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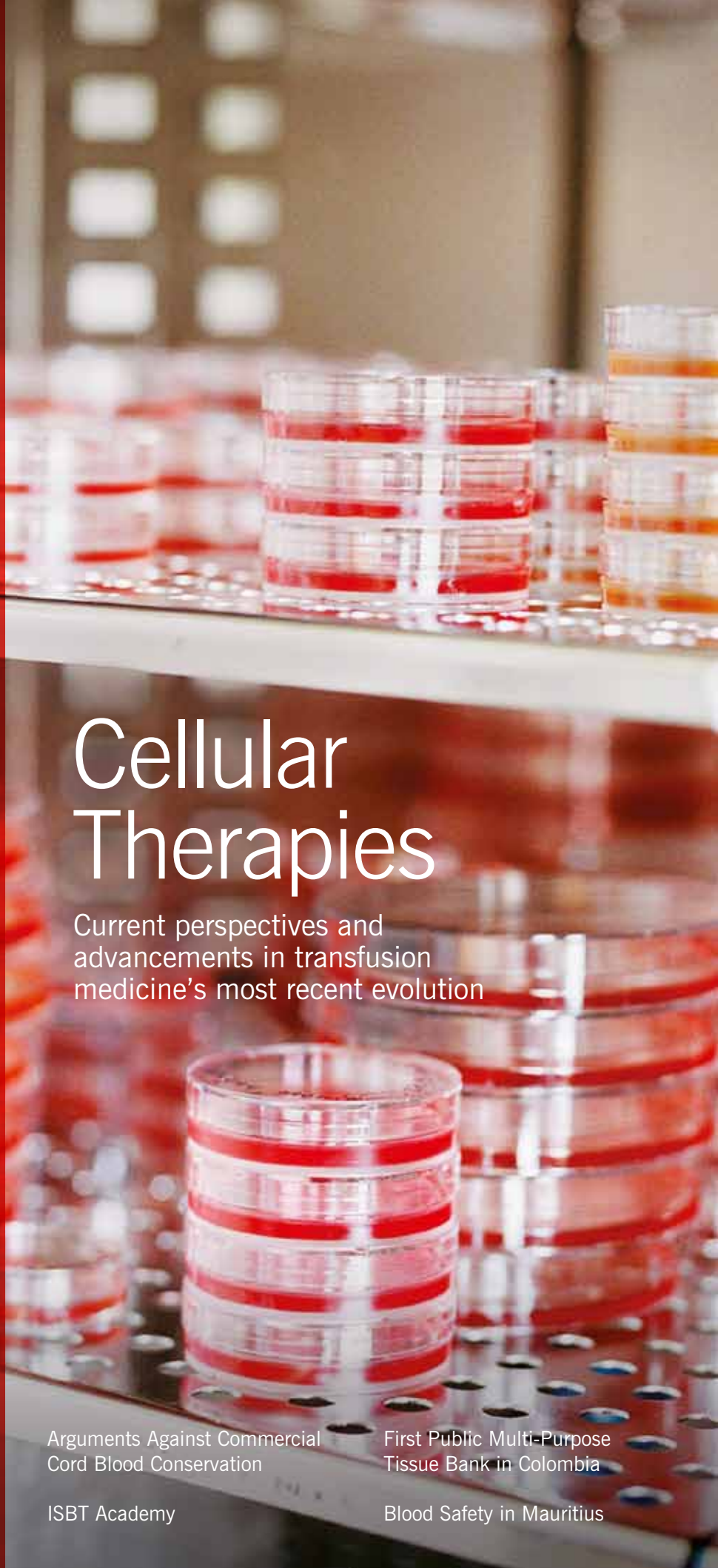

Cellular Therapies

Current perspectives and advancements in transfusion medicine's most recent evolution

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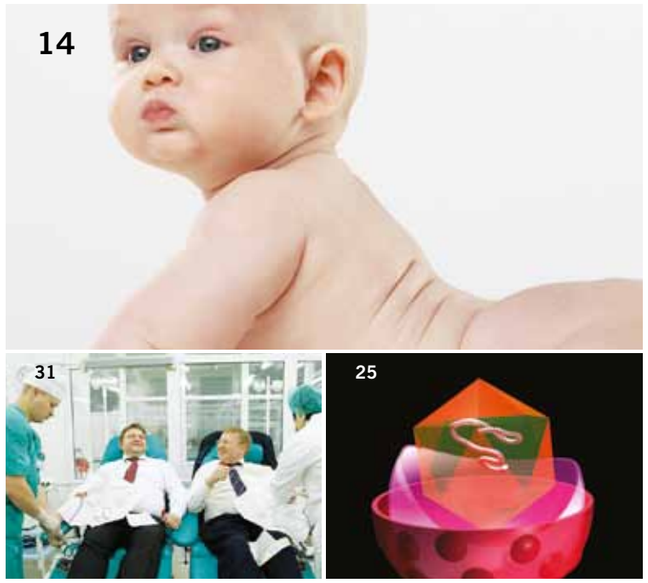


President Silvano Wendel **Secretary General** Geoff Daniels **Executive Director** Judith Chapman **Design** Tomorrow Design **Photography** Transfusion Today **Advertising** Sophie Hamburger, office@isbtweb.org

Send all correspondence to ISBT - J. van Goyenkade 11, 1075 HP, Amsterdam, The Netherlands. T +31 20 5709 636, F +31 20 6737 306, transfusiontoday@isbtweb.org.

Judith Chapman

Editorial

As you know one of the main activities of ISBT is its congresses. The Central Office has been busy with final preparations for the 21st Regional congress of the ISBT in Lisbon. We are encouraged by the number of people who have registered, it seems that the scientific programme has met the requirements of the ISBT membership and you are keen to join us in Lisbon. The preparations for the 22nd Regional Congress to be held in November in Taipei are going well. No congress would be complete without the presentation of abstracts from the delegates, either as an oral or a poster. A reminder that the abstract submission deadline is July 3, 2011.

This issue of Transfusion Today has a focus on cellular therapies. Last year ISBT established a joint Working Party for Cellular Therapies with AABB, both societies wished to embrace the field of cellular therapies and it seemed appropriate to form a joint Working Party. Paolo Rebulla and John McMannis, the joint chairpersons have written a short piece about the Working Party. Other articles in the section include aspects of stem cell donors, stem cell donation and sterility testing and the challenges of interdisciplinary co-operation in cellular therapies.

The regional pages include two short papers; one from Egypt and one from Mauritius, reports on the celebrations of a regional blood bank in Russia and the ideal donor in the United Arab Emirates and a report on the International Haemovigilance Network meeting held in Amsterdam in February. This meeting was supported by the ISBT Academy. In the section 'from the Central Office' there is a brief update on the Academy and how to apply for support for an Academy event. The Board wishes to increase the activities of the Academy and to expand the Academy to countries where workshops and meetings have not previously been supported by ISBT. To this end the Board has set aside substantial funds in its budget for the current financial year.

The Central Office staff looks forward to meeting you in Lisbon.

Paolo Rebulla and John McMannis
Co-chairs

The ISBT-AABB Working Party on Cellular Therapies

After preliminary talks and formal deliberations, in February 2009 we were invited to co-chair a new Working Party on Cellular Therapy (WPCT) with the specific purpose of developing and sharing common views on the clinical use of cellular products between the ISBT and the AABB.

This article reports the WPCT objectives and a brief summary of activities performed to date.

The need for a new joint working party involving two major international professional organizations dealing with blood transfusion stemmed from the consideration that the future development of regenerative medicine – the most recent evolution of transfusion medicine – requires improved logistics for the procurement of novel blood and cellular products transported across national borders. These products would be prepared and distributed in full compliance with norms and regulations of the home countries of their donors and recipients.

The original letter of invitation to co-chair the WPCT included an expression of interest in joining the WPCT previously expressed by three members of the ISBT from Finland and from the Netherlands. The WPCT quintet, including three members and two co-chairs, exchanged communication in 2009 to define a program for activities, as required in the WP terms of reference. It was soon realized that there was no need for a replica of other active groups of scientists dealing with the complex pathways of systems biology and the different 'omics' which regulate the fate of cell development. Rather, there was a need for a possibly humbler but nonetheless crucial activity impacting on the clinical effectiveness of novel cellular therapies: the harmonization of a plethora of local and national practices regulating the production, storage, distribution and therapeutic use of these products. Simply stated, our main concern was to remove impediments to the widespread exchange of products across national borders which may depend on lack of critical review and harmonization of relevant norms and regulations.

These preliminary activities were carried out with a clear appreciation of related issues being addressed by the recently formed Alliance for the Harmonization of Cellular Therapy Accreditation (AHCTA). The WPCT members met at the ISBT congress in Berlin and at the Annual Meeting of the AABB in Baltimore to plan the WP activities. It was agreed that a good starting point was the development of consensus articles on donor selection and product release criteria. Selected members of the CTWP are currently finalizing these materials.

Anneke Brand, Sanquin Blood Supply & Leiden University Medical Centre, Leiden, the Netherlands & **Ina Perez** H Servicio Bancos de Sangre y Medicina Transfusional. Hospital Edgardo Rebagliati Martins. Securo Social Peruano, Peru; on behalf of the ISBT/AABB Joint Working Party on Cellular Therapies

Uniform Examination of Stem Cell Donors

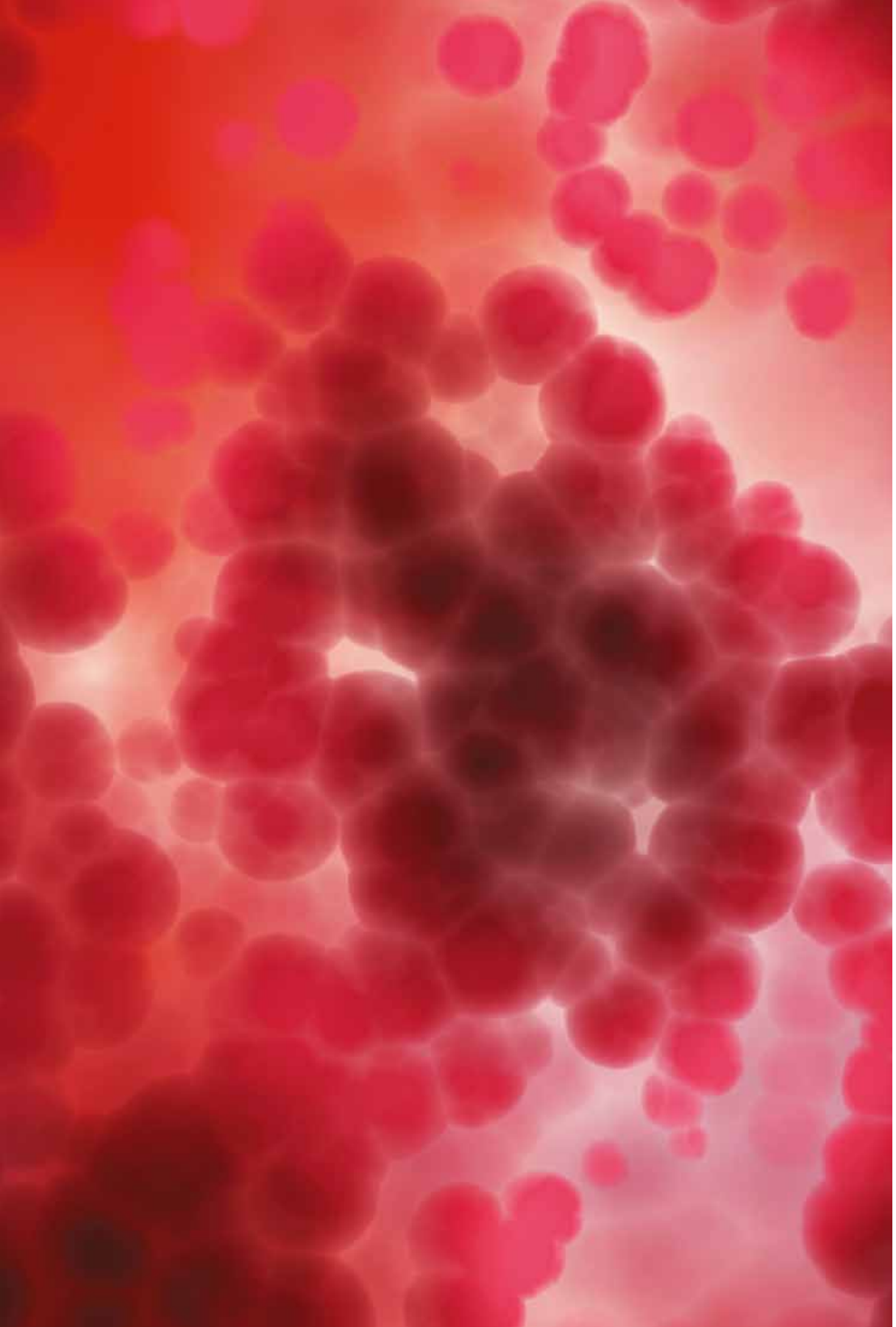
For allogeneic haematopoietic stem cell transplantation (HSCT) three sources of stem cells (Bone Marrow/BM, G-CSF mobilized peripheral blood stem cells/PBSC and umbilical cord blood/UCB) can be used.

All types of stem cell donation include donor recruitment, information and consent, HLA-typing, medical checks intended for donor safety to undergo donation and product safety for the recipient, release of the donor to donate, stem cell harvesting, (serious) adverse events reporting, stem cell product quality, short- and long-term follow-up and consent to contact the donor in case of a second donation request. In case of UCB, recruitment and consent regards the mother of the child. Second donation request of UCB donors is impossible, but in the future it is expected that part of the UCB can be manipulated to serve as a second product for immunotherapy.

"In contrast to unrelated donors who are counselled and examined according to international guidelines, for related donors such strict procedures are lacking."

Several organisations are active to safeguard donors and recipients. Guidelines and recommendations are provided by the Foundation for the Accreditation of Cell Therapy & Joint Accreditation Committee-ISCT & EBMT (FACT-JACIE), the World Marrow Donor Association (WMDA), the National Marrow Donor Program (NMDP) and the Council of Europe. The WMDA recommends on criteria of (unrelated) donor eligibility; WMDA, FACT-JACIE and EU formulated requirements for the quality of the stem cell products. The European Bone Marrow Transplantation (EBMT), the Centre for International Blood and Marrow Transplant Research (CIBMTR) and the World Wide Group for Blood and Marrow Transplantation (WBMT) mainly register patient outcome. The 3rd edition of the EU guide prescribes that all living donors of organs, tissues and cells must be registered and offered life-long follow-up; this applies to related and unrelated donors. Because G-CSF mobilizes higher numbers of CD34+ cells, older patients are eligible for non-myeloablative transplantation. These patients have older siblings, which may suffer co-morbidity. In contrast to unrelated donors who are counselled and examined according to international guidelines, for related donors such strict procedures are lacking.

All these organizations and registries offer their expertise and experience or have already installed subcommittees to give recommendations. However, in practice for related donors often local/hospital-based policies are in use. The ISBT and AABB have large experience ranging from donor recruitment to hemovigilance registration, which is also applicable for new cellular products including haematopoietic stem cell products. The ISBT represents a wide network including well- and less resourced countries. It is the purpose of the WPCT to offer the complementary experience of the ISBT and AABB blood supply organizations and in collaboration with organizations already operating in this field to harmonize procedures for related and unrelated donors providing new cellular blood products.



Melanie Stoermer
and Thomas Montag
Paul-Ehrlich-Institut,
Federal Institute for Vaccines and
Biomedicines, Langen, Germany

Advancements in Sterility Testing of Cell Therapeutics

Microbial safety of cell therapeutics

In contrast to blood products like plasma derivatives (e.g. coagulation factor concentrates), microbial safety of cell therapeutics presents an only partly solved problem [1]. Most approaches in pharmaceutical industry are not applicable in case of cell therapeutics (e.g. sterility of source materials not guarantied, no sterilization by heat, radiation or filtration possible). Moreover, cell therapeutics often have a short dating shelf life, which often necessitates administration to the patient before sterility test results are available [2,3].

Established methods for sterility testing

Classical sterility testing is addressed worldwide in respective documents. In principle, they recommend incubation of test samples applying both aerobic and anaerobic incubation for 14 days. The indicator for microbial growth is turbidity. Addition of cell suspensions to the media, however, inevitably causes them to become opaque so that these methods are as a rule not recommendable for sterility testing of cell therapeutics. Automated culturing (BacT/Alert, BioMerieux, France, and Bactec, BD, USA) has been made available for sterility testing of cell therapeutics. These systems are used successfully for microbial screening of cellular blood components [4] representing a major progress, but also have their limitations for testing of cell therapeutics (e.g. unavoidable “sampling error” which does not produce complete information on sterility of the whole product) [3]. Nevertheless, the advantage of the automated culture system is the shortened incubation period of seven days. But considering the extremely short shelf life of much cell therapeutics, novel rapid and effective principles are needed.

Advanced methods for rapid sterility testing of cell therapeutics

Due to many similarities between cell therapeutics and cellular blood components several methodological principles developed in transfusion medicine should be applicable for cell based products [2]. Some methodological models at the Paul-Ehrlich-Institute (PEI, Federal Institute for Vaccines and Biomedicines, Langen, Germany) are presented in the following. To mimic the matrix of cell therapeutics, artificially contaminated Chinese hamster ovarian cells (CHO, 4 x 106 cells/ml) were inoculated with PEI Bacteria References (WHO Repository Transfusion Relevant Bacteria Reference Strains) with a final count of 5-50 CFU per sample (0.5 to 5 CFU/ml).

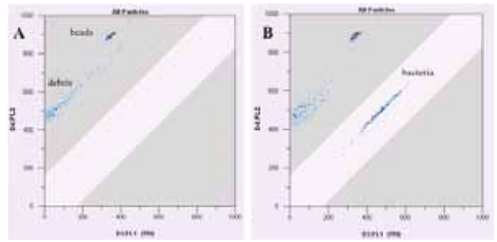
Universal Bacteria Real Time PCR

Detection of sequences of ribosomal nucleic acids conserved in all bacteria using real-time PCR offers a universal tool for their detection. The technique is very sensitive (~ 10 CFU/ml), rapid (1-3 hours), and relatively easy to perform [5]. To the best of the author’s knowledge, no commercial method is available on the market, however, efforts concerning this are being made by various manufacturers. Real-time PCR can be used directly (advantage: very rapid; disadvantage: detection of bacterial cadavers) or in combination with a short pre-incubation of the sample in liquid media as cited above (advantage: “growth based method”, i.e. detection of living microorganisms only; disadvantage: prolongation up to 6-10 hours).

Flow cytometry

Flow cytometry has been described as a feasible tool for rapid detection of microorganisms in PCs [6,7,8,9]. Results are avail-

Figure 1
Detection of microorganisms using the Bactiflow cytometer. Jurkat cell culture samples were inoculated with PEI Bacteria References. After enzymatic digestion of mammalian cells a non-fluorescent fluorochrome that passes the cell membrane of viable cells is added to the sample. Following cleavage by intracellular esterase fluorescence is produced and detected by the Bactiflow cytometer (AES Chemunex GmbH, Germany).
A: negative control (jurkat cell culture sample free of bacteria)
B: positive control (Staphylococcus epidermidis PEI-B-06) inoculated in jurkat cell culture
Upper population: internal validation beads



able within 30 to 60 minutes. There is one approach on the market originally developed for food microbiology (BactiFlow, AES Chemunex GmbH, Germany) having a sensitivity of around 100 CFU/ml. A respective pilot study at PEI demonstrated that the method is generally applicable for cell therapeutics (Fig. 1). As pointed out for real-time PCR, flow cytometry can be used directly or in combination with a short pre-cultivation showing in principle the same advantages and disadvantages. In case of pre-incubation the results are available within 5-20 hours.

Detection of Microcolonies

Another pilot study involves two methods originally developed for microbial monitoring of the environment; the Milliflex Rapid System (MR) and the Milliflex Quantum System (MQ, both Millipore, France) which are based on membrane filtration and visualization of microcolonies via ATP-bioluminescence (MR) or fluorescence (MQ) [10,11]. Applying the CHO cell model, the times for diagnosis were between 4-7 h (MR) and 7-13 h (MQ). Figure 2 shows the detection of three PEI Bacteria References.

Outlook

There is a strong necessity for development of novel principles in microbial safety of cell therapeutics. Moreover, we need a paradigm shift in thinking. Whereas the current asking regarding sterility is “we have to find everything”, the new thinking has to be “we have to find as much as possible within the time frame available”.

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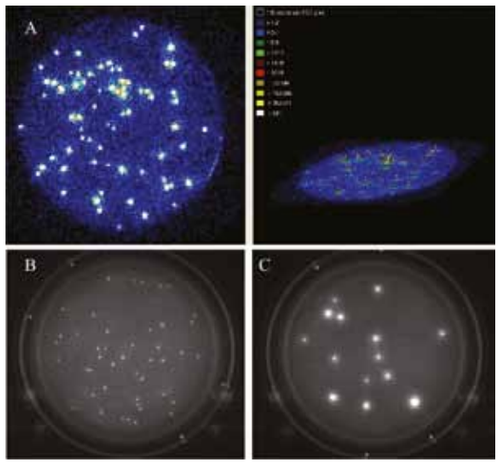
Figure 2

Detection of Microcolonies using ATP-bioluminescence (A) or fluorescence technology (B, C). Membrane filtration was performed after inoculation of PEI Bacteria References into CHO-cell suspensions and lysis of mammalian cells. Membranes were placed onto Trypcase Soy Agar plates and incubated at 32.5°C for different time periods. Detection was performed using the Milliflex Rapid (A) and Milliflex Quantum System (B, C; both Millipore S.A.S., France) after addition of corresponding staining solutions:
A: Microcolonies of Enterobacter cloacae (PEI-A-43) after 5 hours incubation at 32.5°C using the Milliflex Rapid System. The microcolonies are visualised by luciferin-luciferase-mediated luminescence.
B: Microcolonies of Staphylococcus epidermidis (PEI-B-06) after 13 hours, and...
C: Microcolonies of Bacillus cereus (PEI-A-33) after 11 hours incubation at 32.5°C using the Milliflex Quantum System. The microcolonies are visualised by fluorescence.



Erhard Seifried and Reinhard Henschler
Institute for Transfusion Medicine and Immune Hematology,
German Red Cross Blood Donor Service Baden-Württemberg - Hessen, Clinics of the Goethe University, Frankfurt, Germany

The Challenge for Transfusion Medicine in Interdisciplinary Cooperation in Cellular Therapy

ISBT is demonstrating its serious commitment to intensify support of activities in this important field of transfusion medicine. In particular, this has become visible through the recent establishment of an own Working Party on Cellular Therapies at ISBT´s 31st International Congress in Berlin in 2010. In this issue of Transfusion Today, several articles appear which mirror the substantial ongoing activities within the working party. This comprises work on securing donor identification (see article by Dr Anneke Brand), advancement in sterility testing in cell therapeutics (see article by Dr Melanie Störmer), but also takes up such burning issues as the commercialization of cord blood conservation (article by the chair of the Working Party, Professor Paolo Rebulla). In addition, a report is given on a recent European meeting summarizing the current advances in the preclinical and clinical development of mesenchymal stromal cells (MSCs), held in Milan in April 2011.

It is clear that the challenge to safeguard a high and transparent quality of our cellular therapeutics provides an enormous challenge to the entire field of translational medicine. We propose that transfusion medicine, due to its unique profile in expertise and developmental capacities, will be a prime discipline to spur this development through the ability of physicians working in transfusion medicine.

In the normal development of a cellular therapeutic, usually clinicians and scientists who have developed novel cell-based medicines come to us and wish us to convert their cells into a state-of-the-art therapeutic which is GMP manufactured and validated for all currently required regulatory standards. In this situation, transfusion medicine institutes which run their own research laboratories and scientific groups as an own scientific basis, operated by physicians and scientists with a background in preclinical and clinical research, will be at advantage as partners to the clinicians who develop new concepts of cellular therapies.

A main reason for this is the fact that these transfusion medicine doctors will likely speak two languages – the language of basic science but also the language of the manufacturer of a pharmaceutical cell product.

Ideally, the personnel at transfusion institutes will therefore also comprise physicians with experience in conducting clinical studies, and who can either facilitate interactions with the clinical study center or who could run activities of a study center at the same time. We can state that for our own institution of the Red Cross Blood Donor Service Institute of Transfusion Medicine and Immune Hematology at the University Hospital Frankfurt, this concept has proven extremely fruitful and rewarding. We can recommend such a concept for the discipline of transfusion medicine in general, and can recommend ISBT to work on mediating interaction between such centers´ activities, and stimulating young researchers to follow integrated and interdisciplinary approaches in such environments.

We appeal to all physicians and scientists who are active in our Society and beyond in the area of transfusion medicine and in related areas, to consider models of substantiated and scientifically based interactions with their various clinical partners. This would involve taking them into the responsibility when designing a pharmaceutically best qualified clinical grade production process and product. Moreover they should be notified or even involved into the active surveillance of the integrity and preserved efficacy of cellular therapeutics. Of course, this will have to occur in addition to already established quality and release criteria for these medicines. We predict that the reward will be a mutual learning and interaction, and that this will increase the visibility, the quality and the credibility of the cooperative work between the individual involved disciplines. Such an approach should therefore contribute to a maximum benefit of a scientific approach in clinical cell therapy development and shall reward finally and especially our patients.

Stem cells from normal to cancer: The Good, the Bad & the Ugly Strike Again

Federico Colombo
Centre of Transfusion Medicine, Cellular Therapy and Cryobiology, Foundation Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.

The title of the famous 1966 'spaghetti western' by Sergio Leone has given many investigators an opportunity to make a paraphrase of positive and negative properties of stem cells (1-5). Here some good, bad and ugly features of stem cells along the pathway from normal physiology to cancer transformation, are discussed and should be taken into account when developing novel cellular therapy products and therapeutic protocols.

Normal adult stem cells from healthy individuals (the 'good'), share two basic features which distinguish them from all other adult cells: self replication and progeny generation. Both are necessary to ensure the correct function of all body organs, tissues and systems. Blood is a remarkable and well studied example of such tissues, where hemopoietic stem and progenitor cells physiologically resident in a quiescent state in the bone marrow generate billions of red cells, white cells and platelets every day and at the same time self replicate to maintain the regenerative potential for future physiologic needs and for system repair after pathologic events. These processes are finely tuned to ensure the correct maintenance of this crucial homeostatic function. However, during their very long lifespan, these cells can accumulate genetic mutations and epigenetic alterations causing de-regulation of their function (the ' bad'). Included in their sophisticated molecular machinery, stem cells dispose of powerful tools to repair damages caused by mutagens such as chemicals and radiation. Despite their documented and reassuring efficiency, these tools may be challenged by a number of causes including a generally increasing level of pollution, which can exhaust their self reparative capability and lead to cancer transformation.

Cancer stem cells share their origin with normal stem cells and the property of self replication and generation of a progeny consisting of more or less differentiated cancer cells. Unfortunately, cancer stem cells also share another self protective basic feature of normal stem cells, which greatly limits most therapeutic attempts developed for their complete eradication. Although our knowledge of these cells is still limited, their existence has been unquestionably proven in some blood, breast, colon, liver and brain cancers. With regard to the latter, unexpected findings from a recent study by Italian investigators (6) opens new perspectives for the treatment of glioblastoma. It has been known since a long time that tumours in general and glioblastoma in particular can self support through the generation of new blood vessels. This notion has led to the development of treatment modalities including not only 'anti-tumor' but also 'anti-vessel' cell drugs (AKA 'anti-angiogenetic' drugs). Previous information had supported the view that tumours could recruit endothelial cells from vessels in close proximity through the production of endothelial cell growth factors. The observations from the Italian investigators provide novel evidence that most endothelial cells lining along tumour vessels do not derive from normal endothelium but from cancer stem cells, which can harness their differentiation capacity into mature cells to build new vessels able to feed the tumour.

This unexpected finding paves the way to new important therapeutic developments. First, it can provide a clue to understanding the cause of the relative inefficacy of current anti-angiogenetic therapies, which have been designed with the aim of targeting 'normal' endothelial cells and can be ineffective against vessels generated by tumour stem cells. Moreover, as the new vessels play a fundamental feeding role not only for tumour development but also for the survival of the tumour cell mass, preventing cancer stem cell transformation into new vessels could prove an effective therapeutic strategy against glioblastoma and, possibly, other tumours.

Not unexpectedly, studying the 'bad' and the 'ugly' could provide a solution to restore the 'good'. In parallel, improved knowledge on the mechanisms of transformation of normal into cancer stem cells could improve our ability to develop safer and more effective cellular products for the treatment of our patients.

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Paolo Rebulla
Director, Milano Cord Blood Bank, Center of Transfusion Medicine, Cellular Therapy and Cryobiology, Department of Regenerative Medicine, Foundation Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy

In the Best Interest of My Baby

Some valuable arguments against commercial cord blood conservation.

Busy expectant mothers and their partners do not have much time available during the late phase of pregnancy when they are confronted with two alternative and conflicting options: should we store our baby's cord blood in a private commercial bank for his or her future exclusive use – the so called 'autologous conservation' option – or should we generously accept the invitation made by public banks to donate cord blood for the community needs – the so called 'solidaristic' option? Although some mothers may be simplistically attracted by the advice offered by some fashion, sports and entertainment VIPs – in spite of the usually limited knowledge by the latter on the topic under discussion – most mothers duly follow the guidance provided by mother nature which teaches them to act in the best interest of their babies. Accordingly, they seek for 'evidence' supporting their choice in favor or against the understandable 'temptation' of autologous conservation.

Most of the times, they have contacted me in my role as director of a large public bank with a crystal clear argument: we all know how important stem cells are as therapeutic tools and how many studies are currently being performed to find novel applications of these apparently 'magic' cells for the treatment of pathologic conditions of the heart, liver, lung, kidney, brain and other important organs for which current therapies offer no hope. If the above is true, how could a mother deprive her baby of such a formidable source of repair for future illnesses?

We, as professionals involved in maternal counselling, have two options: option one is to refer mothers to many 'position statements' published in scientific journals by respected scientific societies or groups such as the American Society of Pediatrics, the Royal College of Obstetrics and Gynaecology, the World Marrow Donor Association, the Expert Group on Ethics of the EU (1-4), and others. A proportion of mothers with adequate cultural elements and sufficient linguistic skills allowing them to properly manage these documents find in the above sources of information appropriate elements for an informed choice.

For those unwilling or unable to use the above resources, or asking for additional advice, I found the next few arguments particularly enlightening.

Argument one. It is of course totally understandable and fully correct that you, as a mother, want to preserve for your baby 'any best possible chance'. Let's reason on what this chance can be when we talk of stem cells and their therapeutic application. The therapeutic option for today and the next few years to come is the treatment of severe blood diseases (some forms of leukemia, lymphoma, thalassemia, immune deficiencies and metabolic disorders). Clearly, if your baby suffers from a genetic condition, his or her own defective cells do not represent a suitable option for cure. Moreover, also in conditions which do not show a classical heritable pattern – eg leukemia – some cellular defects predisposing to a later development of the condition may be present also during the antenatal phase. Again, autologous cells are not a good option for autologous transplant in such cases. Finally, a slight degree of difference – technically termed 'incompatibility' – between transplant donor and recipient is desirable for the treatment of some tumours as the 'graft versus host reaction' played by the donor transplanted cells against the recipient organs and tissues can eradicate residual tumour cells resistant to chemotherapy. How could a rational mother of an unfortunate baby affected by leukemia in need of a 'donor transplant' (technically called 'allogeneic' to differentiate it from 'autologous' transplants) ask another mother to donate her baby's 'precious' cells for this 'lifesaving allogeneic transplant' if she has not agreed to donate her own baby's cord blood for others in need? Most mothers – being correctly interested in their own baby's 'best chance' - understand argument one.

Argument two. Let's assume that in 40-50 years totally innovative treatments are developed from cord blood stem cells to cure a number of conditions for which there is no treatment available today, eg hearing loss or neural degeneration. No one knows the future, but it is not totally irrational to expect that similar treatements could be developed starting from cells which are quite similar to cord blood stem cells and which mother nature preserves in our bone marrow at no cost and under strict quality conditions that are not so evidently maintained in many commercial cord blood conservation programs (5). Most mothers who are still skeptical after discussing argument one change their views after considering argument two. Last but not least, for some of them the savings linked to public donation as opposed to the expense of 2,000 – 3,000 euros for private conservation provide precious additional resources for the care and education of their baby.

Don't try to convince mothers with 'dry science' only. Follow their natural and correct reasoning to act in the best interest of their babies. Just provide them with elements to determine what this 'best interest' can be.

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In Focus Working Party on Cellular Therapies

Lorenza Lazzari[1], Massimo Dominici[2], Rosaria Giordano[1]

[1] Cell Factory 'Franco Calori', Center of Transfusion Medicine, Cellular Therapy and Cryobiology, Foundation Ca' Granda Ospedale Maggiore Policlinico, Milan;

[2] Laboratory of Cell Biology and Advanced Cancer Therapies, Department of Oncology, Hematology and Respiratory Diseases, University Hospital of Modena and Reggio Emilia, Modena, Italy.

3rd FIRST Meeting Report

Milan, April 18th 2011

The purpose of the "Forum of Italian Researchers on Mesenchymal and Stromal Stem Cells" (FIRST) is to bring together the different experiences currently ongoing in the field of mesenchymal stem cell (MSC) research, also using the potential of the web to get scientists connected on a real time basis.

On April 18th 2011, the third meeting of FIRST was held in Milan, Italy, with the participation of attendants from 5 European Countries. Particular emphasis was put on the contribution of young researchers who were also awarded for the best abstracts. Presentations included studies on neuroregenerative properties of MSC and kidney repair, on MSC senescence, on mechanisms underlying MSC multipotency and their immunomodulatory properties. Moreover, the limits and bottlenecks of induced pluripotent stem cells have been reviewed, with particular attention to cardiovascular applications.

Mesenchymal stem cells and neuroregenerative properties. MSC have been proposed to contrast the progressive dopaminergic depletion caused by the selective death of neuronal subpopulations that is responsible for the symptoms in Parkinson's Disease (PD). In the study presented by Patrizia Bossolasco, undifferentiated human MSCs have been implanted into the striatum of rats bearing a lesion of the nigrostriatal pathway induced by local injection of 6-hydroxy-dopamine (6-OHDA), a widely recognized rodent model of PD (1). MSCs expressed markers of neural cells, but no glial markers were detected. After transplantation, some transplanted cells acquired a glial-like phenotype in animals bearing the nigrostriatal lesion, but no differentiation toward a dopaminergic phenotype was observed. Interestingly, transplanted animals showed increased survival of both cell bodies and terminals of dopaminergic neurons and a reduction of the behavioral abnormalities associated with the lesion. These results suggest that MSCs could stimulate the surrounding microenvironment to support damaged neurons substitution. It was also demonstrated that grafted MSCs sustained the survival of striatal/nigral dopaminergic terminals and enhanced neurogenesis in the subventricular zone and neuroblasts migration. Moreover, MSC protected the murine differentiated Neural SCs (mdNSCs) against the cytotoxic effects of 6-OHDA in a co-culture system and multiplex human angiogenic array analysis on the conditioned media demonstrated a modulation of released cytokines.

The neuroregenerative properties of MSC have also been investigated in the context of peripheral nerve gap injuries that are currently repaired with an autologous nerve graft or biocompatible nerve conduits. The combination of biomaterials and MSC may facilitate improved nerve regeneration. The results presented by Giorgio Terenghi demonstrate that adult adipose-derived MSC differentiated towards the expression of phenotypic and functional characteristics of Schwann cells and transplanted into bioengineered nerve conduits, have beneficial effects in promoting enhanced nerve regeneration (2).

MSC and kidney regeneration. Important advances have recently been made in understanding the mechanisms underlying the effects of MSC in renal regeneration. Several studies support the paracrine action of MSC. It has also been demonstrated that microvesicles (MVs) derived from human bone marrow MSCs may be responsible for the observed effects of MSC. In particular, Benedetta Bussolati demonstrated that MVs are as effective as the cells themselves in accelerating the recovery in models of glycerol-induced acute kidney injury and of acute and chronic ischemia-reperfusion damage (3). MVs released from MSC may reprogram target cells by transferring various bioactive molecules including specific subsets of mRNA and microRNA.

Induced pluripotent stem cells and cardiovascular repair. Massimiliano Gnecchi discussed the current basic science, the techniques, potential and possible risks of induced pluripotent stem (iPS) cells in the light of needs for patient-derived pluripotent stem cells. Data concerning generation, efficient genetic modification, scalable expansion and cardiorespiratory differentiation of iPS cells were presented. Their application for myocardial restoration and tissue engineering, together with the first encouraging results of iPS cells in pharmacological research, were reviewed, suggesting fascinating perspectives for future developments in biotechnology and regenerative medicine.

MSC and senescence. Wolfgang Wagner analyzed genetic and epigenetic sequels upon expansion of MSC from human adipose tissue. Since the early passages the fibroblastoid colony-forming unit (CFU-f) frequency and the differentiation potential are significantly impaired. Indeed, significant chromosomal aberrations are not detected by karyotyping and SNP-microarrays, thus supporting the notion that human MSC possess relatively little genomic instability. DNA-methylation profiles evaluation showed that the profiles of MSC derived from adipose tissue and bone marrow markedly differed. Highly reproducible senescence-associated modifications at specific CpG sites occurred already within the initial expansion phase (between passages 5 and 10). Notably, these DNA-methylation changes correlated with histone marks such as trimethylation of H3K9, H3K27 and EZH2 targets. These results indicate that cellular aging is not just a random accumulation of cellular defects, but that it is precisely regulated by epigenetic means in the course of culture expansion.

MSC and immunomodulatory effects. A general overview on the effects of MSC from different sources was discussed. The results presented by Cedric Menard were collected in the context of two current European Consortia, the CASCADE and the REBORNE projects, aimed at establishing common standards for the production, control and clinical use of MSC in skin, cornea and bone regeneration.

Molecular pathways for multipotency in MSC. Donald Phinney showed recent results on the role of different molecules in maintaining the undifferentiated state of MSC. FGF2 reversibly inhibits multi-lineage differentiation of primary mouse MSC. Moreover, the pre-treatment of MSCs with FGF2 specifically up regulates TWIST2 and SPRY4, which suppresses ERK1/2 activation in response to osteo-inductive stimuli and results in suppression of bone specific gene expression. FGF2 also induces expression of FGFR1 and FGFR4 and suppresses expression of FGFR2 and FGFR3 whereas BMP2, which increases osteogenic differentiation, has the opposite effect. Moreover, FGF2 has dramatic effects on cytokine gene expression in MSCs, such as IL-1α and IL-1β. FGF2-induced up regulation of IL-1β also strongly correlates with suppression of TWIST1 expression as well as several anti-inflammatory proteins belonging or related to the IL-1 family (4). Collectively, these data suggest that TWIST proteins integrate external signals in MSCs to regulate differentiation and cytokine gene expression, thereby providing a critical link between the stem-like and stromal-like functions of the cells.

Taken together, the information presented during the 3rd FIRST meeting defines a new framework of MSC research in which their mechanisms are better clarified, thus opening new options in the fascinating field of regenerative medicine.

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"See you soon in Lisbon!"

Silvano Wendel

The spring in the Northern hemisphere brings a very colorful season, where trees are blossoming and skies are no longer grey. Since my last address (February), I had the opportunity to be in Dubai (United Arab Emirates) and Dublin (Ireland) representing ISBT.

In Dubai, WHO is developing a program focused on Patient Blood Transfusion Management. This certainly requires a multidisciplinary, collaborative effort between all kinds of professionals responsible for transfusions at the patient site (prescribers, nurses, hemovigilance officers, transfusion medicine specialists, and several medical associations). It really represents the final stage of the Blood Transfusion chain, which has not always been completely covered by some Blood Transfusion Centers, where the main focus was to provide adequate and safe blood units. I concur that it is time now to have transfusion medicine specialists working together with the patients' corresponding physicians, so we can promote a more integrated interface between all players. This is certainly a very promising field to be developed by ISBT.

In this aspect, ISBT is starting the development of a new partnership with NATA. Following an invitation from Dafydd Thomas (NATA President) I attended their Board meeting, held in conjunction with their annual meeting in Dublin. After a friendly and fruitful conversation, the ISBT Executive Committee approved my proposal to have NATA brought closer to us, by being more active with the ISBT Clinical Working Party, chaired by Jonathan Wallis. I wish Dafydd and Jonathan success in this new, joint activity, and hope that the fruits are harvested pretty soon.

The current issue of Transfusion Today focuses on the joint ISBT/AABB Working Party on Cellular Therapy, chaired by Paolo Rebulla and John McMannis. It is rewarding to see that after a lag phase, our members have access to interesting articles about the uniform examination of stem cell donors, advancements in sterility testing and the challenge for Transfusion Medicine in Interdisciplinary Cooperation in Cellular Therapy. ISBT and AABB have the same view that Cellular Therapy is very important for the future of our activities, and certainly both Societies are maintaining efforts to allow its development on a global scale. This is a very fascinating field, which will give a substantial change in our future daily activities. We have to be prepared for the future.

In June, before the Lisbon congress, the ISBT Board will meet in Estoril for a 2-day meeting. Our mission is to develop our strategic plan for 2012-2015, our long-term projects need careful planning.

Finally, start to pack for Lisbon. The regional ISBT congress in Portugal had more than 800 abstracts submitted from people representing 67 countries. Although originally intended to be a regional congress, our estimates show that ISBT is not organizing regional congresses anymore, but rather another global congress, albeit in lower scale than our traditional International Congress, whose next one will be in Cancun. This is a clear signal that ISBT represents professionals from all corners of the globe, and we have to promote it even further. The more we include peoples from all countries of the world, understanding their differences and looking for the same principles and targets, the more we will fulfill our mission towards implementing a continuous development of Blood Safety on a global scale.

See you soon in Lisbon!

Silvano Wendel
ISBT President

ISBT Corporate Membership

ISBT has introduced Corporate membership and is pleased to announce that currently two companies have become corporate members; Heamonetics and Roche.

Roche provides diagnostic tests and automation platforms used worldwide to improve the safety of blood products, increase laboratory efficiency, diagnose disease, onitor response to therapy and identify gene-based factors that may aid in treatment selection.

Roche has joined the corporate membership programme as a platinum member.

Haemonetics is a global healthcare company dedicated to providing innovative blood management solutions their customers. Their devices and consumables, information technology platforms and consulting services deliver a suite of business solutions to help customers improve clinical outcomes. Haemonetics has joined the corporate membership programme as a gold member

For further information on corporate membership please contact the ISBT Central Office.

HAEMONETICS®
THE Blood Management Company

Roche

Welcome to our new members

February 2011 - April 2011

Africa
- **CAMEROON:** Claude Tayou Tagny
- **SOUTH AFRICA:** Lesley Bust

Americas
- **MEXICO:** Oscar Jimenez, Juan Carlos Wynter Garcia
- **USA:** Evan Bloch, Anna Ettinger, Lawrence Goodnough, William Greenman, Matthew Murphy, Gorka Ochoa, Adonis Stassinopoulos

Eastern Mediterranean
- **IRAQ:** Yakoob Al-Musawi, Faez Al-Qazzaz, Mohammed Khalid
- **KUWAIT:** Hanan Al-Awadhi, Reem Ameen, Christian Awarasi
- **QATAR:** Mohammed AzharMohiuddin
- **SAUDI ARABIA:** Ali Alsharef, Layla Bashawri, Osama El Fayoumi, Amr Halawani, Ali Mohamoud

Europe
- **BELARUS:** Volha Klimovich
- **BELGIUM:** Alain Alewaeters, Helena Bunkens
- **BULGARIA:** Emiliya Binakova
- **DENMARK:** Helle Abildgaard, Lene Albjerg, Sandal Anny, Susanne Askbo, Christian Erikstrup, Gitte Feldborg, Birthe Hansen, Svend E. Hove Jacobsen, Assing Kristian, Franziska Larsen, Lone Daniel, Laursen Vibeke Ljoerring, Lisbeth Milling, Conni Nielsen, Helle Sarnum
- **FINLAND:** Teemu Laakso, Anne Linnolahti, Jarno Tuimala,
- **FRANCE:** Pascal Bailly, Philippe Ligot
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- **ITALY:** Giuseppe Bresolin, Filippo Buscemi, Michele Cirella , Giovanni Gajo, Donatella Londero, Cinzia Paccapelo, Daniele Prati, Domenico Visceglie
- **LITHUANIA:** Rita Kralikiene, Reda Verbickiene, Evelina Zenkeviciene
- **NETHERLANDS:** Stephanie Agoston, Femmeke Prinsze, René van Lier
- **NORWAY:** Fadi El-Hage, Thomas Larsen, Titze Poland: Aneta, Kopacz
- **PORTGUAL:** Maria Antonia Escoval,
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- **RUSSIA:** Larisa Golovkina, Anastasia Lelekova, Alexey Rukavishikov
- **SERBIA:** Velimir Srejic, Milena Todorovic, Dusan Vucetic
- **SPAIN:** David Garcia-Crespo, Laia, Jofre, Mónica Lopez
- **SWEDEN:** Hans Gullikkson, Camilla Hesse
- **SWITZERLAND:** Christoph Gassner, Peter Gowland, Hein Bovenkant formulier Hustinx
- **UNITED KINGDOM:** Carole Green, Vanja Karamatic Crew, Brian Marcel Graham Smallridge

South East Asia
- **INDIA:** T.R. Raina, Atul Sonker, Saptuti Chunaeni
- **INDONESIA:** Saptuti Aditya, Zainal Arifin Aly
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Western Pacific
- **AUSTRALIA:** Chris Hogan, Sue Ismay, Kylie Rushford
- **CHINA:** Yan Meng, Jinglin Wu
- **JAPAN:** Izumi Toru, Chiaki Yamad
- **REP. OF KOREA:** Ji-Seon Choi
- **MALAYSIA:** IrmaLisa Samsuri
- **NEW ZEALAND:** Christine van Tilburg
- **PHILIPPINES:** Maria Rizalina Chua

November 20-23, 2011

22nd Regional Congress of the ISBT, Asia, Taipei, Taiwan

The ISBT president and Board of Directors are looking forward to welcoming you to Taipei for the 22nd Regional Congress.

All the information regarding the congress e.g. abstract submission, registration, accommodation, key dates is available on the Taipei website **isbtweb.org/taipei**

Abstracts
You are invited to submit an abstract in one of the many topics available. You can share scientific findings with colleagues from around the region and receive expert feedback. The deadline for abstract submission is July 3, 2011.

Key Dates to Remember

Deadline for Abstract Submission	July 3, 2011
Abstract Notification Information	August 13, 2011
Deadline for Early Registrations	August 26, 2011
Deadline for guaranteed Hotel Accommodation	September 30, 2011
Deadline for Cancellation of Registration	October 28, 2011

For more information please visit **isbtweb.org/taipei**

Geoff Daniels

What is the ISBT's strategy into the future?
In order to achieve its vision – 'Facilitating knowledge about transfusion medicine to serve the interests of donors and patients' – the ISBT must have a strategy. Consequently, the ISBT Board of Directors is charged with drawing-up a three-year strategic plan. The goals of the current plan are:

- Expanding the scientific profile of ISBT.
- Developing a portfolio of high quality effective communication channels.
- Positioning ISBT as a global leader in transfusion medicine education.
- Developing a High Standard of corporate governance.
- Strengthening the ISBT congresses.

The term of this strategic plan ends in 2012, so it is now time for the Board to start formulating a new plan. The process began at the Board meeting in Amsterdam in February, where Board members were introduced to two Professors from the Department of Strategy and Business Environment, Rotterdam School of Management at the Erasmus University, who are facilitating the development of the new plan. The Board members then embarked in some 'brainstorming' exercises to start to assess key areas for further examination.

The next stage of the process will take place in Estoril near Lisbon, Portugal, in June immediately before the ISBT Regional Congress. After two days incarceration with the two professors we hope to have made substantial progress towards the formulation of a strategic plan for 2012 to 2015.

Cellular therapy – what about red cells?
The main focus of this issue of Transfusion Today is cellular therapy, the introduction of new cells into a tissue in order to treat a disease. Cellular therapies are not strictly speaking part of transfusion medicine, but as transfusion and transplantation share so much technology and expertise, cellular therapy has become a new and exciting element of our discipline.

Some of you may be aware that I tend to favour blood cells that contain haemoglobin. So with cellular therapies in mind, could it be possible to culture and manipulate red cells for therapeutic purposes? Well, possibly. Erythroid cells have been cultured from three sources of progenitors: (1) blood stem cells derived from adult or cord blood; (2) embryonic stem cells; and (3) fibroblasts manipulated to behave like embryonic stem cells (induced pluripotent stem cells). By culture under the appropriate conditions, these cells can be coaxed to develop along the erythroid line, produce haemoglobin, express red cell surface markers, and even exclude their nuclei. So the result is small quantities of reticulocyte-like or erythrocyte-like cells.

Can the process then be scaled up so that sufficient numbers of red cells for a blood transfusion can be produced, at an acceptable cost? I am not convinced that goal can be achieved at the moment, but it should be only a matter of time. Once that has been mastered, then genetic engineering can be applied to produce bespoke red cells, tailored to the individual patient. Don't hold your breath, but this technology could revolutionise blood transfusion, virtually eliminating the requirement for blood donors. A more modest goal, though, would be to apply this technology to the production of 'designer' red cells, expressing reduced or enhanced levels of selected blood group antigens, for use in antibody detection and identification.

Lisbon in June
Returning to more immediate matters, the programme for the 2011 Regional Congress in Lisbon, Portugal is now complete. The scientific committee has produced a broad and stimulating programme, which should provide plenty to interest everyone involved in transfusion science and medicine. So, if you have not done so already, why not check it out on the ISBT web site? Lisbon in June will be a great place to be.

Geoff Daniels

ISBT Supporting Transfusion Medicine Education ACADEMY

ISBT is willing to help support educational activities such as workshops and symposia.

Are you intending to host an activity related to Transfusion Medicine in 2011? The activity can be about any topic but must be related to Transfusion Medicine e.g. haemovigilance, transfusion transmitted infections, quality management.

ISBT may be able to help you. Information on how ISBT can support you and how you can apply can be downloaded at **www.isbtweb.org**

ISBT Academy

The concept of the ISBT Academy was developed with the intention to organise educational courses, and give support to national or regional courses or congresses. During recent years ISBT has supported workshops and meetings with the use of its logo and occasionally providing speakers for a programme with a particular focus. One of the successes of the Academy has been the Arab Transfusion Medicine courses.

Last year Anne Husebekk, ISBT Senior Vice President and Chairperson of the Academy and Judith Chapman, ISBT Executive Director met to discuss the activities of the Academy and to develop a plan for future activities. The plan was put to the Board meeting in February. The plan included the development of procedures for applying for an Academy event and an application form and a proposal to institute an ISBT Academy Standing Committee which will be chaired by the Senior Vice President. The Standing committee will consist of up to ten ISBT members will have international representation and include the ISBT Junior Vice President and the ISBT Scientific Secretary. This Standing committee will replace the Standing Committee on Education which has been dissolved.

The ISBT Board expressed its commitment to supporting the Academy and to demonstrate this commitment has allocated money to the Academy in the budget for 2011/12.

ISBT has developed a document on the procedure for applying for an Academy event and an application form. These are available on the ISBT website. Once the application form is received it is sent to a small review committee who make the decision for approval of the activity.

So far in 2011 the ISBT will support 12 activities in 11 countries. Two more activities are awaiting agreement.

For more information please visit the Academy page on **www.isbtweb.org**

Nesrine Fathi Hanafi
Lecturer in Medical Microbiology & Immunology
Faculty of Medicine,
Alexandria University, Egypt

Hepatitis C Virus

and Peripheral Blood Mononuclear Cells

Though being a primarily hepatotropic virus, hepatitis C RNA genome sequences have been detected in many different organs. Furthermore, replication of the Hepatitis c virus in cells of the immune system has been linked to the capacity of establishing a chronic status through affecting their normal function. There has been a controversy in reporting the detection of the HCV in the cells of the hematopoietic system. Many authors demonstrated that the bone marrow has been found to be highly infiltrated by the virus, proven via HCV RNA sequences detection in peripheral and medullar hematopoietic cells in HCV antibody positive patients.[1] mainly B cells. A reported high tropism of HCV for B cells has been linked to the development of lymphomas described in cases of HCV-infected carriers.[2] There has been no reporting of HCV RNA detection in T lymphocytes and platelets although T lymphocytes which constitute the most abundant population in PBMCs.

Traces of HCV RNA may persist in liver or PBMC for up to 9 years justifying the persistence of humoral and cellular immunity for years after viral clearance. This poses the potential risk for transmission and reactivation. In case of immunosuppresion, PBMC all together with hepatocytes have been speculated to be a potential source for viral recurrence as in case of liver transplantation. These findings suggested that complete elimination of the virus is unlikely to be achieved.[3]

Other studies failed to demonstrate the viral sequences in those cells.[4-6] These controversies have been explained by the limited number of cases which varies in type of genotype causing the infection and the viral load which is usually of low level in chronic cases. Some authors proposed the hypothesis that favoring extrahepatic reservoirs by HCV viruses could differ according to the genotype and not the viral load.5 Some findings reflected a higher preferential tropism of genotype 1 viruses for PBMCs compared to genotype 2 isolates. Other studies reported preferential tropism of specific HCV viral quasi species for PBMCs.[4]

More recent studies using sensitive assays such as "Transcription Mediated Amplification" have confirmed that in the successfully treated or aviremic seropositive cases for HCV failed completely to demonstrate any HCV RNA in PBMC while it has been detected in the majority of viremic cases.[6] Thus they demonstrated that PBMC does not serve as reservoir for HCV patients who have clear sera for HCV RNA. It has been suggested that the detection of HCV viral particles previously reported have been attributed to adsorption of antibody-coated viral particles to Fc-receptor on the surface of the immune cells (monocytes, granulocytes, and B cells0 and not to invasion of the virus to inside the cell as part of viral replicaton.[6-8] Another justification of the detection of viral RNA in the polymorphs, is the take up of cellular debris of virally infected cells by the phagocytic cells which might include viral RNA.

Some reported clinical evidences can support the fact that PBMC does not act as long lived reservoir for HCV. This includes the slow decrease in anti-HCV antibody titers in cases with spontaneous clearance of viremia and the sero reversion detected in 7% of transfusion

> "There has been a controversy in reporting the detection of the HCV in the cells of the hematopoietic system

transmitted infections. This reflects the cis of antigenic stimulation inducing the antibody production.[8]

This debate is still not solved though there is an increasing evidence of excluding PMNC of being the host for maintenance of the virus within the carrier cases. This could impact strategies not only for management of cases but also for blood transfusion screening protocols.

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EASTERN MEDITERRANEAN

May Raouf
Medical Director Sharjah Blood Transfusion Centre, UAE

Gold Medal for the Ideal Blood Donor

United Arab Emirates – Sharjah Voluntary Work Award, 2010

Under the patronage of HH. Sheikh Dr. Sultan Bin Mohammed Al Qassimi, Member of Supreme Council, Ruler of Sharjah; Sharjah Voluntary Work Award in it's eighth session has awarded four voluntary, regular blood donors with gold medals during the celebration of the award on 16th December, 2010.

The board of trustees for the above mentioned award has set a group of criteria for the ideal blood donor who can win the medal. The blood donor should be a voluntary, regular donor who has donated 30 times.

Sharjah Voluntary Work Award includes different categories of awards, all support humanitarian voluntary acts, and voluntary, regular blood donation is one of these categories.

The blood donation centers in United Arab Emirates are requested to nominate their ideal blood donors to the board of trustees of Sharjah Voluntary Work Award every year for getting the above shown beautiful golden medal.

This reflect the government support of United Arab Emirates to voluntary blood donations program which is the stone base for safe blood transfusion practice in all countries. It is also worthy to mention that United Arab Emirates has hosted World Blood Donor Day in 2008 as the fifth country in world and 1st Arabic country; under the theme "One Is Not Enough".

Bernardo Camacho Rodríguez
Scientific Director Blood,
Tissue and Cells Bank
Hemocentro Distrital- Secretaría
de Salud de Bogotá

First Public Multi-Purpose Tissue Bank

Hemocentro Distrital, Secretaria de Salud de Bogotá, Colombia

A new welfare discipline, based on solid technical and scientific evidence called Tissue Therapy and supported by the technological advances in the cell and tissue preservation field has contributed to the development of transplants and implants. During the development of these advances, an essential component has been the participation of manipulation, cryopreservation and storage units, named Tissue Banks. These units or services have begun to be essential and necessary in all our Latin-American countries with the aim to offer therapeutic alternatives to many patients. Regretfully these services do not exist in some of our countries, or they are limited and do not procure or process all the different kinds of tissues that today are the object of transplant or implant.

The District Tissue Bank (Banco Distrital de Tejidos) of Bogota´s District Health Department is the first centralized public tissue bank in Bogotá and in Colombia. It was created and put into operation in 2010, in order to procure, process and cryopreserve different human tissues to be used in transplant and implant procedures by the public and private hospital network in Bogotá and other Colombian cities. Its activity is directed to supply primarily the poorest and most vulnerable population, lowering inequities and making the right to health a reality.

The implementation of the tissue bank has been carried out in phases: in 2010 the tissue bank started with skin, amniotic membrane, corneas and sclera. In 2011 osteoarticular tissues: bone, ligaments and tendons were introduced and in 2012 cardiac valves and vascular segments.

Bogota did not have a human skin bank, to satisfy the demand of many patients that have lesions, burns, ulcers or skin traumas, conditions which are treated by implanting skin obtained from cadaveric donors. This skin works as a temporary biological dressing while the patient generates his own new skin; these grafts benefit greatly the patients decreasing fluid and electrolyte loss, the risk of infection and pain and promoting epithelization, decreasing hospital stay and health cost. In some cases the allograft precedes the use of autologous grafts. The amniotic membranes are processed in the same way as the skin.

Although there are other eye banks in the city and in the country, the tissue bank wanted to be a service alternative in terms of the quality of the corneal tissue and sclera being processed and the access to the poorest and most vulnerable population.

Our muiltitissue bank was designed with high standards of quality and biosafety: we also have instruments and equipment of the latest technology. We have developed a robust quality assurance system; and the sanitary conditions certification granted according to the Colombian sanitary legislation and the registration to the Regional No. 1 of the National Donation and Transplantation Network of the country.

An outstanding aspect is constituted by the need to strengthen and develop a culture in the community for the donation of organs and tissue: religious, cultural and traditional aspects and the misinformation of the public about the therapeutic use of human tissues have become barriers to obtain them.

It is worth to note that in the same perspective and direction we are in the final phase of assembly of the first public umbilical cord stem cells bank (BSCU) of the country, which will begin operations in 2012.

We are committed not only to the needs of the population, but also to become a centre of excellence and reference center for teaching and academic training as well as the development of research projects in the fields of tissue and cell therapy.

Thus in a single center and headquarters, but interdependent, we have implemented a blood bank, a tissue bank and a cell bank (BSCU).

It is necessary to thank various tissue centers in Spain, for their support and collaboration and for their successful operating model that has become a global reference especially for Latin American countries.

Prithviraj Thumaiah[a], Janaki Sonoo[b], Marie France Lan Cheong Wah[c]
a Medical student, University of Pretoria; University of Mauritius (UoM), (2006-2009)
b Senior Specialist Pathologist, Head of National Blood Transfusion Service, Victoria Hospital, Candos, Mauritius.
c Senior lecturer, Faculty of Science, Department of Medicine, UoM, Réduit, Mauritius.

Blood Safety in Mauritius

A Knowledge, Attitude and Practice (KAP) survey of blood donors in a small island nation.

The reorientation of Mauritian economic activities into medical tourism has caused a drastic increase in the demands for safe blood and blood products. A nationwide Knowledge, Attitude, and Practice (KAP) sample survey provided the clues on how to expand, and retain the pool of regular, voluntary blood donors. The main focus was to increase the safety of blood, maximize efficiency of donor-recruitment programs, and provide empirical demographic data about Mauritian donors and non-donors.

A randomized, cross-sectional study was carried out on a population of 200 blood donors and 200 non-blood donors, who were approached in several regions of the island. A KAP questionnaire, adapted to the Mauritian folklore and practices, was designed, pre-tested, and used to harvest information from the population.

The survey found that males make up 82% of Mauritian blood donors while non-blood donors are predominantly young female adults with disproportionate fear of the phlebotomy process (Table 1). Socio-demographic profile, ethnicity, socio-economic profile, unawareness, and knowledge are the 5 principal factors determining willingness to donate blood. Altruism is absent among Mauritians

The ageing of the blood donors, in tandem with misconceptions from these subjects represent a direct threat to blood safety. Targeting the Mauritian young adults, an untapped pool of blood donors, is the answer to improved safety, and long-term sustainability of safe blood supply.

The full article can be found at **www.isbtweb.org**

Table 1 Characteristics of survey population
(Taken from a paper by Dr. Thumaiah. The full text is available on the ISBT website.)

	Blood donor	Non-blood donor
Percentage registered over total population	2.92 (35,000 registered)	97.08
Sample	200 (of which 80% regular blood donor)	200
Profile	38 years old married males of Indian origin with middle to high education and income.	29 years old single females of Indian origin with middle to high education and income.
Gender	M = 82% (164) F = 18% (36)	M= 35% (70) F = 65% (130)
Age	32.5% ages 18-30, 40% ages 31-45, 27.5% ages 46-60; Mean= 37.78	64.5% ages 18-30, 22% ages 31-45, 13.5% ages 46-60; Mean= 29.76
Marital status	74.5% married 25.5% single/ divorced/other	41% married 59% single/ divorced/other
Ethnic group	Indian origin: 81.5% (163) African origin: 11% (22) European origin: 3% (6) Chinese origin: 1% (2) Mixed origins: 3.5% (7)	Indian origin: 78% (156) African origin: 9.5% (19) European origin: 2.5% (5) Chinese origin: 0.5% (1) Mixed origins: 9.5% (19)
Level of education	No academic education: 2.5% (5) Primary education: 12% (24) School Certificate: 31.5% (63) Higher School Certificate: 23% (46) Certificate/Diploma: 9.5% (19) Degree: 21.5% (43)	No academic education: 1% (2) Primary education: 13.5% (27) School Certificate: 14% (48) Higher School Certificate: 37.5% (75) Certificate/Diploma: 12% (24) Degree: 12% (24)
Total household income	Low income (<Rs.10,000)= 25% (50) Medium income (Rs.10,000-25,000)= 51.5% (103) High income (>Rs.25,000)= 23.5% (47)	Low income (<Rs.10,000) = 34% (68) Medium income (Rs.10,000-25,000) = 46% (92) High income (>Rs.25,000) = 20% (40)
Residence	Rural: 55% (110) Urban: 45% (90)	Rural: 55.5% (111) Urban: 44.5% (89)

Eugene Zhiburt,
ISBT Regional Director,
Eastern Europe

Kirov Regional Blood Bank:

75 years, renewal and unusual regular blood donor

Figure 1 Blood donations in Kirov

Справка №

Серия АВ 057086

Дана донору Белых Н.Ю.

в том, что он(она) дал(а) кровь 11 АПР 2008

Дана для предъявления по месту работы.

В день сдачи крови за донором сохраняется средняя заработная плата по месту работы и предоставляется дополнительный день отдыха, который по его желанию может быть присоединен к очередному отпуску.

Основание: Распоряжение Совета Министров СССР от 30.11.55 г. № 805-Р и решение Государственного Комитета Совета Министров СССР по вопросам труда и заработной платы от 12.05.56 г. № 109/АВ.

М.П.

Дано, данное справку

Figure 3 Nikita Belykh blood donor certificate

The Jubilee conference "75 years anniversary of Regional Blood Bank" took place in Kirov in March 2011. Kirov is a city located 1000 km to the east of Moscow. Founded in 1936 the regional blood bank became the heart and source for the Kirov "transfusion hub": Research Institute of Haematology and Blood Transfusion, Medical Academy and Plasma fractionation plant (under construction).

The old-fashioned blood bank has been renewed in the last couple of years with the Federal and regional government investing about 5 million euros in reconstruction and in purchasing new equipment (Figure 1).

Russia consists of 83 regions each having a governor. Eight regional governors are blood donors. Only the Kirov Governor, Nikita Belykh, is a regular blood donor. He and his team donate blood every two months (Figure 2).

Figure 2 Nikita Belykh (left) blood donation

Nikita Belykh was born on 13th June 1975 and on 8th of December 2008, was nominated governor of the Kirov Region. Even among the youngest Russian Governors he is healthy and modern-styled. For example, he received a reprimand from President Dmitry Medvedev for tweeting during an official meeting. He has also become a victim of his own blogging activity.

Belykh wrote an entry describing how he became a blood donor. In the post he made a link to a scanned-in PDF copy of his certificate (Figure 3). That certificate according Russian low gives the right to a day off of work. So it is useless for the governor.

This was just what a woman in the northern Russian city of Vologda needed to falsify a similar document. The woman saved the certificate on her computer and made the necessary changes in a photo editing program. She added in her name and a relevant date, printed the copy and gave it to her boss. The director decided to check the authenticity of the document and sent an enquiry to the Health Department of the Kirov region. The reply was that the certificate that matched this number was issued earlier to Nikita Belykh.

The Health Department is going to hand over the fraud evidence to local law enforcement bodies. While Belykh says the incident is shameful, he added, *"That's what you get for giving free access to documents. It's both funny and sad,"* he wrote in his blog.

J.C. Wiersum-Osselton,
R.R.P. de Vries,
The Netherlands

Successful International Hemovigilance Seminar

Amsterdam, February 2011

Some 250 participants from over 35 countries and five continents attended the thirteenth seminar organized by the International Haemovigilance Network (formerly the European Haemovigilance Network). The Network and the ISBT Working Party on Hemovigilance are in communication with each other and collaborate on certain projects. Hemovigilance, their common focus, is defined as "a set of surveillance procedures covering the whole transfusion chain from the collection of blood and its components to the follow-up of its recipients (…)", intended to make recommendations to improve transfusion safety.

Throughout the seminar there were ample opportunities for exchanges between professionals. Plenary speakers on the first half day (Hemovigilance and transfusion safety: a global affair) set the scene by triggering reflection on cost of interventions. We were also reminded that hemovigilance should be rooted within and backed up by a functioning quality management system within blood service and hospitals. Actual focuses may differ between different parts of the world, as was made clear in presentations on blood safety in developing countries and hemovigilance in the US.

The programme on Hemovigilance in The Netherlands in the morning of the second day continued the challenge to reflect critically and systematically improve the hemovigilance activity, for instance by agreeing on definitions and addressing new developments such as transfusion outside hospitals. Interactive presentations from the Dutch transfusion experts and the national hemovigilance office TRIP (Transfusion Reactions in patients) using electronic voting highlighted differences between participants, both in transfusion practice and in interpretation and classification of hemovigilance reports. TRIP director Martin Schipperus presented the 2009 annual report and trends in 7 years of hemovigilance reporting: the encouraging rise of numbers of reports and the slower progress on implementation of recommended measures. A large part of the practical work of hemovigilance in hospitals is performed by transfusion safety officers (hemovigilance workers). An international survey among TSOs by Dutch members of the national hemovigilance platform pointed up the range of tasks and responsibilities, against a widespread lack of any formal requirement for specific training.

In the afternoon of the second day the parallel sessions and poster walk offered lectures by invited speakers as well presentations of submitted abstracts. All areas of the transfusion chain were covered, from donor vigilance (recording and vigilance of complications of blood donation, with a view to improving care and safety for blood donors) to errors and incidents in the blood transfusion chain and evaluation of the effectiveness of transfusion. The poster prize was awarded to Dr Dialina Brilhante and colleagues for their poster describing a pilot of RFID technology in the transfusion chain of a Portuguese hospital.

Future directions of hemovigilance were the focus on the final morning. Attention was given to physiology of vasovagal reactions to blood donation and possible preventive measures. Participants were stimulated to consider vigilance relating to autologous blood management techniques, such as the re-infusion of salvaged blood after surgery. The wider, international perspectives of hemovigilance and of biovigilance (which includes tissues, cells and organs) were presented and will become increasingly important.

What therefore have been the successes of hemovigilance? These were summarized in the results of a recent international survey of hemovigilance experts, presented by Dr. Jean-Claude Faber. Numerous improvements in transfusion practice have been seen in the 17 years since the first national hemovigilance system was created (in France). Some of the improvements might have come about without the work of the hemovigilance offices, but nevertheless hemovigilance can claim to have brought transparency and triggered action to reduce transfusion risks.

The concluding part of the seminar was the presentation of the second IHN award to Dr Lorna Williamson, co-founder of the well-known SHOT (Serious Hazards of Transfusion) office in the United Kingdom. In her award address Dr Williamson shared reflections on the first stages of SHOT, the major results of the past and new developments.

The full programme and list of speakers as well as most of the seminar presentations (in pdf) can be found on the IHN website (**www.ihn-org.net**). The next Seminar will be held in Montreal, Canada, on April 25-27, 2012.

2011

July 15 – 17

7th IABS Symposium On Advances In Transfusion Safety
Singapore, Singapore
www.iabs-singapore.org

August 10 – 12

XIII Congreso Argentino de Medicina Transfusional y del VII Congreso del Grupo Cooperativo Iberoamericano de Medicina Transfusional
Buenos Aires, Argentina
www.aahi.org.ar/2011/congreso/index.html

August 29 – September 3

24th World Congress of the International Society for Forensic Genetics ISFG
Vienna, Austria
www.isfg2011.org
isfg2011@interconvention.at

September 14 – 17

IX Congreso Anual de la Asociacion Mexicana de Medicina Transfusional
Mazatlan Sinaloa, Mexico
www.ammtac.org
ammtac@cablevision.net.mx

September 27 – 30

44. Jahrestagung der Deutschen Gesellschaft für Transfusionsmedizin und Immunhämatologie
Hannoverf, Germany
www.dgti2011.de/
Jasmin.Schlangen@thieme.de

October 5 – 7

I Ukrainian Transfusion Medicine Congress & Exhibition
Kiev, Ukraine
www.ukrainetransfusion.com

October 7 – 9

5th National Transfusion Conference
Kuala Lumpur, Malaysia

October 20 – 21

IVth National Conference of BAATA
Sofia, Bulgaria
www.baata.org
baata@mail.bg

October 22 – 25

AABB Annual Meeting
San Diego, USA
www.aabb.org

November 20 – 23

22nd Regional Congress of the ISBT, Asia
Taipei, Taiwan
www.isbtweb.org/taipei
taipei@isbtweb.org

2012

July 7 – 12, 2012

32nd International Congress of the ISBT
Cancun, Mexico
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