ESID Newsletter

Reminder call for membership fee payment 2008-2009 !!

European Society for ImmunoDeficiencies

2008-3

ESID Newsletter

Contents

The ESID Newsletter is made for the members of ESID – the European Society for Immuno Deficiencies.

It is published under the responsibility of the ESID Board, and at this moment it is edited by Esther de Vries (editor in chief), Lucia Bianchi, Ales Janda, Gustavo Lazo, Nima Rezaei, and Crina Samarghitean.

Any ESID member who is interested in publishing his or her views, research, new ideas or other material in the ESID Newsletter is cordially invited to submit copy to the Editor. Suitability for publication is assessed by the Editor in consultation with the other members of the ESID Board.

Editorial address:
Dr. Esther de Vries, pediatric immunologist, Jeroen Bosch Hospital loc GZG, P.O. Box 90153, 5200 ME 's-Hertogen bosch, the Netherlands, tel. +31-73-6992965, fax +31-73-6992948.

Please only use my *new email address*: esid@ estherdevries.nl

Front page: Dutch tulips.

Dear ESID members,

The heat of summer has descended upon us, even in Holland, which is often an area of Europe where temperatures are a bit lower. Not so now, however, and flowers and birds are thriving!

You will find a lot of information about the various Working Parties in this issue of the ESID Newsletter, and also additional candidates for ESID offices. This time, we will have online voting for ESID officers for the first time, so look at your email box for the alert!

The preparations for the ESID—INGID—IPOPI meeting in `s-Hertogenbosch are ongoing, and we hope to meet you all there. We have had an even greater number of submitted abstracts than last time, and it looks like we can have a very interesting meeting scientifically speaking, not to mention all the possibilities for social activities among Society members.

Best wishes to all of you, and hope to see you all in `s-Hertogenbosch.

Esther DE VRIES

ESID is the European Society for Immunodeficiencies. It was formed in 1994. The forerunner of ESID, the informal European Group for Immunodeficiencies (EGID) was established in 1983. The aims of this society are, among others, to facilitate the exchange of ideas and information among physicians, scientists and other investigators who are concerned with immunodeficiencies and to promote the research on these diseases. Anyone who is interested in primary immunodeficiency diseases can become a member of ESID. Registration is possible online at www.esid.org/members.php.

Within ESID, seven Working Parties are actively engaged in coordinating the member's joined efforts in patient care and research in primary immunodeficiency diseases: Stem cell transplantation and gene therapy (chair: Mario Abinun), Registries (chair: Gerhard Kindle), Clinical (chair: Bobby Gaspar), Genetics (chair: Naomi Taylor), Education (chair: Andrew Cant), PID-care in development (chair: Laszlo Marodi), and ESID *juniors* (chair: Eleonora Gambineri). Anyone who is interested in participating in one or more of these Working Parties is invited to do so. Please contact the chairman of the relevant Working Party (contact information is available at www.esid.org /board.php).

In 1994, a main registry of patients with various forms of immunodeficiency in Europe was established. Altogether, data from some 10,000 patients from 26 countries was compiled until 2002. However, given various shortcomings of this registry, ESID decided to develop a new state-of-the-art database for primary immunodeficiencies. This online registry was launched in 2004 and contains subregistries for more than 150 primary immunodeficiencies. It combines both clinical and laboratory data of PID patients and offers the possibility to document genetic data as well. Up to date, more than 5,500 patients have been registered in that database. Information, database statistics and a demo version of the registry can be found at www.esid.org/registry.php, or send an email to registry@esid.org.

The new ESID Online Registry is connected to the mutation databases (IDbases) in Tampere, Finland. These were created since 1995, when the first locus-specific immunodeficiency mutation database accessible through the internet was established (BTKbase for X-linked agammaglobulinemia). Since then, more than 100 additional locus-specific databases have been established. Information is available at http://bioinf.uta.fi.

ESID organizes a biennial congress to facilitate international contact between primary immunodeficiency specialists. The last congress was organised in 2006 in Budapest, Hungary , and the next one will be October 16-19 in `s-Hertogenbosch, The Netherlands, in 2008. Information is available at www.esid2008.org.

= ESID Information =

President's letter

Dear ESID members,

We are getting closer to the ESID and ASID international meetings, respectively in Holland and Morocco, and I am inviting you all to attend both meetings!

We have received more than 400 abstracts for the ESID meeting and expect more to be submitted to the 'late breaker" session. These abstracts are extremely diverse and most interesting, announcing a formidable ESID meeting.

You will soon be able to submit abstracts to the ASID too. For any information about the ASID meeting in Morocco, please contact Pr Aziz Bousfiha at aabousfiha@menara.ma.

I look forward to seeing you soon in Holland, where Esther de Vries and her colleagues have organized a great ESID meeting, and subsequently in Morocco.

All best wishes,

Jean-Laurent CASANOVA

Secretary's report

Dear ESID members,

The next General assembly (GA) of ESID is coming closer, to be held on Friday, October 17th in 's-Hertogenbosch during the 13th ESID meeting. I would full-heartily like to invite you to attend!
Please find attached the agenda for the GA and the minutes of the last GA in 2006.

A. Elections for the ESID officers

Please note: This time we will vote online prior to the GA and just announce the results at the GA. Electronic voting will be possible from September 15th through October 15th, noon CET.

The following ESID officers can be re-elected for two more years:
President: Jean-Laurent Casanova
Secretary: Bodo Grimbacher
Registry WP: Gerhard Kindle
Genetics WP: Naomi Taylor
Educational WP: Andrew Cant
PIDcare in development: Laszlo Marodi

For the other posts, we have the following applicants:
President Elect: Amos Etzioni
Treasurer: Eleonora Gambineri
Clinical WP: Klaus Warnatz
SCT and GT: Bobby Gaspar
ESIDjuniors: Crina Samarghitean

Please look at their application on:
http://www.esid.org/news.php?show=1&sub=2&offset=0&id=178

B. New ESID constitution

Moreover, we will discuss the new constitution, which will be posted on the website shortly:
http://www.esid.org/home.php?sub=2&id=174

Please read it prior to the general assembly so that we can discuss any possible issue and improve the wording. We will vote online on the new constitution after the GA in 's-Hertogenbosch.

In essence the change to the last draft is the following: "The ESID meeting is organized by a local steering committee in close collaboration with a congress organizing company. The scientific content of the meeting is proposed by a scientific committee. This scientific committee is suggested by the congress president but approved by the ESID board. The ESID board needs to approve the scientific content of the meeting. In case of a dispute, the ESID board will have the final say."

C. ESID meeting 2012

I also hereby call for applications to host the 2012 ESID/IPOPI/INGID congress. From 2012 onwards we will have a core congress organisation which shall ease things a lot. We are asking for centres to present their bid with a short powerpoint presentation at the GA in s'Hertogenbosch but then vote for the 2012 venue for the 15th ESID meeting ONLINE after the GA.

D. The ESID Legal Act

The legal act and the papers for the chamber of commerce were signed by the ESID board. The papers will now be submitted.

E. With which congress organization shall ESID go?

ESID has put out a tender for a permanent congress organizer and administration support. I am still in the process of collecting offers, but already have started to talk to KENES in more detail. ESID has used KENES before, and was very happy with how Kenes dealt with relocating the ESID congress from Jerusalem to Geneva in 2000. Moreover, ESPID has good experiences with KENES as core PCO. An elected set of congress organizers will present their proposals at the GA in 's-Hertogenbosch.

F. Relation to FOCIS and ECI

I am currently looking into the possibility for ESID to become a FOCIS member. We can discuss at the GA. The ESID board offered to the congress organizers of the ECI in Berlin 2009 to draft the program for an immunodeficiency session. ESID will not get involved in the sponsoring of this meeting.

G. What is an ESID activity?

The ESID board decided that all ESID members who plan to use the societies name "ESID" in any of their activities, the ESID board needs to be involved. The secretary will maintain a list of these ESID activities.

H. Who is an ESID member?

In case the new constitution is accepted by the GA, at the time of membership renewal, the respective ESID members will have to tick that they are fulfilling the criteria for an ESID member as laid down in the new constitution. There will be links provided to INGID and IPOPI websites to guide nurses and patients.

Yours,

Bodo GRIMBACHER

Agenda for the ESID General Assembly on October 17th, 2008

Time: 14:30 - 16:00 hrs

Location: Theater aan de Parade, 's-Hertogenbosch, The Netherlands

Topics:

1. Approval of minutes from the last GA and matters arising from these minutes (Secretary)
2. Presidential Report
3. Report of the Treasurer
4. Report of the Working Parties
5. Report of the Secretary
6. Discussion on New Constitution
7. Presentation of congress organizers
8. Discussion on the Congress Organization
9. Presentations on possible venues for the 2012 ESID meeting
10. Results of Elections for ESID board members
11. Varia

Treasurer's report

— REPEATED MESSAGE —

Dear ESID members, it is time to pay your membership fee for 2008-2009. The amount you have to pay is the same as for 2006-2007. If you haven't yet paid 2006-2007, you will have to do this first!

It will not be possible to register as a member for the `s-Hertogenbosch meeting if your membership fee has not been paid in time. The congress organisation will check this before sending you your invoice, and will charge the non-members registration fee if you haven't paid your ESID membership fee 2008-2009. You can correct that, but if you do that after the early registration deadline, you will be charged the late registration fee for the meeting, albeit the fee for members.

So, don't forget to pay in time, and join us in October in `s-Hertogenbosch !!

— REPEATED MESSAGE —

Up to now (June 29) 195 members have paid their membership fee 2008-2009. **Please all take the time to pay your membership fee !!!**

Esther DE VRIES

News & Views

Casablanca, June 10, 2008

Dear Colleagues, Ladies and Gentlemen,

The African Society for Immunodeficiencies, ASID, in partnership with the Moroccan Society of Hematology and the Moroccan Society of Pediatrics, organizes in Casablanca, Morocco, from October 30 to November 1, 2008 the 1st African Congress on Primary Immunodeficiencies PID.

We invite you to actively participate in this conference by scientific work related to the DIP in a comprehensive manner. For African countries with no sufficient explorations to support the diagnoses, observations or series of cases involving suspects PID will be accepted, as well as projects to organize PID units. Enclosed is a pre-program of this scientific event.

The deadline for submission of abstracts is scheduled for September 1, 2008. Abstracts must be submitted electronically to the address of the ASID e-mail: asid.casablanca @ gmail.com.

Aziz BOUSFIHA

Additional candidates for ESID offices

Dear friends and colleagues,

My interest in immunodeficiencies started in 2002 when I met Prof. Mauno Vihinen. His group was already well established and had many achievements and successes in this field. I liked his spirit and enthusiasm from the beginning so it was a pleasure to accept his proposal to work as a research scientist in his group. Having done an MD, and then an M.Sc. in Medical Informatics, I wanted to move into research. So, I fit well in an environment where most of my colleagues were more technical orientated.

At that time, I didn't know that what first started by a fortunate chance would be transformed in a long and passionate commitment, and that I will be so involved in this field. The more I learned about this field, the more fascinating I found it. My main task was to maintain, curate and develop ImmunoDeficiency Resource (IDR), (http://bioinf.uta.fi/idr), a comprehensive knowledge base for PIDs, and IDdiagnostics (http://bioinf.uta.fi/IDdiagnostics), a database for genetic and clinical test for PIDs.

Soon after, I also got to know more deeply the people behind this challenging and exciting field, people I had previously only known from articles and books. My first official meeting was the Nordic Patient Organisation meeting, organised in Tampere, Finland, in 2002. I was very touched by the patient's stories I heard there. I decided to put all my energy and effort in this field and try to make a difference. My first encounter with ESID community was in the same year at the conference organized in Weimar. There, I could meet personally the big names in the field and I learned a lot, like in all ESID meetings I participated thereafter. All the meetings have been characterized by the same spirit, innovation, communication and friendship, and after each of these meetings I have been more motivated to work to improve the services and increase public awareness for PIDs. There were exciting meetings and times, with lots of good memory. In 2005, I had the chance to visit Texas Children's Hospital, Houston, Texas, USA, where the first SCID transplant was performed. I met Prof. Hans Ochs there, and I was very touched by his speech and stories. I gained deeper insight into immunodeficiencies and have been motivated to start developing a decision support system (PIDexpert), to help clinicians to make correct diagnosis for these rare and difficult disorders. Another part of my research is to apply new innovative datamining techniques for classification of PIDs. Currently, I am finishing the last two papers from my PhD dissertation and about to release PIDexpert for testing in clinical setting. In order to be near from the clinical practice in 2003 I have been accepted as a trainee in Tampere University Hospital, in Paediatric department, under the supervision of Dr. Merja Helminen, who is also actively involved in this field.

Since 2005, when I became a member of ESID, I have been involved in many activities of ESID juniors WP and in the ESID editorial board; I have also tried to raise awareness of this field at the conferences and other events I have attended.

If I am elected I will continue the work started by my previous enthusiastic colleagues and friends. I will seek out new funding opportunities for ESID juniors; introduce and refine innovative techniques for PIDs; increase the awareness of PIDs in those countries in which PID are not well recognized; and foster collaboration between ESID juniors and other ESID parties, as well as with European and non - European societies dealing with clinical immunology.

I thank you for your support and hope to see you all in 's Hertogenbosch!

Crina SAMARGHITEAN

Dear colleagues,

My name is Klaus Warnatz and I ask for your support for my candidacy as head of the Clinical Working Party of ESID.

After my medical training in Germany and a 2.5-year post-doctoral period in Basic Immunology at the laboratory of Prof. Carson, UC San Diego, United States, I joined the division of Rheumatology and Clinical Immunology at the University Medical Centre Freiburg (Prof. H.H. Peter) in 1997. I was appointed senior consultant in 2006 and currently oversee the outpatient clinic in adult rheumatology, PID and HIV of our department.

My main research interest is the pathogenesis of adult antibody deficiency disorders. Having had my basic immunology training in B-cell immunology and deregulation of B-cell differentiation in autoimmunity, the initial approach to a better understanding of CVID was through B-cell phenotyping. This led to the European trial in CVID classification through which I had the chance to get to know several of you and learned to appreciate the great value of networking under ESID. It is because of this experience that I would like to help advance the collaboration between the associated PID centres.

I am fully aware of the challenge of a Clinical Working Party in the broad field of immunodeficiency and that this task cannot be fulfilled by one person. Therefore, I would see my role as an initiator and facilitator, to further the exchange between the many European centres and to combine efforts across ESID and beyond.

If elected, I would like to approach these goals by:

- Developing a platform for immunophenotyping of primary immunodeficiency (IPID), as I had announced in the ESID newsletter 2/2008. This platform is meant to serve as a reference website to look up typical changes of immune phenotype associated with certain primary immunodeficiency syndromes.
- Defining together with you the most urgent clinical questions in the different fields of immunodeficiency and by setting up working groups to develop specific recommendations.
- A special interest of mine has always been the coexistence of immunodeficiency and autoimmunity. At this time there are no satisfactory, let alone evidence-based recommendations for immunosuppressive therapies for most immunodeficiency syndromes. In the first phase, current disease specific treatment protocols will be collected from participating centres, which subsequently will build the basis for clinical trials in selected disorders.
- Encouraging and supporting initiatives from you, which will serve the aim of improving diagnosis and treatment of PID patients.
- Evaluating the possibility with the ESID board and especially the future treasurer, for creating a funding system by the ESID, allowing for small grants to initiate clinical multi-centre trials, in order to achieve the goals mentioned above.

If you approve of the suggested goals and entrust me with the task to jointly tackle them, I ask for your support for my candidacy as head of the Clinical Working Party of ESID.

Klaus WARNATZ

Registry Working Party

This year, we will see the fourth round of bonus payments to the participating centers since the establishment of the new ESID Online Database for Primary Immunodeficiencies. With the deadline of June 30th just around the corner, we want to give the readers a look at the development of patient numbers over the years.

The total number of patients in the ESID Database as of the editorial deadline for this newsletter (June 15th, 2008) is 6'422. Of these, France by far contributes the largest share with 2'505 patients. However, many other countries have also shown remarkable increases in patient numbers over the years. This can be seen in the charts below.

Further routinely updated statistical information on categories, diseases and age distribution as well as numbers on Ig-replacement are available at www.esid.org/statistics.php.

SCT & GT Working Party

End-of-office: What is the best conditioning regimen for haematopoietic stem cell transplantation (HSCT) in primary immunodeficiency (PID)?

When I attended my first ESID BMT/WP meeting over 20 years ago at Schloss Elmau, the main topic was how best to unify conditioning regimens for BMT in PIDs, mainly SCID, throughout Europe. Most of the time was spent in discussions on how to improve the outcome of haplo-identical T cell depleted transplants and in producing our 'guidelines' – the term 'protocol' was always felt to be somewhat more defined!

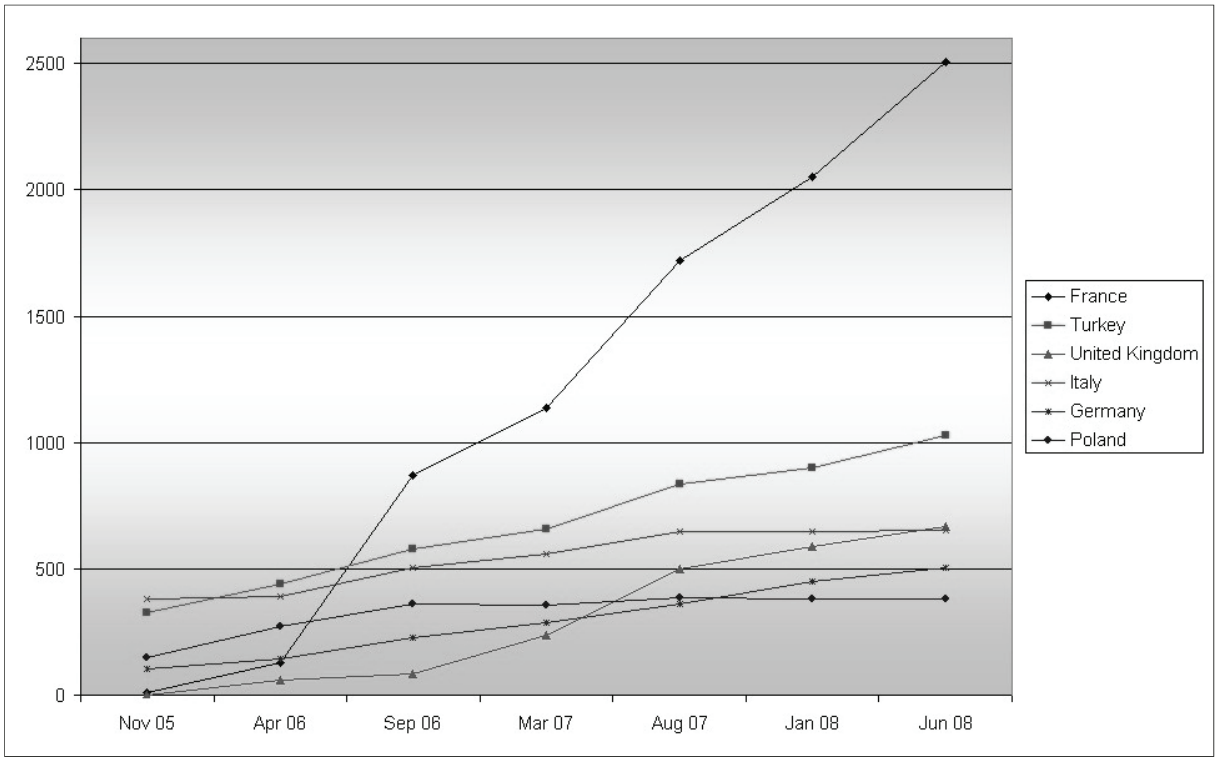

Fig. 1 Development of patient numbers in countries with currently more than 100 entries

Oral busulphan and cyclophosphamide were the mainstay regimen and T cell depletion was just in its infancy. Besides divides to 'TBI or not TBI' centres, there was already a 'Channel divide' on the issues of sheep red blood cell (SRBC) and lectin rosetting versus monoclonal antibodies, mainly Campath 1M. Early 90's brought more 'regulation' in the field, and for a very brief period of time Campath 1M (than G, followed by H) was in favour till the emergence of Miltenyi technique with positive selection versus previous T cell depletion. As they say, the rest is history!

Simultaneously, there was some progress with i.v. busulphan to replace the oral formulation, but the real change was the emergence of the low intensity regimen (LIC) with fludarabine, melphalan, and anti-T lymphocyte globulin (ATG). This coincided with many European centres starting transplanting their cohorts of 'old and sick' patients with often undetermined PIDs, the combined immunodeficiencies (CID) (1). As well, advanced tissue typing techniques allowed wider use of HSC from really well 'matched' unrelated donors.

All this is mirrored in the development of WP's 'Guidelines'. The latest version available on the website, which is not really different in many details from the preceding one, is from 2004. We never produced a 'newer version' as in the meantime the reduced intensity (RIC) regimens further mushroomed into a whole range of varieties (see the pyramid) (2). Haplo-identical T cell depleted HSCT became a rarity, even for SCID, even in Newcastle! Basically, depending on the nature of the underlying PID condition (proven or otherwise…), age of the patient, complications (end-organ damage, infections, etc.), donor availability (matched or 'mismatched') and source of haematopoietic stem cells (bone marrow, peripheral blood, umbilical cord blood), and

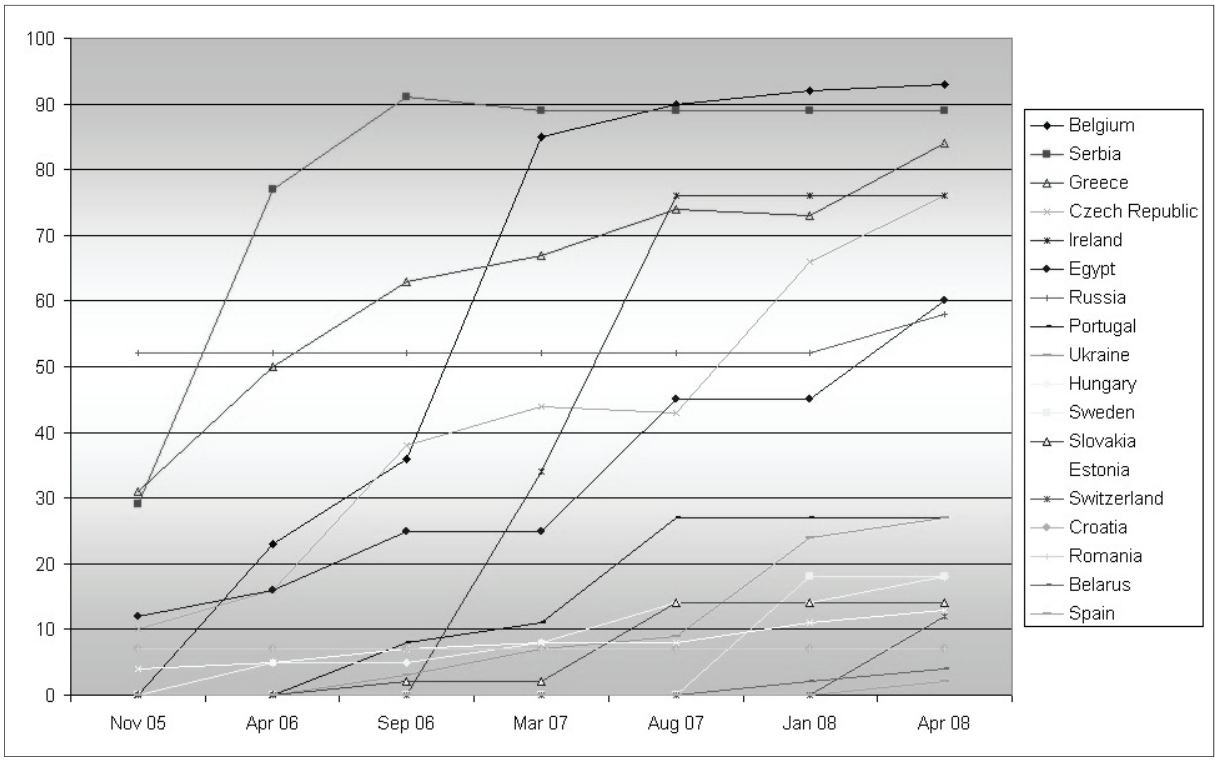

Fig. 2 Development of patient numbers in countries with currently less than 100 entries

of course 'the character' of the transplanting centre, a regimen is being tailor-made for almost each and every patient. Welcome to the era of 'engineered grafts' (and gene therapy).

So, have we reached the 'optimal' state in conditioning regimens for HSCT in PIDs? As is the answer with other similar questions, only the future will tell. We are just now getting to know what we really achieved by the 'old fashioned' conditioning regimens used all those years back, again mainly for patient with SCID, by looking into the data on real long-term (10-20 years and more) follow up (3-6). The main issues to address remains the long term immune reconstitution and the quality of the immune system function – the exact reasons we do these transplants in the first place.

References:
1. Berthet F et al. Clinical consequences and treatment of primary immunodeficiency syndromes characterized by functional T and B lymphocyte anomalies (combined immune deficiency). Pediatrics 1994;93:263
2. Satwani P et al. Reduced intensity conditioning and allogeneic stem cell transplantation in childhood malignant and non-malignant diseases. Bone Marrow Transplantation 2008;41:173
3. Borghans JA et al. Early determinants of long term T cell reconstitution after hematpoietic stem cell transplantation for severe combined immunodeficiency. Blood 2006;108:763
4. Cavazzana-Calvo M et al. Long term T cell reconstitution after hematpoietic stem cell transplantation in primary T cell immunodeficient patients is associated with myeloid chimerism and possibly the primary disease phenotype. Blood 2007;109:4575
5. Mazzolari E et al. Long term immune reconstitution and clinical outcome after stem cell transplantation for severe T cell immunodeficiency. J Allergy Clin Immunol 2007;120:892
6. Slatter MA et al. Long term immune reconstitution after anti-CD52 treated or anti-CD34 treated hematpoietic stem cell transplantation for severe T lymphocyte immunodeficiency. J Allerg Clin Immunol 2008; 121:361

Mario ABINUN

ESIDjuniors Working Party

Dear ESID Juniors, the winter is gone everywhere in Europe and with the approaching lovely and sunny season here are some exciting news for you all!!!

First of all visit the newly shaped ESID Junior site on the ESID website! In this regard I would like to thank Benjamin Gathmann and Viviane Knerr for the technical support J!

Here in brief the new sections you can access:

- New ESID Junior Activities (our activities since the last ESID Meeting in Budapest 2006)
- Latest news: What's new in PID....
- Call for Collaboration
- Recent discussions….
- And finally a nice Photo-Gallery that only members can access!!

So please login and have a look! Your inputs are very welcome!

"1,000 Euros" Scholarship for Short-term Programs: three scholarships of 1,000 Euros each will be awarded to ESID Junior members, who are physicians or scientists in training, interested in learning diagnostic/ therapeutic procedures or lab techniques in the field of Primary Immunodeficiencies. This scholarship will enable to spend two weeks up to one month in other European institutions willing to accept young trainees. If you are interested in applying please visit the dedicated section within this issue or the

TOP NEWS section on the ESID website.

Together with the Educational working party a "new" Educational Day within the 2008 ESID meeting has been organized! Juniors will actively take part with oral presentations or posters on clinical cases or research activities. Visit the official website of 2008 ESID meeting: www.esid2008.org! Looking forward to meeting you there!!!

Travel grants to ESID 2008 in s-Hertogenbosch will be available for Junior members!!! Details and further info are posted on the TOP NEWS section of ESID website.

As you have probably seen, I have decided to run for the Treasurer's post during this upcoming election, so unfortunately I have to step down from ESID Junior chair. It has been very tough trying to establish this new working party, but very exciting and mostly a great learning experience! I thank you all very much for your valuable support! I believe that the role of Treasurer will enable me to handle contacts, deal with sponsors, raise money for educational activities…therefore promoting the future growth of the Society, somehow more firmly progressing what I have been working out for ESID Junior so far. I hope I can count on your vote J!

Have a super summer!!!

Eleonora GAMBINERI

Educational Working Party

How quickly the academic year passes! Only 4 months before the Educational Day on Thursday 16 October at the beginning of ESID 2008 in s-Hertogenbosch! It has been very encouraging to see so many interesting abstracts submitted for what looks set to be an interesting and stimulating day. It will start with a breakfast session hosted by 5 members of various immunology summer schools, followed by sessions on:

· CVID (Jacques van Dongen & Helen Chapel)
· Autoimmunity /immune dysregulation (Hans Ochs)
· Deficit of innate immunity (Jordan Orange & Terry Flood)
· Infectious diseases / PID (Andrew Cant)

These sessions will be interspersed with presentations by juniors and a poster session, so do come and contribute to the lively debate and interaction!

If it is only 4 months until the Educational Day at ESID 2008, then it is only 15 months until the next Summer School which takes place from 2 September to 6 September '09 in the beautiful lakeside resort of Bled in Slovenia; a purposeful decision to move into Eastern Europe having taken us here. The speakers have been confirmed. Further details will appear on the ESID website in January '09, so look out for this and do apply!

Finally, congratulations to Andre Hennigs, Medical Student from the University of Freiburg who was awarded the 'ESID Young Investigators Award'. Andre will perform an 8 month research project at the Royal Free Hospital, University College London under the supervision of Bodo Grimbacher. The purpose of the project is to identify molecular causes of Chronic Mucocutaneous Candidiasis (CMC).

Don't forget, ESID also offers scholarships for short-term programs and travel grants to support and encourage those who will be the next generation of Clinical Immunologists across Europe. Please check the ESID website for further details.

Andrew CANT

Interesting Papers

A short selection of interesting papers for this ESID newsletter number cover atypical clinical cases on different PIDs, new techniques applied in therapy and management, and different review articles.

An atypical clinical picture of the forms of RAG1 or RAG2 deficiency has been described recently. The late onset and the extensive granulomatous disease involving the skin, mucous membranes, and internal organs may prompt the inappropriate use of chemotherapy or immunosupression. RAG deficiency should be a consideration in older patients with combined humoral and cellular immunodeficiency and unexplained granulomatous lesions. (Schuetz C et al. An Immunodeficiency disease with RAG mutations and granulomas, N Engl J Med 358; 19, May, 2008)

Another atypical case comes from XLA patients diagnosed late in life. An unusual adult-presentation of XLA, a humoral immunodeficiency usually diagnosed in childhood, may have significant implications in family counseling, female carriers detection and early treatment of affected male descendents.(Sigmon JR et al, X-linked agammaglobulinemia diagnosed late in life: case report and review of the literature, Clinical and Mollecular Allergy 2008, 6:5)

A novel use of DNA microarrays to improve the diagnosis and management in SCID is shown in a recent detailed case report. This relatively simple and inexpensive way to identify potential tissue donors for SCID may have broader clinical and financial implications and should work within any biological family. (Strauss K.A. et al., Clinical application of DNA microarrays: Molecular diagnosis and HLA matching of an Amish child with severe combined immune deficiency, Clin. Immunol. 2008)

Radiosensitivity has been reported in selected immunodeficiencies such as ataxia telangiectasia and other DNA repair deficiencies. Only few studies have shown an increased radiosensitivity in CVID patients. These patients should be protected from unnecessary diagnostic and therapeutic procedures using ionizing radiation. The authors suggest that the strong relation found between radiosensitivity and consanguinity may help to classify CVID patients and find the genetic cause of the disease. (Aghamohammadi et al. Chromosomal radiosensitivity in patients with common variable immunodeficiency, Immunobiology 213 (2008) 447-454)

A comprehensive review about the immunopathology and genetics of chronic granulomatous disease was recently published. The article covers a short history of this disease, study of different CGD variants, clinical features and management of CGD, as well as functional and molecular CGD diagnostic test. (Stasis JM, Li Jun X, Genetics and immunopathology of chronic granulomatous diseas, Semin Immunopathol, 2008)

Another interesting review details the genetic basis of partial T -cell immunodeficiencies, a heterogeneous cluster of disorders characterized by an incomplete reduction in T-cell number or activity. This review focus on recent advances in mouse models to propose mechanisms by which a reduction in T-cell numbers or function may disturb the population-dependent balance between activation and tolerance. (Liston A et al, Unravelling the association of partial T-cell immunodeficiency and immune dysregulation, Nat Rev Immunol. 2008 Jun 13)

An elegant review, just came from press, focus on a series of conditions not commonly viewed as PIDs. The twelve examples presented in this paper illustrate how the field of PIDs has advanced in the last 10 years and expanded the conventional view of PIDs. The dissection of PIDs is useful for immunological and medical purposes. (Casanova JL et al, Revisiting human

primary immunodeficiencies, J Intern Med. 2008 Jun 6)

It has been exciting this time again to search for interesting papers and it would be even more exciting receiving your feedback. So, if you have other interesting papers and want to draw attention on them send and email to :

Crina.Samarghitean@uta.fi !

Wish you a great summer and many ideas and inspiration for many interesting and challenging papers!

Crina SAMARGHITEAN

Young Researchers' Corner

Dear ESIDJunior members,

This time we're going to talk about:

CYTOKINE OR CHEMOKINE ANALYSIS

The ability to measure soluble mediators involved in immune regulation has been the focus of researchers for over three decades. To this point, immunologists and cell biologists have focused on the in vivo and in vitro measurement of multiple analytes and their associated receptors. The importance of assessing the relative levels of these mediators is evidenced by the fact that they form the basis of a sophisticated cellular communication network for normal immune function as well as in disease states.
The direct quantification of appropriate cytokine and chemokine, is critical for basic researchers and investigators involved in the field of immunology. Several methods have been developed that allow cytokine expression profile to be measured like ELISA, RT-PCR, ELISPOT, in situ hybridization (ISH) and flow cytometry. Numerous commercial reagents are available for this purpose. The correct (statistical) analysis of standard curves and (multiplexed) data are critical for proper interpretation.

ELISA-based technology

A majority of techniques for the measurement of soluble analytes employ a classical solid-phase sandwich immunoassays such as enzyme-linked immunosorbent assay (ELISA). In this approach, target proteins are captured by the arrayed capture antibody and then detected in a sandwich ELISA format using a cocktail of biotinylated detection antibodies. The signals are visualized by either horseradish peroxidase (HRP)-conjugated streptavidin and enhanced chemiluminescence, or cy3-conjugated streptavidin and laser scanner. Several key factors and steps are included: selection of solid supports, selection of suitable antibodies, determination of specificity and sensitivity of cytokine protein arrays, array design, sample preparation, and detailed experimental procedures for macroarray and microarray formats. An account of the successful development and application of cytokine protein arrays has been presented in the last years. Although this is a methodology well suited for single-analyte analysis, it is more desirable to simultaneously quantitate multiple analytes from a relatively small sample size in a rapid fashion. Sample size becomes a critical factor for the evaluation of multiple analytes, especially when monitoring disease states.

Cytometric bead array (CBA) system

The melding of ELISA-based technology with flow cytometry has alleviated most of these issues. The utilization of fluorescent-labeled microspheres has been the key to this success. Flow cytometry may be used as a readout for sandwich immunoassays. Bead-

based flow cytometric immunoassays have been described for single analytes. The single-analyte assay principle was expanded to the detection of multiple analytes from a single sample, using this technology. Beads of different sizes or colors are used for multiplexed immunoassays.

The introduction of flow cytometric bead-based technology has added a new approach for investigators to simultaneously measure multiple analytes in biological and environmental samples. This new technology allows for (1) evaluation of multiple analytes in a single sample; (2) utilization of minimal sample volumes to glean data; (3) reproducibility and results comparative with previous experiments; (4) direct comparison with existing assays; and (5) a more rapid evaluation of multiple samples in a single platform. Results have been presented for the analysis of a variety of human cytokines. In addition, the technology allows for the design and creation of assays to measure a variety of analytes including inflammatory mediators, chemokines, immunoglobulin isotypes, intracellular signaling molecules, apoptotic mediators, adhesion molecules, and antibodies.

What do you think about these different protocols? Is CBA technology really better suitable for cytokine detection? That is to say: is a wide range of beads available for any demand? I'm waiting for any suggestions from all of you!! I'm particularly interested in protocols and methods you would like to advise!

Lucia BIANCHI
(l.bianchi@meyer.it)

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ESID MEETING IN `S-HERTOGENBOSCH

Dear ESID members,

I heartily invite you all to attend the next biennial meeting in `s-Hertogenbosch from October 16-19. We have an interesting program on research and clinical topics, a new format Educational Day with talks and posters by ESIDjuniors, and an impressive >400 abstracts which will be presented to you as orals, posters or 'abstract only' (abstract available in the Abstract Book).

The social program is also very interesting, and gives you all a good chance to renew all friendships, and start new ones!

The Hotel Central on the Markt, one of the Congress hotels, during Carnaval this year

Typical Dutch landscapes: flat and full of water !

Hope to see you all! **Esther DE VRIES**

XIIIth meeting of the European Society for Immunodeficiencies

ESID

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October 16-19, 2008

together with

the Xth Meeting of the International Patient Organization for Primary Immunodeficiencies

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