:** The authors developed and validated an alternative version of the Thomas plot, plotting RET-He against transferrin/log (ferritin) instead of soluble transferrin receptor/log (ferritin). It was concluded that the alternative Thomas plot delivered similar results in sub-categorising IDA and in reducing the number of anaemias of unknown causes. In the overall distribution of anaemia cases a shift from IDA in the Thomas plot to functional IDA in the alternative Thomas plot was observed.

Almashjary MN et al. (2022)
Reticulocyte Hemoglobin-Equivalent Potentially Detects, Diagnoses and Discriminates between Stages of Iron Deficiency with High Sensitivity and Specificity.
J Clin Med; 11(19): 5675
Free online: https://www.mdpi.com/2077-0383/11/19/5675

**Summary:** The authors found that RET-He predicted ID/IDA with a sensitivity of 92.7%/90.6% and specificity of 97.9%/92.3% using serum ferritin as a reference. Also RET-He predicted early stages of ID better than RDW and gave indications of iron therapy success after 7 days, whereas HGB was not changed yet.

Auerbach M et al. (2021)
Using Reticulocyte Hemoglobin Equivalent as a Marker for Iron Deficiency and Responsiveness to Iron Therapy.
Mayo Clin Proc; 96(6): 1510
Free online: https://www.mayoclinicproceedings.org/article/S0025-6196(20)31376-8/fulltext

**Summary:** Data from CBC and RET-He were able to identify patients with iron deficiency anaemia (RET-He <30.7 pg, 68.2% sensitivity and 69.7% specificity) and determine the need for and the responsiveness to intravenous iron defined as an HGB increase of 1.0 g (RET-He <28.5 pg and HGB <10.3 g/dL, 84% sensitivity and 78% specificity).
Hoenemann C et al. (2021)
J Clin Med; 10(18): 4250

Free online: https://www.mdpi.com/2077-0383/10/18/4250

Summary: This review paper summarises literature with regards to Patient Blood Management. It focuses on RET-He and Delta-He in the context of pre-, during-, and postoperative patient management for anaemia in elective surgeries. They present the advantages in septic patients compared to classical anaemia parameters, and also explain their roles in ICIS and COVID-19 prognostic score.

Neef V et al. (2021)
The Reticulocyte Hemoglobin Equivalent as a Screening Marker for Iron Deficiency and Iron Deficiency Anemia in Children.
J Con Med; 10: 3506

Free online: https://www.mdpi.com/2077-0383/10/16/3506

Summary: The study shows that the cut-off value for RET-He to screen for ID was 33.5 pg (sensitivity 90.7%; specificity 35.8%) and 31.6 pg (sensitivity 90.6%; specificity 50.4%) to screen for IDA.

Hoenemann C et al. (2021)
Reticulocyte Haemoglobin as a Routine Parameter in Preoperative Iron Deficiency Assessment.
iMedPupJournals; 5(1): 154


Summary: The authors of the review recommend RET-He as a routine preoperative parameter to identify patients at risk for latent iron deficiency. RET-He helps to proactively avoid complications during surgery and prevent extended hospitalisation. In contrast to other biochemical parameters it is much cheaper and already available in many hospitals.

Bahr TM et al. (2020)
Reconciling markedly discordant values of serum ferritin versus reticulocyte hemoglobin content.
J Perinatol; 41(3):619

https://www.nature.com/articles/s41372-020-00845-2

Summary: In a multicentric study discordances between RET-He and serum ferritin were found in rare cases. 15 out of 16 of these discordances had a low RET-He and high serum ferritin and 13 out of the 15 had a confirmed or suspected infection or inflammation.
Kumar U et al. (2020)
Role of Reticulocyte Parameters in Anemia of First Trimester Pregnancy: A Single Center Observational Study.
J Lab Physicians; 12(1): 15

Summary: A prospective study on first trimester pregnant women revealed that RET-He values were different among normal, borderline and true anaemia, and RET-He <27.8 pg had an AUC of 0.93 for diagnosis of IDA with a sensitivity of 93%.

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/

Summary: 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

Summary: RET-He (n = 953) was investigated in a variety of conditions, involving inflammation, and its diagnostic performance was evaluated in assessing the iron status, in this study. 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

Summary: The authors suggest that RET-He could be 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 in this study to be a more reasonable test than conventional iron parameters.
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

Summary: The authors concluded that 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.

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

Summary: This study demonstrates the clinical efficacy of RET-He, %Hypo-He and %Micro-R for detecting ID in nonanemic pregnant patients. The authors point out that this is 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
[108x616]Free online: https://www.researchgate.net/publication/319877155

Summary: In this study, reticulocytes indices (Sysmex RET-He and Siemens CHr) were directly comparable. RET-He showed a slightly better predictive power for iron deficiency identification in IDA. Hypo-He (Sysmex) and %HYPO (Siemens) were not exchangeable, the authors recommended to use them 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

Summary: 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. The authors concluded that RET-He and CHr can both be used for assessing iron status.
Toki Y et al. (2017)
Reticulocyte hemoglobin equivalent as a potential marker for diagnosis of iron deficiency.
Int J Hematol; 106(1): 116
http://rd.springer.com/article/10.1007/s12185-017-2212-6

**Summary:** In this publication, 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

**Summary:** In this study, RET-He 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

**Summary:** 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

**Summary:** In this study, HYPO-He and RET-He presented as being reliable parameters for the study of erythropoiesis status in haemodialysis 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


Summary: In this study, 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.

Weimann A et al. (2016)
Delta-He, Ret-He and a New Diagnostic Plot for Differential Diagnosis and Therapy Monitoring of Patients Suffering from Various Disease-Specific Types of Anemia.
Clin Lab; 62(4): 667

Summary: A diagnostic plot using RET-He and Delta-He was developed based on differences between different patient groups suffering from anaemia. The authors showed several case examples to demonstrate the clinical utility of this plot for therapy monitoring.

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

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

Peerschke EI 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

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

Summary: In this study, RET-He and %HYPO-He are helpful in assessing erythropoiesis and iron status.

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

Summary: In this study, 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

Summary: In patients with community-acquired pneumonia, acute inflammation at an early-stage results in decreased RET-He levels reflecting acute erythropoietic dysfunction.

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

Summary: 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

Summary: The authors created a special algorithm by combining RBC-He, RET-He, and lactate dehydrogenase and used it as a marker for haemolysis which presented a strong correlation 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

Summary: 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

Summary: The authors recommended the Thomas-plot as helpful in diagnosing patients referred from general practitioners and differentiating functional iron deficiency from classical iron deficiency.

Schoorl M et al. (2010)
Free online: https://www.nvkc.nl/sites/default/files/NTKC/2010-3-p206-208.pdf


Summary: In this study, RET-He 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 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

**Summary:** This study showed that RET-He could prove superior to transferrin saturation (TSAT) and ferritin in monitoring iron status of haemodialysis patients due to a lower biological variation.

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

**Summary:** RET-He is equivalent to CHr and useful in managing haemodialysis patients with iron deficiency as it responds more rapidly than HGB, in this study.

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

**Summary:** RET-He and CHr correlate and agree well in evaluating CKD patients needing iron support, in this study.

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

**Summary:** The authors concluded that 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

Summary: A review article about anaemia of chronic disease, markers for iron deficiency and the ‘Thomas plot’, that includes RET-He. Results from a small study with 26 six critically-ill patients receiving epoetin therapy were also discussed. The ‘Thomas plot’ could predict the response to therapy to those patients that had increased erythropoietic activity after treatment.

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

Summary: In dialysis patients the authors identified RET-He as a reliable marker of cellular haemoglobin content and suggested it usage to identify iron-deficient states. RET-He and Chr presented a good agreement in this study.

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

Summary: In this study, 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

Summary: A study in 474 anaemic patients showed that RET-He and Chr had an excellent correlation (r=0.92). RET-He could replace Chr in the original ‘Thomas plot’, resulting in an agreement rate of 94.7%.
**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*

**Summary:** According to the present study RET-He may be useful to support 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*

**Summary:** The authors concluded that RET-Y closely correlates with CHr and can be used for diagnosis and early monitoring after the administration of intravenous iron.
Extended RBC parameters (HYPO-He / HYPER-He / MicroR / MacroR)

Amir N et al. (2019)
Percentage of hypochromic red cells as a potential screening test to evaluate iron status in blood donors.
Int J Lab Hematol; 41(3): 418

Summary: HYPO-He with a cut-off value of 0.6% is presented as a potential screening parameter with high sensitivity and specificity for evaluating iron status among blood donors, in this study. The authors concluded that the parameter is suitable for screening because of faster turnaround time than biochemical markers.

Schoorl M et al. (2012)
Am J Clin Pathol; 138(2): 300
Free online: https://academic.oup.com/ajcp/article/138/2/300/1761358

Summary: The authors conclude that the advanced algorithms, derived from extended RBC parameters provided by the Sysmex XE-5000 analyser, 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

Summary: The authors analysed the hereditary spherocytosis diagnostic tool by Mullier et al. and concluded that it is a useful and working tool 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

Summary: In this study it is shown that 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
Free online: https://academic.oup.com/ajcp/article/135/3/374/1766023
Summary: In this study, the new index %MicroR-%HYPO-He was the most reliable index in the differential diagnosis of microcytic anaemias due to its high sensitivity and specificity.

Urrechaga E. et al. (2011)
Erythrocyte and reticulocyte parameters in iron deficiency and thalassemia.
J Clin Lab Anal; 25(3): 223
Summary: In this study, 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
Summary: In this study, the new index %microcytic-%hypochromic was the most reliable index in the differential diagnosis of microcytic anaemia due to its high sensitivity and specificity.

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
Summary: In this study, 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.
Nucleated red blood cells (NRBC)

**Piggott K et al. (2021)**
Nucleated red blood cells as a biomarker for mortality in neonates following cardiac surgery. Cardiol Young; 32(7):1048
https://www.cambridge.org/core/journals/cardiology-in-the-young/article/abs/nucleated-red-blood-cells-as-a-biomarker-for-mortality-in-neonates-following-cardiac-surgery/1CBA9B0C143F3CCC320EF71F8466CBD1

**Summary:** In this retrospective single centre study in neonates an NRBC value of ≥10/100 WBC following cardiac surgery and an elevated NRBC value in the 14-day period post-cardiac surgery was associated with mortality (AUC of 0.9 and 0.914).

**Hüseyin N et al. (2021)**
Nucleated red blood cells as predictor of all-cause mortality in emergency department. Am J Emerg Med; 46: 335

**Summary:** A retrospective analysis of 204 samples from emergency department patients showed that NRBC was higher in patients that died compared to the ones that were discharged. NRBC was an independent predictor for mortality, with an AUC of 0.95, and a cut-off > 0 NRBC/μL had a sensitivity of 94.1% and specificity of 82.3%.

**Valina O et al. (2020)**
Free online: https://www.sysmex.co.jp/en/products_solutions/library/journal/vol30_no1/summary01.html

**Summary:** The authors compare manual NRBC count to an automated counting by XN-Series analyser for neonates, which correlates well. In addition, the mean NRBC count on different postnatal days were analysed and reference values have been stated.

**Morton SU et al. (2020)**
Association of nucleated red blood cell count with mortality among neonatal intensive care unit patients. A Pediatr Neonatol; 61(6): 592
Free online: https://linkinghub.elsevier.com/retrieve/pii/S18759572(20)30109-1

**Summary:** Neonatal ICU patients with NRBC count >0 had a significantly higher risk of mortality, and time to mortality decreased with higher NRBC counts. The authors claim that NRBC counts may be useful in refining prognostic models for neonates.
Menk M et al. (2018)
Nucleated red blood cells as predictors of mortality in patients with acute respiratory distress syndrome (ARDS): an observational study.
Ann Intensive Care; 8(1): 42

Summary: The study results confirmed previous findings in critically ill patients suggesting that NRBC are equally predictive of mortality in acute respiratory distress syndrome (ARDS). NRBC-positive patients were found to require longer treatment with mechanical ventilation, extra-corporeal gas exchange and had prolonged ICU stay when compared with NRBC-negative patients.

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/

Summary: Quote: ‘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

Summary: 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

Summary: The authors suggested that 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, in this study.
Hotton J et al. (2013)
Am J Clin Pathol; 140(6): 845
https://academic.oup.com/ajcp/article/140/6/845/1761105

**Summary:** 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

**Summary:** An excellent correlation was found between manual NRBC counts and NRBC counts from the XE-2100 (r² = 0.94) in umbilical cord blood. The authors suggest using this number 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

**Summary:** In this study, an increased count of nucleated red blood cells in preterm new-borns 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.

**Summary:** 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

Summary: In this study, 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

Summary: NRBC were found in nearly all onco-haematological diseases in this study at diagnosis and frequently during therapy. They were 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

Summary: The authors found that 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: https://ccforum.biomedcentral.com/articles/10.1186/cc5932

Summary: In this study, 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

Summary: The NRBC count is one indicator of mortality independent of other in this study analysed 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

Summary: NRBC count is an early indicator of mortality – daily screening is recommended, by the authors.

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

Summary: In this study, the NRBC count correlated 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

Summary: The authors revealed that 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

Summary: The automated NRBC count was highly correlated with the manual reference count ($r^2=0.97$). In this study the ‘optical’ platelet count significantly improves the reliability of low platelet counts.
RBC fragments (FRC)

Hisasue M et al. (2021)
Modification of the Algorithm Used by Automated Hematology Analyzer XN-3000 Improves Specificity in the Detection of Schistocytes.
Clin Lab; 67(1): 15
https://www.clin-lab-publications.com/article/3614

**Summary:** A retrospective analysis in 1,026 blood samples showed that the 'Fragments?' flag had a sensitivity of 100% and a specificity of 41.6% in detecting schistocytes. Combination of the flag and the research parameter FRC% balanced the performance of the analyser (sensitivity 86.5%, specificity 70.3%).

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

**Summary:** 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 JF et al. (2015)
Fragmented red cells reference range for the Sysmex XN®-series of automated blood cell counters.
Int J Lab Hematol; 37(5): 583

**Summary:** Normal values were determined on the XN-Series for the percentage fragmented red blood cells, FRC%: 0.14 +/- 0.35% (mean 0%). It was also found that HYPO-He correlates with FRC% so, samples with both a high HYPO-He and FRC% should be interpreted with care.

Lesesve JF 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

**Summary:** The automated FRC count offered a better degree of certainty than microscopy to exclude the presence of fragmented RBC in this study.
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

Summary: In conclusion, the FRC level was a simple and useful marker for thrombotic microangiopathy (TMA), and an FRC level of 1.2% was recommended by the authors as the cut-off 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

Summary: In this study, sequential monitoring of FRC% was a reliable marker for a specific type of complication (TTP-HUS; thrombotic thrombocytopenic purpura 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

Summary: The determination of FRC% by the XE-2100 enables early diagnoses and monitoring of TTP (thrombotic thrombocytopenic purpura) or TMA (thrombotic microangiopathy) in this study.
Malaria-infected RBC (MI-RBC)

Komaki-Yasuda K et al. (2022)
Clinical performance testing of the automated haematology analyzer XN-31 prototype using whole blood samples from patients with imported malaria in Japan.
Malaria J; 21: 229
Free online: https://malariajournal.biomedcentral.com/articles/10.1186/s12936-022-04247-x

Summary: In the present study the low malaria mode and pre-diluted mode of the XN-31p (prototype) analyser showed similar sensitivity (97%/94%) and same specificity (100%). Changes in parasitaemia during treatment monitoring were concordant in 4 out of 6 cases between microscopy and XN-31p, whereas in 2 cases were deviated.

Kayange M et al. (2022)
Automated measurement of malaria parasitaemia among asymptomatic blood donors in Malawi using the Sysmex XN-31 analyser: could such data be used to complement national malaria surveillance in real time?
Malaria J; 21: 299
Free online: https://malariajournal.biomedcentral.com/articles/10.1186/s12936-022-04314-3

Summary: The authors found that malaria prevalence in blood donors in Malawi (endemic area), measured by XN-31, correlated with seasonal and local prevalences of the disease as known from household survey. This study demonstrated the powerful utility of screening blood donors for malaria parasites using the XN-31, which not only improves the safety of blood transfusion, but provides valuable complementary surveillance data for malaria control.

Kagaya W et al. (2022)
Potential application of the haematology analyser XN-31 prototype for field malaria surveillance in Kenya.
Malaria J; 21: 252
Free online: https://malariajournal.biomedcentral.com/articles/10.1186/s12936-022-04259-7

Summary: The authors investigated the feasibility of a hub-and-spoke model for malaria diagnosis by XN-31p. Identical results for presence of malaria were found between capillary and venous blood, also short-term storage under chilled conditions, simulating storage and transport of the suggested hub-and-spoke model, had no adverse effect.
**Picot S et al. (2022)**
Diagnostic accuracy of fluorescence flow-cytometry technology using Sysmex XN-31 for imported malaria in a non-endemic setting.
Parasite; 29: 31

[Free online: https://www.parasite-journal.org/articles/parasite/full_html/2022/01/parasite210161/parasite210161.html](https://www.parasite-journal.org/articles/parasite/full_html/2022/01/parasite210161/parasite210161.html)

**Summary:** In a study conducted in the University Hospital in Lyon, France the XN-31 analyser exhibited a sensitivity of 100%, specificity of 98.4%, NPV of 100% and PPV of 96.5% when compared to microscopy. Correlation of XN-31 and microscopy regarding parasitaemia and species identification was deemed excellent. The authors consider XN-31 as a more efficient screening tool than LAMP and RDT during patient follow-up.

**Khartabil TA et al. (2022)**
Fast detection and quantification of Plasmodium species infected erythrocytes in a non-endemic region by using the Sysmex XN-31 analyzer.
Malaria J; 21: 119


**Summary:** In this study from the Netherlands the XN-31 exhibits a positive and negative predictive value of 100% while three out of 112 samples showed abnormal scattergrams. In a set of 920 samples with RBC abnormalities abnormal scattergrams occurred in 50% at a false positive rate of 4.6%. Sickle cell disease was the most frequent underlying condition. However, with a review of the scattergram, false positives can be well distinguished from true positives.

**M’Baya B et al. (2021)**
Evaluation of the Sysmex XN-31 automated analyser for blood donor malaria screening at Malawi Blood Transfusion Services.
Vox Sang; 117(3): 346


**Summary:** The malaria detection rate in 5,281 donor blood samples from malaria endemic area (Malawi) was significantly higher using XN-31 (11.6%) when compared with routine microscopy (6.5%). The latter only detected 22% of samples with low parasitaemia (< 100 parasites/μL). The XN-31 had superior sensitivity to routine microscopy (100% vs. 75%) whilst maintaining excellent specificity (98.9%).
**Zuluaga-Idárraga L et al. (2021)**

Performance of the hematology analyzer XN-31 prototype in the detection of Plasmodium infections in an endemic region of Colombia.

Malaria Sci Rep; 11(1): 5268

https://www.nature.com/articles/s41598-021-84594-y

**Summary:** The XN-31 prototype (XN-31p) was evaluated against qPCR exhibiting a sensitivity of 90.0% and a specificity of 99.8%, thus similar to the performance of microscopy and Rapid Diagnostic Test (RDT). Sensitivity of XN-31p is inferior to microscopy and RDT in detecting *P. falciparum*, however, sensitivity and specificity for detecting *P. vivax* is similar to both. Results in a small number of samples indicate similar diagnostic accuracy in capillary blood as in venous blood.

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**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/

**Summary:** 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 in this study.

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**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/

**Summary:** 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 in this study.

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**Tougan T et al. (2018)**

An automated haematology analyzer XN-30 distinguishes developmental stages of falciparum malaria parasite cultured in vitro.

Malaria J; 17(1): 59

Free online: https://malariajournal.biomedcentral.com/articles/10.1186/s12936-018-2208-6

**Summary:** Using a modified algorithm, the XN-30 research analyser could be used to recognize cultured red blood cells infected with different developmental stages of Plasmodium falciparum parasites. In addition, purified merozoites and gametocytes could be detected. The analyser may therefore be useful for research studies done on the malaria parasite.
Dumas C et al. (2018)

Automated Plasmodium detection by the Sysmex XN hematology analyzer.
J Clin Pathol; 71(7): 594

https://jcp.bmj.com/content/71/7/594.long

Summary: The study describes abnormal WDF scattergrams on the XN-Series for samples from patients infected with malaria. Most WDF scattergrams were not affected by Plasmodium falciparum infections but about 50% of non-falciparum infections caused scattergram abnormalities.
Erythrocyte sedimentation rate (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

**Summary:** Indicated by the high correlation coefficient of 0.96 the InteRRliner showed an excellent comparability to the HumaSed ESR method.

**Kratz A et al. (2017)**
ICSH recommendations for modified and alternate methods measuring the erythrocyte sedimentation rate.
Int J Lab Hematol; 39(5): 448
Free online: https://onlinelibrary.wiley.com/doi/full/10.1111/ijlh.12693

**Summary:** The gold standard for the determination of the erythrocyte sedimentation rate is still the Westergren method. The authors suggest that alternative methods should be accepted when they have been appropriately validated and their results are expressed by comparison with the gold standard.
General

**Schoorl M et al. (2022)**
Effects of iron supplementation on microcytic and hypochromic red blood cells during the third trimester of pregnancy.
Int J Lab Hematol; 44(6): 1060

**Summary:** A study in 145 third trimester pregnant women showed an increase in MicroR and Hypo-He and a decrease in RET-He, RBC-He and Delta-He in women developing iron-deficient erythroidosis (IDE) (n=39) compared to non-IDE (n=106). After four weeks of iron supplementation in the IDE group, Hypo-He, RET-He and Delta-He showed significant improvements towards their normal reference ranges.

**Combaluzier S et al. (2022)**
Detection of unstable haemoglobin variants with Sysmex XN-10.
Int J Lab Hematol; 45(2): e21

**Summary:** WDF channel of XN analysers shows a decreased fluorescence signal in blood samples of patients with unstable haemoglobin variants causing an abnormal scattergram. The optimal threshold combination to specify unstable haemoglobin variants is LY-SFL < 42 and NE-SFL < 41.2 resulting in a sensitivity of 100% and specificity of 99.9%.

**Adam AS et al. (2022)**
Rare unstable and low oxygen affinity haemoglobin variant, Hb Hazebrouck, detected on Sysmex XN-9000.
Clin Chem Lab Med; 60(5): e116

**Summary:** This is the first case of Hb Hazebrouck, an unstable Hb variant, detected with XN-9000. It shows the same distinctive pattern in the WDF measurement channel as reported in previous cases. This confirms the importance to continue investigations for the presence of 'WBC Abn Scattergram' flag and abnormal scattergram distribution.

**Nivaggioni V et al. (2022)**
Detection of Southern Asian Ovalocytosis with Sysmex XN-10: A complement to the decision tree previously described.
Int J Hematol; 44(2): e84
Summary: The authors improved the algorithm described in the Nivaggioni et al. 2020 publication with the addition of a step to detect Southeast Asian ovalocytosis (SAO) cases. All SAO samples were correctly classified using the Hypo-He/MicroR ratio, which achieved an AUC of 1.0.

Shaikh MS et al. (2021)
Ensuing adequate mixing of blood samples before analysis—A proposed method for verification of satisfactory sample mixing by automated red blood cell count analyzers.
Int J Lab Hematol; 43(3): e141

Summary: The authors report an excellent correlation (r value of 0.99) between manual and automated blood sample mixing with a minimal bias (0.009), proving an exceptional pre-analysis mixing of samples on the XN-1000 analyser.

Van der Vorm LN et al. (2021)
Performance of the CellaVision DC-1 digital cell imaging analyser for differential counting and morphological classification of blood cell.
J Clin Pathol; 76(3): 194
https://jcp.bmj.com/content/early/2021/10/18/jclinpath-2021-207863.long

Summary: The accuracy, within-run precision, clinical sensitivity and specificity of the DC-1 were all adequate compared with prespecified acceptance criteria and the DI-60. Altogether the authors state that the DC-1 is a reliable automated cell imaging analyser for the differential white blood cell (WBC) count and morphological classification of both WBCs and red blood cells on peripheral blood smears.

Rosetti M et al. (2021)
Parasitised red blood cells misclassified as giant platelets by an automated digital morphology analyser (Sysmex DI-60/ CellaVision): a case report and a retrospective EQA analysis.
Br J Haematol; 192: e66
Free online: https://onlinelibrary.wiley.com/doi/10.1111/bjh.17276

Summary: The DI-60 is not intended to be used for diagnosing malaria, however this study shows how the capturing of abnormal cells by the instrument can aid laboratory technicians to reach a diagnostic conclusion for the patient. The study emphasises the usefulness of remote review.

Albichr IS et al. (2020)
Cross-evaluation of five slidemakers and three automated image analysis systems: The pitfalls of automation?
Int J Lab Hematol; 42(5): 573

Summary: Sysmex SP-10 and SP-50 showed in the study an acceptable performance for differential leucocyte counting and a good correlation with haematology analyser results and manual differential on
HemaPrep smears. SP-10 and SP-50 showed superior performance compared with the Siemens Advia Autoslider 1, Autoslider 2 and Abbot Alinity Hs slide maker stainers.

Falvella FS et al. (2020)
Validation of the reticulocyte channel of Sysmex XN-9000 system for blood cell count in samples with suspected cold agglutination for use in a total laboratory automation setting.
J Clin Pathol; 73(12): 847
https://jcp.bmj.com/content/73/12/847.long

Summary: 40 samples with increased MCHC (> 37.0 g/dL) due to cold agglutination were tested with two different methods: 1. manual heating at 37°C for two hours and 2. XN RET channel measurement. Both methods equally resolved the falsely altered MCHC and the authors support the implementation of automated reflex tests in Extended IPU to minimise manual operations and shorten the time to result.

Ortiz A et al. (2020)
Performance Comparison of Sysmex Hematology Analyzers XN-550 and XN-10.
Sysmex J Int; 30(1): 9

Summary: The XN-550 is highly reliable with functionality comparable to the XN-10. It has shown high correlation coefficients and excellent comparative performance in all CBC, DIFF and RET parameters (except BASO%). The overall flagging comparison was excellent among the XN-10, the XN-550 and the manual differential.

Smit B et al. (2020)
Massive hemolysis due to Clostridium perfringens: a laboratory’s perspective.

Summary: A case report describing laboratory findings in two patients with Clostridium perfringens sepsis. The authors state that massive haemolysis, ghost cells in peripheral blood smear, differences in haemoglobin parameters (total haemoglobin and intraerythrocytic haemoglobin) and distinct microcytic RBC populations may occur as indirect indicators and support early recognition.
Nivaggioni V et al. (2020)
Use of Sysmex XN-10 red blood cell parameters for screening of hereditary red blood cell diseases and iron deficiency anaemia.
Int J Lab Hematol; 42(6): 697

Summary: A two-step algorithm, based on the XN RBC and reticulocyte parameters, delivers a good prediction and classification between patients with a hereditary RBC disease from iron deficiency anaemia and other patients. The proposed flowchart recommends how to manage MCHC < 36.5 g/dL (22.7 mmol/L) samples in addition to the CBC-O application to assist the diagnosis of RBC diseases. Overall, it reaches a very good classification rate of 99.4%, confirmed by an external cohort.

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

Summary: 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 × 10e9/L in combination with positive CBC criteria can identify JAK2 V617F mutation-positive PV patients.

Moioli V et al. (2019)
Mozhaisk haemoglobin variant effects on leukocyte differential channel using the Sysmex XN series.
Chem Lab Med; 57(12): e324
https://www.degruyter.com/view/journals/cclm/57/12/article-pe324.xml

Summary: Case study showing an abnormal WDF scattergram with a decrease of the fluorescence signal, causing the flag 'WBC Abn Scattergram'. In association with the microscopic revision and further genetic analysis an unstable haemoglobin (Hb Mozhaisk) was confirmed.

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

Summary: 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 in this study.
Jongbloed W et al. (2018)
Unstable haemoglobin variant Hb Leiden is detected on Sysmex XN-Series analysers.
Clin Chem Lab Med; 56(9): e249
https://www.degruyter.com/view/journals/cclm/56/9/article-pe249.xml

**Summary**: Case study with an abnormal WDF scattergram observed on the XN-9000 causing the flag "WBC abnormal scattergram" which highlighted the inability to separate the white blood cell population. Further genetic analysis confirmed an unstable haemoglobin.

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
Free online: https://doi.org/10.1093/labmed/lmw072

**Summary**: 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

**Summary**: The XN-550 showed a good analytical performance and strong correlation with XE-2100 and XN-3000 analysers for routine CBC parameters.

Teixeira C et al. (2017)
Automated detection of unstable hemoglobin variants by Sysmex XE-Series analyzers.

**Summary**: The authors tested 9 samples with known unstable HGB variants and reported that only the XE-2100 flagged the samples in contrast to the SIEMENS Healthineers ADVIA.
Tailor H et al. (2017)
Evaluation of the Sysmex XN-550, a Novel Compact Haematology analyser from the XN-L® series, compared to the XN-20 system.
Int J Lab Hematol; 39(6): 585

**Summary:** Samples from adult patients (N=202) were measured on the XN-550 and compared with an XN-20. Good correlations and low bias were observed for all parameters except for BASO%. PLT-O from the XN-550 showed no significant bias compared to PLT-F from the XN-20.

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

**Summary:** The use of the optical RBC parameters from the XN-Series saved time and helped in the determination of the cause of increased MCHC, in this study.

Tamigniau A et al. (2017)
From XE-2100 to XN-9000, from SIS Standard to GFHC recommendations for slide review: potential impact on review rate and turnaround time.
Ann Biol Clin (Paris); 75(3): 285
https://doi.org/10.1684/abc.2017.1242

**Summary:** Changing from the XE-2100 to XN-9000 and implementing the Biomedical Validation ruleset led to a significant reduction in review rate (from 35.8% to 25.9%) and TAT. In this hospital this resulted in a cost reduction of 7000 Euros over 6 months.

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

**Summary:** The authors report the cut-off values for most of the RBC abnormalities that can be detected by the Advanced RBC Morphology software.
**Geara C et al. (2016)**
Comparative study of quantitative performances between the new Sysmex XN-L (XN-550) haematology analyser and the XN-9000 in a routine laboratory.
Int J Lab Hematol; 38(1): e10

**Summary:** The XN-Series and XN-L Series were compared; correlations were good and the study showed that the XN-L Series provided the same high quality as the XN-Series.

**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

**Summary:** In this study 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

**Summary:** Using the biomedical validation criteria, 21.3% of samples triggered a smear review. Modification of four criteria by the authors reduced the number of smears from 21.3% to 15.0% without loss of clinical value.

**Bruegel M et al. (2015)**
Clin Chem Lab Med; 53(7): 1057
https://www.degruyter.com/view/journals/cclm/53/7/article-p1057.xml

**Summary:** 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.


**Summary:** 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.

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**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


**Summary:** The authors report excellent detection of teardrop cells in samples from patients with myelofibrosis and MDS, using the Advanced RBC Morphology software.

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**Ferrero-Vacher C et al. (2015)**

Utilisation des paramètres érythrocytaires Sysmex dans un cas d’hémolyse sèvere (Erythrocytic parameters Sysmex in a case of severe haemolysis).
Annales de Biologie Clinique; 73(6): 729

[Article in French: https://doi.org/10.1684/abc.2015.1093](https://doi.org/10.1684/abc.2015.1093)

**Summary:** 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.

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**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/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6807107/)

**Summary:** This paper gives a good overview of the technology behind the XE-Series and the benefits of flow cytometry and automatic cell counting. In this study 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

Summary: 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

Summary: 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)
Am J Clin Pathol; 140(6): 845
Free online: https://academic.oup.com/ajcp/article/140/6/845/1761105

Summary: 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

Summary: 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.
**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](https://jcp.bmj.com/content/65/11/1024.long)

**Summary:** 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.

**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/e-docs/anomalies_et_erreurs_de_determination_de_lhemogramme_avec_les_automates_dhematologie_cellulaire_partie_3_hemoglobine_hematies_indices_erythrocytaires_reticulocytes_292317/article.phtml](http://www.jle.com/fr/revues/e-docs/anomalies_et_erreurs_de_determination_de_lhemogramme_avec_les_automates_dhematologie_cellulaire_partie_3_hemoglobine_hematies_indices_erythrocytaires_reticulocytes_292317/article.phtml)*

**Summary:** 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.

**Urrechaga E et al. (2011)**
Erythrocyte and reticulocyte parameters in iron deficiency and thalassemia.
J Clin Lab Anal; 25: 223


**Summary:** In this study beta-thalassaemia was recognised through high RBC, small MCV, high %MicroR and moderately increased IRF, whereas iron deficiency showed high RDW and %HYPO-He.
Reference intervals

Becker M et al. (2022)
Differences between capillary and venous blood counts in children—A data mining approach.
Int J Lab Hematol; 44(4): 729
Free online: https://onlinelibrary.wiley.com/doi/10.1111/ijlh.13846

Summary: In this multicentric study the differences between capillary and venous bloods were investigated in paediatric samples specifying a delta for the CBC parameters dependant on measurement range of the parameter value, time difference in sampling and age of the patient.

L van Pelt J et al. (2022)
Reference intervals for Sysmex XN hematological parameters as assessed in the Dutch Lifelines cohort.
Clin Chem Lab Med; 60(6): 907

Summary: The publication provides reference intervals for 105 XN parameters (incl. functional and cell activation parameters) based on data of 15,803 healthy individuals from the Lifelines cohort in the Netherlands. The reference intervals were calculated in accordance to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) recommended statistical methods.

Song MY et al. (2021)
Establishment of pediatric reference intervals for complete blood count parameters in capillary blood in Beijing.
Int J Lab Hematol; 43(6): 1363

Summary: The authors established reference intervals for 22 CBC+DIFF parameters from capillary blood in 6799 children aged 3 months to 18 years from Beijing area in China.

Mrosewski I et al. (2021)
Indirectly determined hematology reference intervals for pediatric patients in Berlin and Brandenburg.
Clin Chem Lab Med; 60(3): 408

Summary: The study presents indirectly determined CBC reference intervals (RI) for paediatric patients (0-18 years) in Berlin and Brandenburg area in Germany.
Wilson S et al. (2021)
Continuous reference curves for common hematology markers in the CALIPER cohort of healthy children and adolescents on the Sysmex XN-3000 system.
Int J Lab Hematol; 43(6): 1394

**Summary:** First study that generated continuous reference intervals (curves) of healthy children and adolescents for 19 haematological XN parameters. Seven parameters required sex-specific reference curves. Continuous reference intervals were found to be accurate estimate of haematological reference ranges over the paediatric age range.

Bahr TM et al. (2021)
Neonatal Reference Intervals for the CBC Parameters "Micro-R" and "HYPO-He": Sensitivity Beyond the Red Cell Indices for Identifying Microcytic and Hypochromic Disorders.
J Pediatr; 236: 95
https://www.jpeds.com/article/S0022-3476(21)00757-5/fulltext

**Summary:** The authors created retrospectively neonatal reference intervals for MicroR% and HYPO-He. They were measured as part of a neonate’s CBC with no additional phlebotomy volume or run-time and identified identify microcytic and hypochromic disorders even when the red cell indices were normal.

Angelo A et al. (2021)
Umbilical cord blood hematological parameters reference interval for newborns from Addis Ababa, Ethiopia.
BMC Pediatrics; 21: 275
Free online: https://bmcpediatr.biomedcentral.com/articles/10.1186/s12887-021-02722-z

**Summary:** This pilot study enrolled 139 umbilical cord blood samples from healthy newborns to establish reference values for the KX-21N. For WBC, RBC, and NEUT significant differences were found between caesarean and natural birth.

Florin L et al. (2020)
Establishment of common reference intervals for hematology parameters in adults, measured in a multicenter study on the Sysmex XN-series analyzer.
Int J Lab Hematol; 42(3): e110

**Summary:** The study provides reference intervals (CBC+DIFF+RET) that could serve as reference values for haematology parameters in adults for laboratories that use the XN-Series analysers.
**Bohn MK** *et al.* (2020)
Int J Lab Hematol; 42(6): 750


**Summary**: The study establishes comprehensive paediatric (birth to 21 years) reference intervals for haematology parameters using the XN analyser. The data highlight the dynamic haematological profiles observed in healthy children and adolescents and the need for reference interval stratification by age and sex.

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**Ianni B** *et al.* (2020)
Defining Normal Healthy Term Newborn Automated Hematologic Reference Intervals at 24 Hours of Life.
Arch Pathol Lab Med; 145(1): 66


**Summary**: Reference intervals on Sysmex XN-Series for normal healthy term new-borns at 23-25 hours of life were prospectively established for CBC, IG%, IG#, IRF, RET-He, IPF and IPF#.

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**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/)

**Summary**: 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.

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**Ozarda Y** *et al.* (2017)
A nationwide multicentre study in Turkey for establishing reference intervals of haematological parameters with novel use of a panel of whole blood.
Biochem Med (Zagreb); 27(2): 350


**Summary**: Using the Cell Dyn and Ruby (Abbott), LH780 (Beckman Coulter) and XT-2000i (Sysmex) analysers, Turkish reference intervals were obtained for CBC-DIFF parameters. Analyser-specific reference intervals were reported for BASO%, BASO#, MCHC, RDW and MPV.