

Towards New Horizons From The Land Of Explorers

The Sysmex European Haematology Symposium 2007 in Lisbon, Portugal

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When people think of Lisbon they usually think of a beautiful city at the Atlantic coast in the very West of the Iberian Peninsula, they think of castles, monasteries, Fado music and sparkling lights at night in the Old Town. From the 15th century on Portuguese sailors embarked on expeditions to Africa, Asia and South America, driven not only by dreams of wealth and riches but also by the desire to discover new horizons. The *Monument to the Discoveries* in Lisbon is also symbolic for the *Sysmex European Haematology Symposium 2007*, devoted to the exploration of new clinical applications of new and existing haematological parameters.

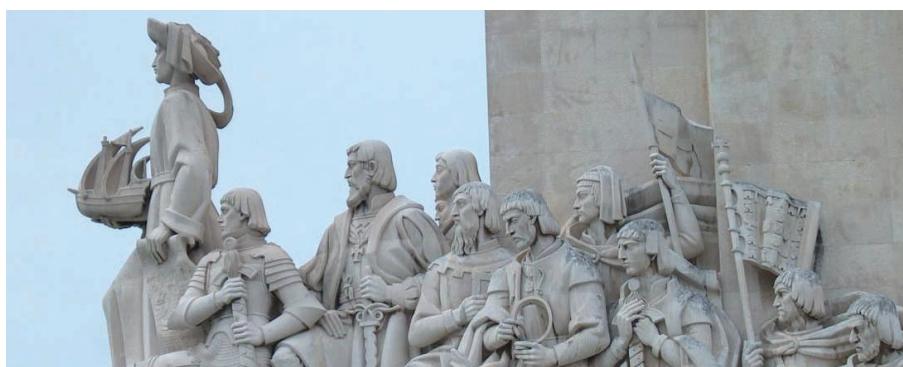
The symposium which took place on June 13th and 14th, 2007, was the fourth in a row of biannual haematological symposia in different European countries: 2001 in Pfäffikon, Switzerland, 2003 in Sirmione, Italy, and 2005 in St. Wolfgang, Austria. Perhaps due to the reputation of its high quality this year's symposium could attract close to 400 visitors from 38 different countries, mostly European but also from Africa, Asia, America and the

Austral-Pacific region.

After the opening of the symposium by **Dr. Rolf Hinzmann**, Head of Medical & Scientific Affairs at Sysmex Europe, the introductory lecture was held by **Dr. Michael Schaefer**, President, Sysmex Europe. Dr. Schaefer asked the question "*Clinical information from the IVD laboratory - end in itself or appreciated support for optimised patient management?*" and made it very clear that laboratories will have to provide more direct support to patient management in the future instead of delivering "just data". Necessary is a collaborative, multi-specialty approach that puts the focus where it belongs - on the patient and the disease - breaking down departmental barriers that can delay diagnosis and treatment. This has become possible by using computerized patient records. Essential, however, is to guarantee adequate, respectful communication between the different specialists and the patient since this is the only way to build up confidence. Growing confidence is actually the key term for improvement and success - try it !



View over the Tejo River and the City of Lisbon.



The Monument to the Discoveries faces West towards the Atlantic Ocean, depicting former voyagers as a symbol of the ambition to explore new horizons.



Dr. Michael Schaefer during his introductory lecture.

Session 1:

It's all about red blood cells: News on blood doping, fragmented red blood cells and malaria

Blood doping has been a persistent problem in endurance sports for a long time. **Dr. Neil Robinson** from the Swiss Laboratory for Doping Analyses in Lausanne, Switzerland presented on *"Fighting for fair competition - Blood doping, a persistent challenge and smart approaches to detect it"*. In the light of the fact that just a few weeks before the symposium a Belgian ex-cycling professional had published a book on systematic doping in cycling and that shortly later members of the German cycling team Telekom confessed what many had suspected for long - that doping seems commonplace in endurance sports - made the lecture red-hot. Dr. Robinson described the race between professionals and scientists who develop more and more sophisticated tests to detect blood doping. The blood profiling or blood passport strategy that uses long-term monitoring of the athletes' haematological parameters and looks at deviations from the individual "normal values" is possibly the best tool to exclude from competition all athletes with abnormal data without knowing necessarily the origin of the abnormality.

Diagnosis of thrombotic microangiopathies must be rapid since they can be fatal when left untreated. The measurement of red cell fragments contributes to the detection of these conditions. **Prof. Dr. Gina Zini** from Rome, Italy, presented her investigations on the *"Clinical usefulness of red cell fragments identified by the Sysmex XE-2100 haematological analyser"*. The most frequent cause of erythrocyte fragmentation is formation of thrombi in the microvasculature in thrombotic microangiopathies such as thrombotic thrombocytopenic purpura (TTP) or haemolytic uraemic syndrome (HUS). Fragmentation occurs after the passage of red blood cells through the

fibrin of microthrombi. Fragmented red blood cells are usually evaluated on peripheral blood films using optical microscope observation and are estimated as a percentage after counting 1,000 erythrocytes. The availability of automated haematological analysers which provide enumeration of fragmented red cells is very useful in terms of accuracy and precision. The measurement of fragmented red blood cells can be used for diagnosis, during the follow-up of patients with thrombotic microangiopathies as well as for routine screening to promptly identify positive, clinically still unsuspecting cases. The main value of the automated enumeration of fragmented red blood cells in daily routine work resides in its high negative predictive value.

In Europe malaria infection may go unnoticed since it is often unsuspected in patients without a history of recent travel to Plasmodium-infested regions. **Dr. Erzsébet Pintér** from Budapest, Hungary, revealed the *"Secret of the clouds - Detection of malaria infection by the Sysmex XE-2100 haematology analyser"* by explaining that in some cases malaria infection can cause atypical patterns in the reticulocyte and / or white blood differential channel of the Sysmex XE-2100 analyser. The appearance of "pseudo-reticulocytes" with elevated fluorescence or of "pseudo-neutrophil" or "pseudo-eosinophil" clouds should always trigger a suspicion of the presence of malaria parasites although the instrument is not considered sensitive enough to serve as a screening device for malaria. (For more details see Dr. Pintér's separate article in this edition of the Sysmex Journal International.)

Session 2:

It's all about leukocytes: AIDS, sepsis and radiation-induced haematological malignancies

AIDS is a global human tragedy that has its strongest impact in the sub-Saharan countries where the number of infections with HIV is still on the rise. During the 3rd South African AIDS Conference in Durban this month, it was reported that in the 15 to 49 year age group 71 percent of all deaths in South Africa are due to AIDS, while more than 500,000 new infections occurred in 2005 alone. Anti-retroviral treatment requires careful staging and monitoring using CD4⁺ T cell measurements. **Dr. Ilesh Jani** from Maputo, Mozambique, is an expert in this field. In his lecture *"The monitoring of HIV infection in countries with limited resources by point-of-care CD4 measurement on the Sysmex KX-21N haematological analyser"* he presented the results of a method measuring CD4⁺ T cell nuclei after immunomagnetic separation on a Sysmex KX-21N system. The method has been designed to provide CD4⁺ T cell counts and a complete blood count with 3-part differential leukocyte count in resource-limited settings where flow cytometry is not available. He concluded that in the hands of a well trained technician, the precision of the method is comparable to that of a CD4⁺ T cell count on a conventional flow cytometer. The KX-21N system generates absolute CD4⁺ T cell counts that are in close agreement with those yielded by a Becton Dickinson FACSCalibur for both adult and paediatric HIV positive patients. The percentages of CD4⁺ T cells generated by the KX-21N sys-



The event took place at the superb Corinthia Hotel.

tem also closely agree with those yielded by the FACSCalibur but mainly for paediatric patients. In summary, this is a technology that can potentially be used in settings with a low- to medium-throughput of specimens.

Sepsis is still a severe and heavily underestimated problem, having a death-toll in the industrialised countries exceeding that of myocardial infarction. Important is early detection of sepsis since this is a prerequisite for early treatment. **Prof. Dr. Kurt Herkner** from Vienna, Austria, works on the detection of early-onset (EOS) and late-onset (LOS) sepsis in - primarily pre-term - infants: *"When time is vitally important: SIC - A novel approach for early detection of sepsis on the Sysmex XE-2100"*. The aim of his ongoing study is to find a new marker for early diagnosis of infection and sepsis by mathematical transformation of instrument parameters generated by the Sysmex XE-2100 haematology analyser, e.g. an algorithm based upon the quantitative information about myeloid precursor cells (IMI). The parameter is called single haematological infection marker and control parameter (SIC). In 155 sepsis episodes SIC presented with significantly increased values more than 24 hours earlier than clinical signs or traditional sepsis markers such as interleukin-8, immature to total granulocyte ratio (I/T-ratio) or IMI. For proprietary reasons details of the mathematical calculation of SIC could not be provided at this stage. The study is still continuing.

The next lecture was likewise focussing on sepsis: **Mr. Jo Linssen**, Scientific Marketing Manager, Sysmex Europe, gave a presentation on *"Highly fluorescent lymphocyte count (HFLC) on the XE-5000: Can these T-cell independent plasma cells help to differentiate between infectious and non-infectious SIRS in adults?"*. Firstly, Mr. Linssen compared HFLC on the Sysmex XE-2100 in 85 selected patients (systemic haematological diseases were excluded) with immunophenotyping flow cytometry on the Becton Dickinson FACSCalibur and morphological assessment of the peripheral blood film with the automated microscopic blood cell recognition system CellaVision DM96. HFLC showed an excellent correlation with activated B lymphocytes and no other cell lineage. For clinical utility he then investigated HFLC kinetics in 240 adult intensive care patients (including 68

classified as having systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis, or septic shock) and 320 neonate intensive care patients (including 65 with clinical and serological signs of early-onset bacterial infection (EOBI)). The preliminary data are promising and demonstrate a significant increase of HFLC in sepsis patients compared to non-infectious SIRS patients.

The explosion at Chernobyl Nuclear Power Plant in Ukraine on April 26, 1986, was followed by radioactive contamination of the surrounding geographic area. The extent of contamination by radioactive fallout and the size of the affected population far exceed that of any previous nuclear accident. Radioactive fallout drifted over parts of the Western Soviet Union, Eastern, Western and Northern Europe, and Eastern North America. Large areas of Ukraine, Belarus, and Russia were badly contaminated, resulting in the evacuation and resettlement of approximately 300,000 people. **Prof. Dr. Danylo Gluzman** from Kiev, Ukraine, investigated *"The development of haematological malignancies in clean-up workers after the Chernobyl nuclear accident"*. In a follow-up study a representative sample of 246 cases with leukaemia or lymphoma was compared to an age-matched control group of 2697 individuals. Although a dramatic increase in the incidence of thyroid cancer has been observed among those exposed to radioactive iodine in most contaminated areas, at present a clear radiation-related increase in the risk of other forms of solid tumours has not been demonstrated. The question as to whether the incidence of leukaemia and malignant lymphomas among Chernobyl clean-up workers is increased is still a point of much controversy. In this comprehensive study increased incidence for multiple myeloma, a tendency for increased non-Hodgkin's lymphoma and an increased rate of chronic lymphatic leukaemia (CLL) were demonstrated. A peculiar feature of acute myeloid leukaemia (AML) in the clean-up workers under study was the development of leukaemia on the background of a preceding myelodysplastic syndrome (MDS) in 19% of all AML cases studied. The overall incidence of AML, however, was higher in the control group. At this stage there is no explanation for this observation.

Session 3:

The Sysmex Outstanding Science Award 2007 - The participants presented their results

Sysmex has embarked on spearheading the development of modern technology for the clinical laboratory and strongly supports the endeavour to develop clinical applications for new and existing parameters. As a logical consequence, Sysmex Europe has initiated the Sysmex Outstanding Science Award which is focused on haematological cellular diagnostics involving Sysmex technology and available to all healthcare institutions. The award is supervised by an independent Scientific Expert Committee and coordinated through local Sysmex representatives. It is well financed with prizes worth €50,000 altogether to honour excellent scientific work improving cellular diagnostics in haematology and its clinical applications. The first of these awards is called The Robert Martin Rowan Memorial Award in memoriam Dr. R. M.

Rowan, the former scientific advisor of Sysmex, enthusiastic teacher, chair in many symposia and good friend to many of us. The award was opened in 2005. Out of all applications the Scientific Expert Committee, consisting of **Prof. Dr. Giuseppe D'Onofrio**, Rome, Italy, **Prof. Dr. Andreas Huber**, Aarau, Switzerland, **Prof. Dr. Sam Machin**, London, United Kingdom, **Prof. Dr. Pranav Sinha**, Klagenfurt, Austria, and **Prof. Dr. Lothar Thomas**, Frankfurt, Germany, selected ten to finally compete for three prizes. Each project received initial funding of €1,000. In May 2007 the three winners were selected by the committee. At the symposium eight of the ten investigators presented their data:

Ms. Kim Alexander from Johannesburg, South Africa, presented her *"Evaluation of the immature platelet fraction (IPF) in HIV/AIDS and malaria in the Southern African population"*. The elevated IPF levels seen in thrombocytopenic HIV patients could potentially assist in explaining the pathophysiology which is as yet poorly understood. The elevated levels seen in the patients with malaria and thrombocytopenia possibly prove peripheral platelet destruction.

Dr. Caroline Brusselmans and **Dr. Willy Goossens** from Leuven, Belgium, did *"A feasibility study of the CellaVision DM96 in a tertiary care hospital"* to investigate the correctness of the instrument's pre-classification of ca. 1.5 million randomly selected cells from pathological blood samples. They concluded: The CellaVision DM96 is an automated cell analysis system with sufficient intrinsic qualities to be capable of satisfactory classification of leukocytes in peripheral blood films. The instrument's pre-classification of cells correlates well with microscopy for most cell types at all leukocyte count ranges, including leukopenic samples. Repeatability of the differential is significantly better than microscopy for any cell type. Blood sample ageing effects are observed after 24 hours.

Dr. Mauro Buttarello from Padova, Italy, showed in his *"Evaluation of immature platelet fraction (IPF) and mean platelet volume (MPV) as risk index of vascular complications in patients with type 2 diabetes"* that IPF and MPV were not different between controls and diabetes type 2 patients with and without micro- or macrovascular complications and are therefore not useful as markers of vascular complications in these patients.

Except in the neonatal period, the presence of nucleated red blood cells (NRBCs) in peripheral blood is always pathological - even if the concentration is low. The investigation of the blood film has some natural limitations to detect and quantify NRBCs. The routine quantification of NRBCs on a haematological analyser can shed more light on the role that NRBCs play in a variety of diseases. **Dr. Paolo Danise** from Naples, Italy, undertook a comprehensive *"Evaluation of NRBCs in peripheral blood in haematological diseases"*. He could show by analysing more than 4,000 blood counts from 1,149 patients that NRBCs are indeed present in peripheral blood in a high number of haematological diseases. This new automated diagnostic tool forms the starting point for studies inves-

tigating the diagnostic, therapeutic and prognostic consequences of the presence of NRBCs.

"The immature platelet and immature red cell fraction - Novel and potent markers for targeted therapy and bone marrow regeneration after stem cell transplantation in children?" asked **Dr. Andreas Weimann** from Berlin, Germany, in his presentation. Contrary to earlier work by others Dr. Weimann could not derive decision criteria for platelet transfusion after stem cell transplantation from the measurement of immature platelets. He stated, however, that at his hospital platelet pools were transfused frequently and only due to clinical symptoms in all patients and presumably often in a rather prophylactic way. Since platelet transfusion temporarily inhibits thrombopoiesis IPF is rather useless under this condition. As a conclusion, IPF is most likely a much more clinically useful and potent predictive marker in a rather strict setting for platelet transfusions.

Session 4:

The Sysmex Outstanding Science Award 2007 - The three happy winners !!

Ms. Marianne Schoorl from Alkmaar, The Netherlands, received the **3rd prize**, worth € 5,000, for her study about *"Changes in platelets in morphology and RNA content during treatment with haemodialysis"*. In subjects treated with haemodialysis haemostatic balance is disturbed as a consequence of extracorporeal blood circulation. Hypercoagulability is demonstrated to be strongly influenced by surface characteristics of the dialyser membrane and anticoagulation mode. Thrombogenicity may result in reduced haemodialysis efficacy because the membrane area does not function appropriately. During treatment with haemodialysis, platelet interaction with the dialysis membrane results in activation, adhesion to the membrane surface, and release of platelet-derived factors. In



Ms. Marianne Schoorl is happy about the 3rd prize.

case of platelet activation, increased amounts of degranulated platelets are present in the peripheral blood circulation. Degranulated platelets are less viable and demonstrate a shortened life span. In a longitudinal study deviations in platelet morphology and RNA content were established in combination with analysis of markers of platelet activation during haemodialysis. In a group of 20 patients Ms. Schoorl took blood samples at various points of time during haemodialysis and determined platelets, platelet distribution width (PDW), mean platelet volume (MPV) and immature platelet fraction (IPF) on the Sysmex XE-2100. Blood films were microscopically screened for qualitative evaluation of morphological aspects of platelets with a CellaVision DM96 analyzer. CD62p expression on platelets, secretion of PF4 from alpha granules and release of serotonin from dense granules in plasma are indicative for the degree of platelet activation. CD62p expression on platelets was detected flowcytometrically with a Beckman Coulter EPICS-XL and PF-4 and serotonin were measured with immunoassays. Apparently healthy subjects and uraemic subjects not undergoing haemodialysis served as controls. The results are indicative of continuous platelet activation during haemodialysis. Alterations concern decreased mean values for platelet counts, IPF, and MPV and increased mean values for the percentage of degranulated platelets. Increase of CD62p expression on platelets and release of PF4 and serotonin in plasma occurs simultaneously with an increase of the percentage of degranulated platelets.

The **2nd prize**, worth €10,000, went to **Dr. Carmen Canals Suris** from Barcelona, Spain, for her study "*Haematopoietic stem cell mobilisation and transplantation: Clinical utility of the immature reticulocyte, haematopoietic progenitor cells (HPCs) and immature platelet fraction (IPF) assessed by the Sysmex XE-2100 haematological analyser*". Several studies have shown

that HPCs correlate with CD34⁺ cells circulating in peripheral blood after stem cell mobilization and can be used as a guide for initiating apheresis. It has also been reported that the immature reticulocyte fraction can be used to predict adequate harvesting of peripheral blood progenitor cells and serve as an early indicator of engraftment following haematopoietic stem cell transplantation (HSCT). Finally, some studies have suggested that the quantification of IPF can be useful in evaluating thrombopoietic recovery after chemotherapy. Aim of the study was to investigate the kinetics of immature reticulocyte fractions, HPC, and IPF in patients mobilised for stem cell collection and during the haematological recovery phase after autologous HSCT (ASCT). The clinical utility of these parameters in timing apheresis, predicting engraftment, and optimising red blood cell and platelet transfusion after ASCT was studied. During 74 mobilisation courses including 142 samples HPC showed a good correlation with CD34⁺ cells in peripheral blood from mobilised patients. Using the two thresholds >10,000 and <3,000 HPC/mL, HPC values can successfully guide apheresis timing in 70% of the patients. For the remaining 30% a determination of the CD34⁺ cells is needed before taking the final decision of starting apheresis. The study also suggests that the enumeration of HPC can be very useful in evaluating the efficiency of different chemotherapy regimens to mobilise stem cells to peripheral blood. Reticulocyte parameters are good indicators of engraftment after ASCT, correlating not only with the red blood cell transfusions needed, but also with the kinetics of leukocyte and platelet recoveries. However, the absence of circulating HPCs does not preclude a successful haematological recovery. After ASCT an increase in IPF was observed in all the patients, reflecting recovery of thrombopoiesis after the aplastic period. Their potential utility to optimise the use of prophylactic platelet transfusions needs further investigation.

Winner of the **1st prize**, worth €25,000, was **Prof. Dr. Florence Cymbalista** from Bobigny, France, with her study "*Usefulness of NEUT-X determination in routine diagnostic procedures: Application to myelodysplastic*



Dr. Canals Suris receives the 2nd prize.



Prof. Florence Cymbalista receives congratulations for the 1st prize from Prof. D'Onofrio, Mr. Azuma, Dr. Rolf Hinzmann and Dr. Michael Schaefer (right to left).



The audience is listening with passion to the discussions.

syndromes". Myelodysplastic syndromes (MDS) are malignant disorders with a poor prognosis. There have been recent advances in the treatment of MDS, more treatments are available for high risk MDS, and early diagnosis of these forms is warranted for optimal benefit from treatment. MDS diagnostic features are polymorphic and non-specific. They include anaemia in the majority of cases. All the haematological features are highly non-specific and the standard parameters given by an automated haematology analyser rarely brings any diagnostic argument towards the diagnosis of MDS. The aim of this study was to investigate if certain structural parameters which are not routinely provided by blood analysis with the Sysmex XE 2100 analyser could help the diagnosis of MDS in a simple way and be adapted to routine practice. In this study 184 MDS cases and 3545 control patients were investigated. Dr. Cymbalista successfully demonstrated that the neutrophil parameter NEUT-X (= mean value for side scatter of the neutrophil population), representative of the structure of the neutrophils, could be used for this purpose. She converted NEUT-X into a semi-quantitative parameter, the granularity index GI. Negative GI in the context of anaemia proved highly suggestive of MDS. The association of isolated anaemia and low GI was taken as an additional criterion for blood film review. Thereby, the number of MDS that received blood film review increased from 67% to 96%. This proves that this association is highly suggestive of MDS and extremely useful to flag otherwise unrecognised MDS in routine practice. Moreover, Prof. Cymbalista confirmed that this rule was not leading to a large excess of unnecessary blood film reviews among non-MDS patients as concomitantly only 2% of controls were reviewed in excess. For example, isolated anaemia in controls mostly had a GI index = 0. Therefore, Dr. Cymbalista proposes to include the GI index in the routine parameters of the blood counts provided by the Sysmex XE-2100 analyzer.

Session 5:

Learn your lesson on prevalence & incidence, hard facts about functional iron deficiency and automated anaemia diagnostics

Do you believe in sensitivity and specificity? Perhaps

most people would be impressed by tests that can demonstrate something like 99% sensitivity and 99% specificity. "These two figures alone tell you nothing" said **Dr. Hans-Hermann Dubben** from Hamburg, Germany, in his interactive lecture on *"Sense and crime and prophecy - Some aspects of the art and science of prediction"*. Prevalence and incidence are the magic words. They determine the so-called positive and negative predictive value (PPV and NPV, respectively) which tell you the likelihood that you are ill when your test is positive or that you are healthy when your test is negative. PPV and NPV depend not only on sensitivity and specificity but as well on the prevalence. A 99% specific test might be false positive much more often than correctly positive if the disease measured by it is very rare. This influence of prevalence of PPV and NPV is often neglected. Although intellectually understandable, our mind is often fooled by this phenomenon when intuitive guessing is performed instead of analytical calculation. Another intuitive misunderstanding is that the feature a test measures and the conclusions we draw from the measurement are two different things: A hair sample found at the site of a crime with a DNA pattern identical to that of a suspect might - or might not, depending on the circumstances - prove that the hair belongs to the suspect. It does not prove that he committed the crime. The question how the hair got to the site of the crime is an entirely different one. Our superficial belief that DNA samples can identify the genitor in paternity issues or the culprit of a crime simply by demonstrating genetic identity with a sample of a suspect is entirely wrong. Likewise, diagnostic tests must be used and interpreted intelligently. A diagnostic test shows that a marker is present or absent, elevated or decreased. It does not tell why this is the case. This is left to the swift interpretation of the physician in the laboratory or of the clinician.

In his presentation *"The red revolution - 2007"* **Dr. Ivor Cavill** from Cardiff, United Kingdom, described the problems associated with prediction of the effect of erythropoiesis stimulating agents (ESAs) such as erythropoietin and its artificial homologues. The chief factor limiting the effectiveness of ESAs in both renal anaemia and the anaemia of chronic disease is functional iron deficiency (FID). This is most readily detected by looking at the haemoglobin content of newly produced red blood cells, i.e. reticulocytes. (This test is called RET-He on Sysmex analysers and CHr on Bayer analysers). The recognition of FID and the administration of intravenous iron to correct the iron supply to the marrow is the key to unlocking the full potential of ESAs. It's impossible to make red blood cells red without an adequate iron supply. It is important to recognise that erythroid iron supply is not the same as the iron "stores". These "stores" are really iron that has been deposited in quarantine - mainly in the macrophages - and play no active part in iron supply to developing red bloodcells. It is quite common to find FID at the erythroid level albeit normal or raised storage iron levels as detected by the serum ferritin concentration. The ability to detect decreased reticulocyte haemoglobin content gives a rational and specific basis for the administration of intravenous iron. The optimum way to detect the failure of iron supply is to measure the

haemoglobin content of the reticulocytes. Automated cell counters which can do this give us the tools to do the job. Long live the revolution!

Anaemia remains as an enormous problem worldwide with more than 2 billion people affected. Despite the high number of individuals living with anaemia, the importance and the impact of this disease has been neglected and the health care community has not focused on anaemia as a serious and common problem, said **Dr. Sebastián Garzón** from Jerez de la Frontera, Spain. Anaemia is not only a frequent condition, it also has an adverse impact on the patients' health and wellbeing and causes a large economic burden that is difficult to calculate since many factors must be taken in consideration such as laboratory tests, drug prescriptions, hospital admissions, physicians' office visits, absenteeism, etc. Anaemia is often underrecognised and undertreated. Frequently it is masked by symptoms of the disease by which it is caused. Its very high prevalence means that nearly all type of medical specialists must manage patients with anaemia and obviously not all of them have an equal skill and knowledge for it. In addition, there are more and more new parameters with difficult standardisation and interpretation. For all that, it is common to observe a long delay in the diagnosis and investigation of anaemia. As a solution, Dr. Garzón presented *"Automated diagnostic algorithms for the investigation of anaemia - Towards more efficacy and efficiency in the haematological laboratory"*. The process starts with a complete blood count and the measurement of creatinine and C-reactive protein. If anaemia is detected a reticulocyte count and a blood film inspection will be performed. Depending on the results, parameters of iron metabolism, vitamin B12, folic acid, or haptoglobin will be determined. The approach uses defined algorithms and reflex testing via the laboratory information system to screen every patient for anaemia and to investigate the cause.

Session 6:

The new Sysmex XE-5000 haematological analyser - and what comes next in laboratory medicine?

Ms. Tanja Tornow, Product Marketing Manager Haematology, Sysmex Europe, presented the *"Extension of*



Inspiring conversation during dinner.

the X-Class concept - The new features of the XE-5000 haematology analyser". Sysmex's new top-end analyser XE-5000 is the first haematology analyser enabling the use of diagnostic concepts for case management and therapy monitoring. With its Case Manager software it assists the physician in the laboratory not only to report but also to interpret the relevant and important clinical information about the patient's condition, supporting the clinician most efficiently in quick diagnosis and therapy monitoring. Hence, new product performance specifications as well as advanced analytical parameters with proven clinical utility such as immature granulocytes (IG), haemoglobin content of reticulocytes (RET-He), or human progenitor cell counts (HPC) are used together with the available patient information to help laboratory professionals and clinicians in managing patients. Especially some of the newer extended parameters of the XE-5000 like the immature platelet fraction (IPF) have proven their clinical utility only in recent years. But their potential is not always known to all users in the laboratory nor to clinicians on the ward. Using the information out of the 76 parameters provided by the XE-5000 that is relevant for a particular case and helping to correctly interpret it is the clear aim of the new diagnostic concept of the Case Manager. The Case Manager is realised by a tiered software concept including discrete disease and case related information. Body fluid analysis completes the holistic concept of the XE-5000. A dedicated body fluid mode capable of measuring and differentiating blood cells of even very small numbers in body fluids completes the abilities of this new first-class haematology analyzer. Now a fully automated measurement technique can replace a process that currently takes much longer by microscopy with a two-minute automated process. Moreover, the classification of leukocytes in polymorph-nucleated cells (PMN, equivalent to granulocytes) and mononuclear cells (MN, equivalent to lymphocytes plus monocytes) provides additional information about the possible cause of the disease.

[Editorial remark: The Case Managersoftware is currently only available from Sysmex Europe and its distributors.]

"Going beyond blood - Evaluation of the new body fluid mode on the Sysmex XE-5000 analyser" was the lecture provided by **Dr. Joke Boonstra** from Rotterdam, The Netherlands, who was the first to evaluate this new feature of the XE-5000. Quantitative and qualitative analysis of different body fluids such as cerebrospinal fluid (CSF) and ascites is an essential tool in the diagnosis and treatment of patients. Microscopic analysis of body fluids is traditionally used for determination of the total leukocyte count and the leukocyte differential count. There are several disadvantages of microscopic evaluation of body fluids: high imprecision, high costs, a relatively long time before results are reported to the clinician, requirement of skilled personnel, and finally, not everywhere are microscopic analyses available 24 hours a day. The obvious answer to these problems could be automated analysis. Dr. Boonstra evaluated the body fluid mode of the Sysmex XE-5000 analyzer in a prospective study using CSF, pleural fluid, ascites, continuous ambulatory peritoneal dialysis (CAPD) fluid, and synovial fluid. Red



After hours: Relaxing tones from The Nana Sousa Jazz Band.

blood cell, total leukocyte, and leukocyte differential counts were made using a Fuchs-Rosenthal chamber and stained cytopsin slides. The extended cell counting in the body fluid mode was reflected by an improved "functional" detection limit (= cell concentration where CV=20%) for leukocytes which improved from $50 \times 10^6/L$ on the XE-2100 to $10 \times 10^6/L$ on the XE-5000. In summary, the body fluid mode on the Sysmex XE-5000 offered fast and accurate red blood cell, total leukocyte, and leukocyte differential counts in clinically relevant concentration ranges in CSF and other body fluids. Furthermore, the exclusion of high fluorescent cells from leukocyte counting may reduce the number of manual analyses in pleural fluids and ascites.

"Where will we go from here? The near future of laboratory medicine" is the title of the outlook to the future that was presented by **Prof. Dr. Germano Sousa** from Amadora, Portugal. The last ten years have seen advances in all medical sciences, with astonishing changes in laboratory medicine in more recent years. The

advent of molecular pathology will generate opportunities for professionals of laboratory medicine to contribute not only to diagnosis but to accurately predict and prevent disease and to participate in treatment. Genetic engineering and molecular biology promise a revolutionary improvement in medicine with already exciting advances in heritable disease. However, of equal importance is the relationship with other physicians, scientists, healthcare organisations, hospitals, the public, and the governments. The future of laboratory medicine will also be in economic efficiency, provision of diagnostic swiftness, reliable service and expert consultation, and clinical support. Scientific advances will merge the roles of the laboratory and clinical medicine. With the introduction of an enormous number of new tests, the clinician cannot be expected to know what every abnormal result means or what reflex testing would prove helpful in diagnosis. Growing errors are resulting from his lack of knowledge that can be avoided by the interpretation of complex laboratory results by knowledgeable clinical pathologists. Indeed, the application of scientific knowledge to human health is a crucial aspect of laboratory medicine. The clinical pathologists and laboratory medicine scientists are important agents through which scientific understanding is expressed and they must become the bridge between laboratory science and medical practice.

A second day of inspiring lectures and fruitful discussions went by and a very much appreciated meeting came to its end. **Mr. Masahide Azuma**, CEO for Europe, Middle East & Africa, Sysmex Europe, confirmed the mission of Sysmex to shape the advancement of healthcare and its commitment to continue to create unique and innovative values, while building trust and confidence. Although it's over - it will go on. Sysmex Europe will shortly announce the terms and conditions for the next Sysmex Outstanding Science Award on its website www.sysmex-europe.com. And we hope to see you at the next Sysmex European Haematology Symposium.