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HAEMATOLOGY WHITE PAPER | February 2024

HSCT management

Managing haematopoietic stem cell transplantation challenges

Haematopoietic stem cell transplantation

Haematopoietic stem cell transplantation (HSCT) is a treatment that involves suppressing a patient's haematopoietic system by chemotherapy or radiotherapy and replacing it either with stem cells previously harvested from this patient (autologous transplantation) or with cells from another individual (allogeneic transplantation). One of the benefits of this treatment is that it lets one use more aggressive treatment in patients with resistant tumours. In addition, the transplanted cells themselves may have a curative effect on the patient's haematologic malignancies [1, 2].

The advances in the clinical protocols for HSCT have led to a significant increase in the number of transplantations performed worldwide. Starting with the first HSCT in 1957, the millionth transplantation was performed in 2012 [3], and by 2019 that number has reached 1.5 million transplantations [4], showing the continuous increase in the adaptation of this procedure.

Traditionally, haematopoietic stem cells have been harvested from bone marrow. Nowadays, peripheral blood enriched with mobilised stem cells is used several times more frequently than bone marrow [5]. Peripheral blood has several advantages over bone marrow as a source of stem cells. Collecting haematopoietic stem cells from peripheral blood is less invasive than sourcing them from bone marrow and does not require anaesthesia. Neutrophil and platelet reconstitution, the markers of successful post-transplantation engraftment, occurs earlier after peripheral blood stem cell transplantation than after bone marrow transplantation [6].

Cord blood haematopoietic stem cells are also used to a smaller extent, usually in children, or in patients where a compatible bone marrow donor or mobilised peripheral blood stem cells could not be found [7]. It is predicted that peripheral blood will continue to be the major source of haematopoietic stem cells for HSCT in the future, and that the annual number of transplantations will continue to increase [4].

This white paper focuses on the different phases of a haematopoietic stem cell transplantation (see Fig. 1), the challenges faced by clinicians during the process, and how advanced clinical parameters from Sysmex haematology analysers can support the clinician with valuable additional information over these phases.

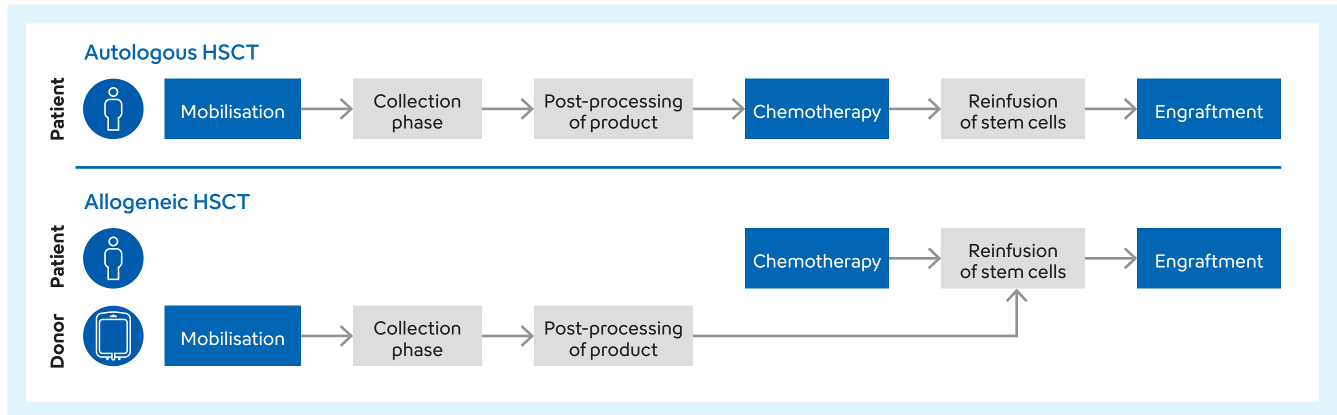

Fig. 1 Simplified schematic of the HSCT phases for autologous and allogeneic transplantations. Blue boxes: phases where Sysmex parameters can be utilised. Grey boxes: phases where Sysmex parameters do not provide information.

Clinical challenges

When caring for the patient, different questions arise depending on the phases of HSCT:

- Have enough stem cells been mobilised?
- Does the patient show signs of an infection?
- Did the platelets reach a critically low level?
- Are there signs of bone marrow recovery?

Stem cell mobilisation

During this phase, the patient or the donor of the stem cells is receiving a cytokine regimen that will mobilise the haematopoietic stem cells (characterised as CD34+ by flow cytometry) and increase their concentration in the peripheral blood. The dose and schedule of the cytokine regimens used for mobilising stem cells, such as G-CSF or plerixafor, vary among transplant centres and depend strongly on the range of the pathologies being treated [8]. Most transplant groups use a five-day regimen, starting stem cell collection on the fifth day. However, some centres report shorter mobilisation periods of four and even three days of cytokine administration [9].

In healthy donors, the percentage of CD34+ cells circulating amongst the total nucleated cell population in peripheral blood in a steady state is approximately 0.06 %, or 2–5/μL. However, the mobilisation of stem cells from bone marrow into peripheral blood prior to stem cell collection increases the concentration of stem cells by a factor of 10 to 100. The optimal concentration of stem cells for successful engraftment is 5 to 10 × 10^6 CD34+ cells/kg of recipient body weight. The minimum concentration is 2 × 10^6 CD34+ cells/kg body weight. Established thresholds for initiating collection may vary across countries and centres, but typically range from 10 to 20 CD34+ cells/μL [6].

Before starting stem cell collection, the mobilisation success has to be assessed to decide whether stem cell collection can be started. Historically, an increase in the WBC count has been seen as a marker for stem cell mobilisation. However, it is reported that a WBC count correlates only weakly with the CD34+ count in mobilised peripheral blood [10].

CD34+ cells are enumerated in mobilised peripheral blood using immune flow cytometry according to the suggested ISHAGE protocol [11]. In general, commercially available kits for staining CD34+, CD45 and apoptosis/cell viability marker 7AAD are used.

On average, the CD34+ count in mobilised blood is performed two to three times in autologous transplantations, and once in allogeneic transplantations on the donor blood. Even though CD34+ flow cytometry is the current 'gold standard' for stem cell evaluation, the method has some limitations.

Firstly, the procedure is lengthy. The sample requires labelling and several washing steps, and the full analysis procedure may take up to 1.5 hours. Secondly, the commercial antibody kits are rather expensive. Thirdly, correct gating of the cell populations on the flow cytometer requires experienced laboratory personnel, and results may vary significantly depending on the flow cytometer's operator. Other factors that affect the variation of the counts within and between the laboratories include the type of flow cytometer, the protocol used, and the antibody manufacturer [12]. Finally, external quality control schemes showed a high variation in CD34+ counts between laboratories [13], and there are reported cases when anti-CD34+ antibodies interacted with substances in the plasma and caused false-positive CD34+ analysis results [14].

Mobilisation assessment with HPC mode
Sysmex haematology analysers equipped with a WPC (white precursor and pathological cells) channel can measure haematopoietic progenitor cells (HPC) (see Fig. 2). Automated progenitor cell counting is a very simple, reliable and standardised method: 190 μL of blood are aspirated and the result is available in a few minutes with no need for manual gating, pre-treatment or sample washing. Four separate HPC counts are performed from the 190 μL aliquot, after which the mean value of the four measurements is reported, making the analysis particularly accurate and reliable. Haematopoietic progenitor cells are reported as an absolute (HPC#) and a relative count (HPC% – a percentage of the total white blood cells).

HPC are enumerated on the Sysmex haematology analyser using fluorescence flow cytometry. During analysis, signals of forward scattered light, sideward scattered light and side fluorescence light are recorded. Forward scatter (FSC) corresponds to the size of the cell and side scatter (SSC) to the internal structural complexity/granularity. The fluorescence intensity (SFL) depends on several factors, such as the cell's state of maturity and whether it is reactive or suspected malignant in origin [15].

In the WPC channel, the fluorescence intensity of cells depends on the cells' permeability to the WPC reagent. A high degree of membrane damage by the reagent leads to cellular content leaking through the pores, a decreased cell size, and higher fluorescence intensity since more fluorescence marker can enter the cell and bind to the DNA.

Immature progenitor cells differ from the more mature cells by their membrane lipid composition. Membranes of progenitor cells are relatively resistant to permeabilisation by the WPC reagent. As a result, progenitor cells are medium in size (medium FSC), have a low granularity (low SSC) and relatively low fluorescence intensity (low-medium SFL) (see Fig. 2).

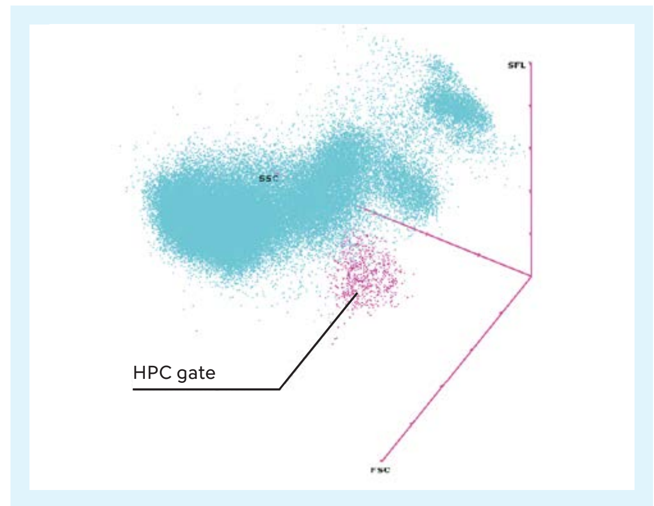

Fig. 2 HPC cluster in the 3D model of a WPC channel scattergram.

Numerous studies have shown a good correlation between HPC and CD34+ count from flow cytometry in mobilised peripheral blood, in both autologous and allogeneic HSCT and in a wide variety of conditions [16–24]. The main findings from these studies are summarised in Table 1.

Table 1 Overview of HPC and CD34 correlation studies.

Study	HPC-CD34 correlation (r)	Cohort	Main diseases in autologous cohorts
Tanosaki R *et al.* [16]	0.919	6 autologous 16 allogeneic	N/A
Peerschke EI *et al.* [17]	0.88	99 autologous 8 allogeneic	43 % myeloma 42 % lymphoma
Grommé M *et al.* [18]	0.917	84 autologous 18 allogeneic	45 % multiple myeloma 25 % non-Hodgkin's lymphoma
Dima F *et al.* [19]	0.926 allogeneic: 0.849 lymphoma: 0.976 multiple myeloma: 0.887	176 autologous 97 allogeneic	47 % lymphoma, 47 % multiple myeloma
Furundarena JR *et al.* [20]	autologous: 0.976 allogeneic: 0.787	50 autologous 30 allogeneic	N/A
Mishra S *et al.* [21]	0.89 autologous: 0.66 allogeneic: 0.87	35 autologous 67 allogeneic	66 % multiple myeloma
Kim SM *et al.* [22]	0.71	171 autologous	43 % plasma cell neoplasm 54 % lymphoma
Reberšek K *et al.* [23]	0.732 autologous: 0.708 allogeneic: 0.923	94 autologous 16 allogeneic	63 % multiple myeloma 20 % lymphoma
Al Mamari S *et al.* [24]	0.79	7 autologous 15 allogeneic	N/A

Several of these studies also examined the use of HPC as a marker to determine the optimal starting point of stem cell collection (apheresis), and identified specific cut-off values according to the underlying disease of the recipient or the graft type of stem cell transplantation [19, 20, 23]. Sysmex recommends that the laboratories evaluate which cut-off value best suits their routine as it will depend on the range of pathologies in their transplantation centre.

Stem cell collection (apheresis)

The next step in the HSCT process is the collection of the mobilised stem cells from the peripheral blood. Mobilised stem cells are collected using a blood separator, in a procedure lasting several hours, usually four to five. On average, three times the body's blood volume is passed through the separator. In some cases, where mobilisation is poor, several apheresis procedures may be required on consecutive days to obtain a sufficient number of stem cells, which is inconvenient for the donors.

After the first apheresis cycle, when a single body's blood volume has passed through the separator, the concentration of stem cells in the donor's peripheral blood drops significantly and keeps falling after each consecutive round due to the removal of stem cells from the blood stream. On the other hand, stem cells continue to be mobilised from bone marrow into peripheral blood during apheresis, and up to 55 % of the stem cells in the final apheresis product represent those mobilised during the apheresis procedure itself. Both the drop in stem cell concentration and the mobilisation during apheresis vary substantially among individuals [25, 26].

Apheresis centres use a formula to calculate the required volume of apheresis and to predict the stem cell yield, based on the CD34+ count pre-apheresis in the mobilised blood, the expected efficiency of apheresis and the weight of the patient [27]. Usually there is no intervention during stem cell collection. However, some laboratories perform a CD34+ count from the apheresis bag after the first collection round to assess whether the collection is running at the predicted efficiency and will yield a sufficient number of stem cells.

Apheresis product post-processing

Following the collection of the mobilised stem cells, some guidelines require a CD34+ count to be performed in the final product [11]. In some hospitals, however, stem cell collection, post-processing of the product, storage and the transplantation itself are carried out at different locations.

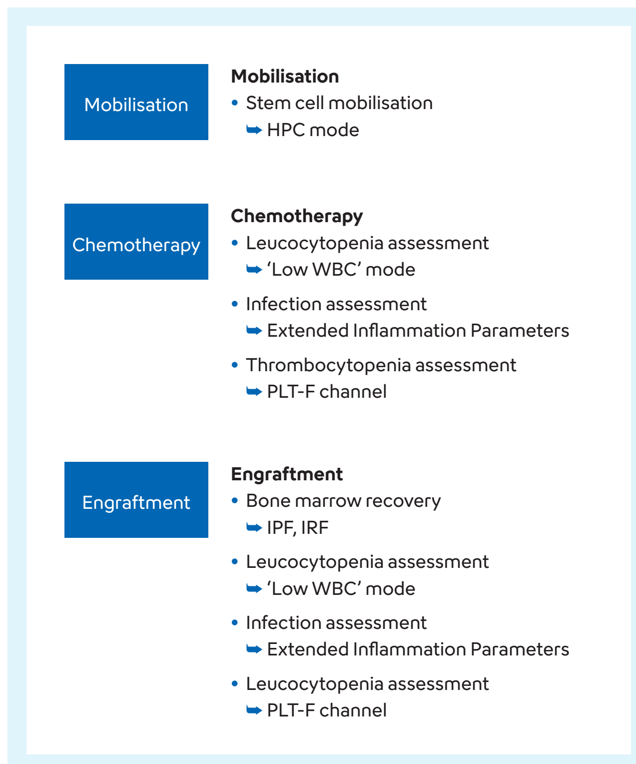

Fig. 3 Application of Sysmex parameters during phases of HSCT.

Chemotherapy

Chemotherapy is an intensive treatment, where the patient's own haematopoietic system is being either completely eradicated or severely compromised. In autologous transplantation, apart from being part of the treatment regimen leading to the transplantation, chemotherapy is conducted after stem cell mobilisation and collection in order to make room for the transplanted stem cells. In allogeneic transplantations, the patient receives a final high-dose chemotherapy prior to stem cell infusion in order to eradicate any remaining cancer cells and also compromise their own immune system to avoid graft rejection. In both cases, patients undergoing chemotherapy are often severely leucocytopenic, thrombocytopenic and have a high risk of infection [1]. Several studies in non-chemotherapy patients presented below have shown how a Sysmex haematology analyser can provide valuable information in those conditions.

Leucocytopenia and infection assessment
Highly precise and reliable white blood cell count and differential results for severely leucocytopenic samples status can be obtained from a routine blood count by the Sysmex haematology analysers using the 'Low WBC' mode [28]. Sysmex analysers can also offer various haematological parameters that quantify activated neutrophil and lymphocyte populations (Extended Inflammation Parameters) [29].

Several research studies have shown that these parameters correlate with the early detection and monitoring of infections [30–32]. The structural neutrophil parameters were shown to predict the appearance of later-stage infection markers such as the presence of immature granulocytes [30].

Furthermore, studies found that both RE-LYMP (reactive lymphocytes) and AS-LYMP (antibody-synthesizing lymphocytes) counts were mainly increased in viral infections. RE-LYMP counts were only increased in some bacterial infections and AS-LYMP counts were only mildly increased in bacterial infections (non-specific T-independent plasma cells) [33].

Further studies in children younger than five years or in HIV patients showed that NEUT-RI (neutrophil reactivity) was increased in patients with bacterial infections compared to controls. However, only RE-LYMP and AS-LYMP counts were significantly higher in patients with viral infections than in patients with bacterial infections or in healthy individuals [29, 34].

These parameters, among others, may therefore help to detect and differentiate infections so that effective countermeasures can be taken without delay. For more detailed information about the inflammation- and infection-related parameters on Sysmex haematology analysers analysers please refer to the white paper 'Novel haematological parameters for investigation of the immune system response'.

Thrombocytopenia assessment
During and immediately after chemotherapy, patients often have a low platelet count due to the depletion of megakaryocytes, the precursors of platelets, in the bone marrow. Low platelet counts are associated with a high risk of bleeding, and often require a platelet transfusion. A range of thresholds from 10 to 50 × 10^9 platelets/L is used to initiate prophylactic transfusion in stable patients or when there is an associated risk factor such as splenomegaly, coagulation factor deficiencies or severe bleeding [35]. However, transfusion can manifest severe side effects, such as higher risk of viral infection, bacterial contamination and alloimmunisation, and should therefore be avoided whenever possible [36]. It is therefore important to accurately count platelets at the transfusion threshold range (10 to 50 × 10^9 platelets/L, depending on the hospital).

Sysmex haematology analysers offer a very accurate platelet count with a fluorescence flow cytometry channel (PLT-F), which has an excellent correlation with the reference method of immune flow cytometry [37] and delivers reliable platelet counts in severely thrombocytopenic patients [38, 39].

Stem cell engraftment

After infusion, the stem cells find their way from the blood to the bone marrow through chemotaxis and a so-called 'homing effect'. After settling in the bone marrow niche, stem cells start to divide asymmetrically to generate another stem cell and a haematopoietic progenitor. These progenitors will eventually replenish the patient's whole haematopoietic system. On average, this process takes up to two weeks, but the time of engraftment depends very much on the prior malignancy and the therapy regimen [40].

While the haematopoietic system recovers (engraftment phase), the patient is very vulnerable to infections and at the risk of bleeding due to severe thrombocytopenia. Sysmex solutions for these complications have been described in the chapter 'Chemotherapy'.

Bone marrow recovery assessment
The main clinical challenge, though, at this phase is knowing as early as possible that the engraftment has been successful and whether functional mature blood cells will soon be at a sufficient concentration to substantially reduce the risk of infection or bleeding. Signs of an activated bone marrow activity can be found in the presence of immature blood cells in the peripheral blood, such as immature reticulocytes and immature platelets [41].

Sysmex haematology analysers can quantify immature reticulocytes and immature platelets with the fluorescence channels RET and PLT-F respectively. Specifically, the immature reticulocyte fraction (IRF) parameter indicates the least mature reticulocytes, and the immature platelet fraction (IPF) parameter indicates the ratio of immature platelets to the total number of platelets. Several studies have shown that the presence or IRF or IPF correlates and predicts successful bone marrow recovery after HSCT [41–43].

IRF, a parameter that describes cells from the erythroid lineage, showed a good correlation with neutrophil engraftment [41, 42]. This phenomenon can be explained as all cell lineages originate from a common progenitor. The IRF increase was observed five days before the neutrophil count increase (see Fig. 4a). The cut-off value for IRF indicating successful transplantation of neutrophils ranged from 6.2 to 10 % in these studies [41, 42].

Research studies presented IPF as a marker for the successful transplantation of the megakaryocyte lineage and for platelet recovery. These studies showed an increase in IPF four to five days before the increase in PLT count (see Fig. 4b) [41–44]. Different studies have used different cut-off values for IPF as a predictor of successful transplantation, ranging from 3.5 to 10 % [41–44]. For the clinician, the IPF value in the transplantation phase after HSCT could serve as an indication of an imminent recovery of the platelet count, thus avoiding unnecessary platelet transfusions. Similarly to IRF, IPF was also shown to correlate with recovery of cells outside of the expected cell lineage, namely red blood cells [43].

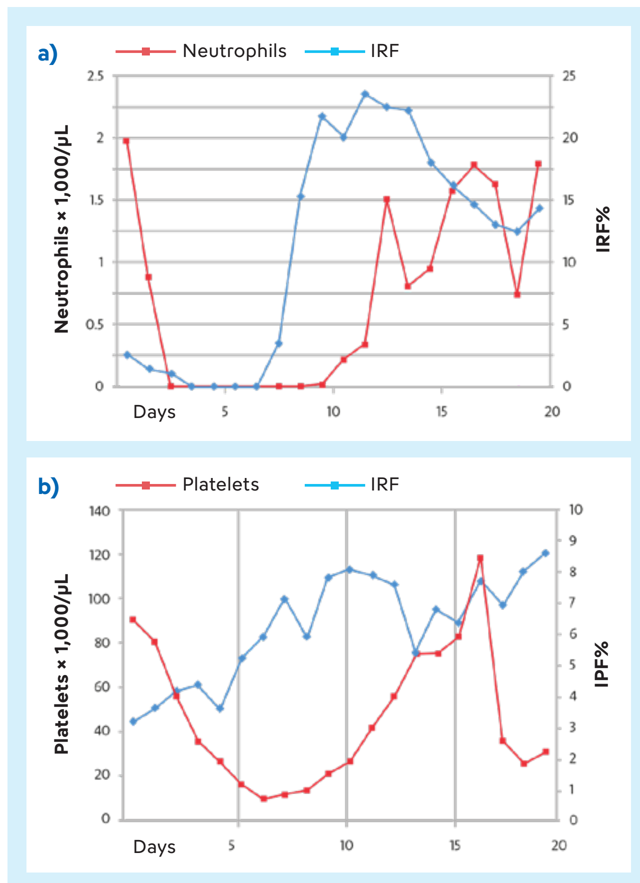

Fig. 4 IRF and IPF as markers of bone marrow recovery after HSCT. Modified from Morkis *et al.* 2014 [12]. a) Neutrophil and IRF kinetics after HSCT. b) Platelet and IPF kinetics after HSCT.

Conclusion

HSCT is an effective but challenging therapy for haematologic malignancies and some other conditions. A successful HSCT depends very much on the care of the patient during the chemotherapy and recovery stage.

The Sysmex haematology analysers provide parameters that can assist in the assessment of patients during chemotherapy, stem cell mobilisation and stem cell engraftment (see Fig. 3):

- Reliable WBC counts and differentials from severely leucocytopenic samples thanks to a special ‘Low WBC’ mode.
- A combination of special white blood cell parameters for the investigation of the immune system response
- PLT-F measurements for a highly accurate platelet count, also in severely thrombocytopenic samples
- HPC count for the enumeration of mobilised haematopoietic stem cells
- IPF and IRF parameters for following-up bone marrow activity after stem cell infusion

All the parameters mentioned above can be obtained alongside a CBC with a routine blood test and so do not place any additional strain on the patient.

References

[1] **Copelan EA. (2006):** Hematopoietic stem-cell transplantation. N Engl J Med 354(17): 1813–26.

[2] **Hatzimichael E *et al.* (2010):** Hematopoietic stem cell transplantation. Stem Cells Cloning 3: 105–17.

[3] **Gratwohl A *et al.* (2015):** One million haemopoietic stem-cell transplants: a retrospective observational study. Lancet Haematol 2(3): e91–100.

[4] **Niederwieser D *et al.* (2022):** One and a half million hematopoietic stem cell transplants: continuous and differential improvement in worldwide access with the use of non-identical family donors. Haematologica 107(5): 1045–53.

[5] **Gratwohl A *et al.* (2010):** Hematopoietic stem cell transplantation: a global perspective. JAMA 303(16): 1617–24.

[6] **Körbling M *et al.* (2001):** Peripheral blood stem cell versus bone marrow allotransplantation: does the source of hematopoietic stem cells matter? Blood 98(10): 2900–8.

[7] **Gupta AO *et al.* (2020):** Umbilical Cord Blood Transplants: Current Status and Evolving Therapies. Front Pediatr 8: 570282.

[8] **Shaughnessy P *et al.* (2013):** Plerixafor and G-CSF for autologous stem cell mobilization in patients with NHL, Hodgkin's lymphoma and multiple myeloma: results from the expanded access program. Bone Marrow Transplant 48(6): 777–81.

[9] **Bonig H *et al.* (2012):** Mobilization of hematopoietic stem/progenitor cells: general principles and molecular mechanisms. Methods Mol Biol 904: 1–14.

[10] **Yu J *et al.* (1999):** The predictive value of white cell or CD34+ cell count in the peripheral blood for timing apheresis and maximizing yield. Transfusion 39(5): 442–50.

[11] **Barnett D *et al.* (1999):** Guideline for the flow cytometric enumeration of CD34+ haematopoietic stem cells. Prepared by the CD34+ haematopoietic stem cell working party. General Haematology Task Force of the British Committee for Standards in Haematology. Clin Lab Haematol 21(5): 301–8.

[12] **Levering WH *et al.* (2007):** Flow cytometric CD34+ stem cell enumeration: lessons from nine years' external quality assessment within the Benelux countries. Cytometry B Clin Cytom 72(3): 178–88.

[13] **Moroff G *et al.* (2006):** Multiple-laboratory comparison of in vitro assays utilized to characterize hematopoietic cells in cord blood. Transfusion 46(4): 507–15.

[14] **Liwski CJ *et al.* (2014):** Discordant CD34+ cell results in peripheral blood and hematopoietic progenitor cell-apheresis product: implications for clinical decisions and impact on patient treatment. Transfusion 54(3): 541–4.

[15] **Schuff-Werner P *et al.* (2016):** Performance of the XN-2000 WPC channel-flagging to differentiate reactive and neoplastic leukocytosis. Clin Chem Lab Med 54(9): 1503–10.

[16] **Tanosaki R *et al.* (2014):** Novel and rapid enumeration method of peripheral blood stem cells using automated hematology analyzer. Int J Lab Hematol 36(5): 521–30.

[17] **Peerschke EI *et al.* (2015):** Evaluation of new automated hematopoietic progenitor cell analysis in the clinical management of peripheral blood stem cell collections. Transfusion 55(8): 2001–9.

[18] **Grommé M *et al.* (2017):** Multicenter study to evaluate a new enumeration method for hematopoietic stem cell collection management. Transfusion 57(8): 1949–55.

[19] **Dima F *et al.* (2020):** Assessment of haematopoietic progenitor cell counting with the Sysmex((R)) XN-1000 to guide timing of apheresis of peripheral blood stem cells. Blood Transfus 18(1): 67–76.

[20] **Furundarena JR *et al.* (2020):** Evaluation of the predictive value of the hematopoietic progenitor cell count using an automated hematology analyzer for CD34+ stem cell mobilization and apheresis product yield. Int J Lab Hematol 42(2): 170–9.

[21] **Mishra S *et al.* (2021):** A study to compare Hematopoietic Progenitor Cell count determined on a next-generation automated cell counter with flow cytometric CD34 count in peripheral blood and the harvested peripheral blood stem cell graft from autologous and allogenic donors. Int J Lab Hematol 43(1): 76–83.

[22] **Kim SM *et al.* (2021):** Correlation between peripheral blood automated hematopoietic progenitor cell counts and flow cytometric CD34(+) cell counts differs according to diagnosis in patients undergoing autologous peripheral blood stem cell transplantation. J Clin Apher 36(5): 737–49.

[23] **Reberšek K *et al.* (2021):** Hematopoietic progenitor cell counting can optimize peripheral blood stem cell apheresis process. J Clin Apher 36(6): 870–7.

[24] **Al Mamari S *et al.* (2022):** Measurement of hematopoietic progenitor cells using XN2000 hematology analyzer. Int J Lab Hematol 44(1): 82–7.

[25] **Humpe A *et al.* (2013):** Successful mobilization, intra-apheresis recruitment, and harvest of hematopoietic progenitor cells by addition of plerixafor and subsequent large-volume leukapheresis. Transfus Med Hemother 40(4): 251–7.

[26] **Hester J. (2000):** Peripheral blood stem cell collection: the interaction of technology, procedure, and biological factors. Transfus Sci 23(2): 125–32.

[27] **Hosing C *et al.* (2014):** Peripheral blood stem cell yield calculated using preapheresis absolute CD34+ cell count, peripheral blood volume processed, and donor body weight accurately predicts actual yield at multiple centers. Transfusion 54(4): 1081–7.

[28] **Seo JY *et al.* (2015):** Performance evaluation of the new hematology analyzer Sysmex XN-Series. Int J Lab Hematol 37(2): 155–64.

[29] **Henriot I *et al.* (2017):** New parameters on the hematology analyzer XN-10 (SysmexTM) allow to distinguish childhood bacterial and viral infections. Int J Lab Hematol 39(1): 14–20.

[30] **Cornet E *et al.* (2015):** Contribution of the new XN-1000 parameters NEUT-RI and NEUT-WY for managing patients with immature granulocytes. Int J Lab Hematol 37(5): e123–6.

[31] **Luo Y *et al.* (2013):** Utility of neut-X, neut-Y and neut-Z parameters for rapidly assessing sepsis in tumor patients. Clin Chim Acta 422: 5–9.

[32] **Park SH *et al.* (2015):** Sepsis affects most routine and cell population data (CPD) obtained using the Sysmex XN-2000 blood cell analyzer: neutrophil-related CPD NE-SFL and NE-WY provide useful information for detecting sepsis. Int J Lab Hematol 37(2): 190–8.

[33] **Prodjosoewojo S *et al.* (2019):** A novel diagnostic algorithm equipped on an automated hematology analyzer to differentiate between common causes of febrile illness in Southeast Asia. PLoS Negl Trop Dis 13(3): e0007183.

[34] **Lemkus L *et al.* (2022):** The utility of extended differential parameters as a biomarker of bacteremia at a tertiary academic hospital in persons with and without HIV infection in South Africa. PLoS One 17(2): e0262938.

[35] **Kaufman RM *et al.* (2015):** Platelet transfusion: a clinical practice guideline from the AABB. Ann Intern Med 162(3): 205–13.

[36] **Kiefel V. (2008):** Reactions Induced by Platelet Transfusions. Transfus Med Hemother 35(5): 354–8.

[37] **Wada A *et al.* (2015):** Accuracy of a New Platelet Count System (PLT-F) Depends on the Staining Property of Its Reagents. PLoS One 10(10): e0141311.

[38] **Schoorl M *et al.* (2013):** New fluorescent method (PLT-F) on Sysmex XN2000 hematology analyzer achieved higher accuracy in low platelet counting. Am J Clin Pathol 140(4): 495–9.

[39] **Tanaka Y *et al.* (2014):** Performance evaluation of platelet counting by novel fluorescent dye staining in the XN-Series automated hematology analyzers. J Clin Lab Anal 28(5): 341-8.

[40] **Caocci G *et al.* (2017):** Bone Marrow Homing and Engraftment Defects of Human Hematopoietic Stem and Progenitor Cells. Mediterr J Hematol Infect Dis 9(1): e2017032.

[41] **Goncalo AP *et al.* (2011):** Predictive value of immature reticulocyte and platelet fractions in hematopoietic recovery of allograft patients. Transplant Proc 43(1): 241–3.

[42] **Morkis IV *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): 259–64.

[43] **Takami A *et al.* (2007):** Immature platelet fraction for prediction of platelet engraftment after allogeneic stem cell transplantation. Bone Marrow Transplant 39(8): 501–7.

[44] **van der Linden N *et al.* (2014):** Immature platelet fraction measured on the Sysmex XN hemocytometer predicts thrombopoietic recovery after autologous stem cell transplantation. Eur J Haematol 93(2): 150–6.

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