

ESID Newsletter

Contents

Introduction	2
ESID information	3
President's letter	4
Treasurer's report	5
Secretary's report	5
News & Views	6
Poland,s second nation-wide meeting of parents with children suffering from ataxia-telangiectasia syndrome.	6
The 3rd Autumn - Winter School of Clinical Immunology: Progress in Education in Clinical Immunology, September 23 - 24, 2005, Gdansk, Poland.	6
J-project meetings	8
Letter to the ESID members about theWHO's list of essential medicines.	8
Important 'Descartes prize' won by famous European PID scientists !	9
European Health Forum Gastein, 5-8 October, 2005.	11
Meetings announced by EuroSciCon.	12
JMF to Develop Newborn Screening Test. Collaboration with NIH and Affymetrix will focus on early detection of PI.	12
Don't forget to register in time for the Budapest meeting in October this year !	13
Working Party reports	14
Clinical Working Party	14
Educational Working Party	14
ESID Summer School 2005	14
ESID Educational Day 2006	16
LAGID meeting November 5 - 7, 2005	16
Registry Working Party, the ESID online registry	17
Registry Working Party, the new ESID website	21
PID-care in development: Costa Rica	21
ADA-questionnaire Clinical Working Party	24

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) and Gustavo Lazo.

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 NOTE !!!

**My email has
changed again :
esid@
estherdevries.nl**

Front page:

*Palma de Mallorca, site
of the ESID Summer
School 2005.*

Dear ESID members,

Let me start by wishing you all the best for the new year 2006 !

A year in which we will meet again, in Budapest this time, for an update of science and friendship. I hope to see many of you there, and, of course, two years later in 's-Hertogenbosch as well. A meeting for which the preparations have already begun.

In this ESID Newsletter, you will find the latest developments on the online Registry, which is thriving, but we always want more ... Also, a contribution from Latin America by Gustavo Lazo, participant of the ESID Summer School 2005, eager young immunologist working in limited circumstances, and achieving a lot, together with his coworkers and his enthusiastic boss dr. Oscar Porras-Madrigal. Gustavo has agreed to join the Editorial Board of the ESID Newsletter, for which I am very grateful. To start with, he will work on interviews for the PID-care in development section from other countries than his own. Furthermore, all kinds of activities undertaken by ESID members all over Europe: J-project meetings, the autumn-winter School in Poland, an A-T family meeting in Poland. The Jeffrey Modell Foundation also sent us some copy, and will continue to do so now and then in the future.

Please, take the time to answer the ADA-questionnaire as requested by Bobby Gaspar from the Clinical Working Party. It is these kind of efforts that help research and patient care another step forwards.

Anyone else interested in joining the Editorial Board of the ESID Newsletter? You are very welcome to do so !

Best wishes to all of you,

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. Anyone who is interested in primary immunodeficiency diseases can become a member of ESID. You can find the necessary information to contact the treasurer Esther de Vries at www.esid.org.

Within ESID, six Working Parties are actively engaged in coordinating the member's joined efforts in patient care and research in primary immunodeficiency diseases: Bone marrow transplantation (chair: Mario Abinun), Patient registries (chair: Bodo Grimbacher), Clinical (chair: Bobby Gaspar), Genetics (chair: Anna Villa), Education (chair: Anders Fasth), and ESID *juniors* (chair: Pim van der Vossen). 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).

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 were received until now. In 1995, the first locus-specific immunodeficiency mutation database accessible through the internet was established (BTKbase for X-linked agammaglobulinemia - curators Mauno Vihinen and C.I. Edvard Smith). Since then, several additional locus-specific data bases have been established: ADAbase (adenosine deaminase deficiency - curators Mauno

Vihinen and Michael Hershfield), BLMbase (Blooms syndrome - curator Mauno Vihinen), CYBAbase (autosomal recessive p22 phox deficiency - curators Dirk Roos and Mauno Vihinen), CYBBbase (X-linked chronic granulomatous disease (XCGD) - curators Dirk Roos and Mauno Vihinen), CD3Ebase (autosomal recessive CD3 epsilon deficiency - curators Mauno Vihinen and Jose R. Regueiro), CD3Gbase (autosomal recessive CD3 gamma deficiency - curators Mauno Vihinen and Jose R. Regueiro), CD40Lbase (X-linked hyper-IgM syndrome - curators Luigi D. Notarangelo and Mauno Vihinen), JAK3base (autosomal recessive severe combined JAK3 deficiency - curators Luigi D. Notarangelo and Mauno Vihinen), NCF1base (autosomal recessive p47 phox deficiency - curators Dirk Roos and Mauno Vihinen), NCF2base (autosomal recessive p67 phox deficiency - curators Dirk Roos and Mauno Vihinen), RAG1base (autosomal recessive severe combined RAG1 deficiency - curators Mauno Vihinen and Anna Villa), RAG2base (autosomal recessive severe combined RAG2 deficiency - curators Mauno Vihinen and Anna Villa), SH2D1Abase (X-linked lymphoproliferative syndrome (XLP) - curators Luigi D. Notarangelo and Mauno Vihinen), TCIRG1base (autosomal recessive osteopetrosis (arOP) - curators Mauno Vihinen and Anna Villa), ZAP70base (autosomal recessive severe combined ZAP70 deficiency - curator Mauno Vihinen), WASPbase (Wiskott-Aldrich syndrome - curators Mauno Vihinen and Luigi D. Notarangelo) (information is available at www.esid.org).

ESID organizes a biennial congress to facilitate international contact between primary immunodeficiency specialists. The last congress was organised in 2004 in Versailles, France; the next congress will be organized in Budapest, Hungary in October 2006, and the one after that will be in The Netherlands, in 2008.

= ESID Information =

President's letter

Dear friends,

With a few months to the next ESID Meeting, significant achievements and new challenges call us to take important decisions.

Let me start by acknowledging the important recognition of excellence of scientific collaborative research that the European Commission has awarded the European PID community. On December 2nd, in London, Alain Fischer and a group of colleagues have been awarded the prestigious "Descartes Prize", the most important scientific award that the European Union attributes every year to distinguished researchers across Europe. As ESID, we should be proud of this award, that officially acknowledges the network of research that we have been able to create during the last decades. Importantly, this is an excellent premise to build new collaborative research projects under the next Framework Programme. A report of the ceremony, that was held at the Royal Society in London, is included in this Newsletter.

I would also like to draw your attention to the new format of the ESID website, for which Bodo Grimbacher has to be congratulated. With a user-friendly format, the website should attract your interest (as well as hopefully that of potential new ESID members).

Important features of the new website include:

- a new ESID Discussion Forum with e.g. the chance to present a clinical case to the community,
- the latest publications in the field of PID (you may even post your papers there),
- a list of current ESID protocols (including those produced by the various Working Parties).

These sections will be accessible to ESID members only, through username and password. In addition, you can now (and have to !) pay your membership fee online. This important long-awaited change should make your life easier and hopefully more enjoyable.

Perhaps, this will also facilitate exchange of opinions among ESID members, something that the Newsletter has not achieved, most likely because it is published only every few months.

I would also like to share with you important aspects that will require extensive discussion and final decisions during the General Assembly in Budapest.

In particular, we will be called upon to decide what type of Society ESID should be. For some reasons, including the possibility to receive funds, we ought to have a proper legal registration. This is not a purely theoretical discussion, since our colleagues in the United States have expressed a strong interest to purchase from ESID the right to use the format of our Registry, and are therefore ready to pay for this. However, in the current situation, we are not able to accept this offer, as it is not clear at all how liability would be in place should legal questions arise after the transaction.

More in general, I believe we need to discuss in detail the organization of ESID, including the number of Working Parties, their composition, and their purpose.

Finally, but importantly, Budapest 2006 (for which Laszlo Marodi is working hard to make it a remarkable success) will be the occasion to renew many positions within the ESID Board, starting from Presidency (for which I welcome Jean-Laurent Casanova, the current President-Elect) to the Chairpersons of several Working parties. **For those of you who wish to play an active role in ESID, it is your time declare your interest by presenting your candidature!**

Luigi NOTARANGELO

Treasurer's report

Dear all,

It is time to pay the ESID membership fee 2006-2007. We have not changed it, so it is still €100 per 2 years for everyone, except those living and working in Eastern Europe, and for those <35 years of age (proof required), who pay €50. From now on, the payment of your membership fee will take place online. Bodo Grimbacher has made an excellent new ESID website, and we have integrated a link on it to a completely safe way of **paying online**. Just click on the 'Saferpay' logo, and you will be helped through the complete process. It is essential that you **DO NOT** pay in any other way anymore !!

Hopefully, this new way of paying the membership fee will decrease the uncertainties and difficulties that were sometimes encountered with payments all over Europe (and the world!), so that everyone, that means all of you and your treasurer, will be happy about it. If you have questions about all this, please send me an email at **my new email address: esid@estherdevries.nl**. However, requests to pay otherwise (by cheque, credit card (not online), or direct bank transfer) will NOT be granted. Other scientific societies use Saferpay and online membership fee payment, and they are satisfied about it. We should be able to do the same! It will save a lot of time and therefore money, which will enable us to keep the membership fee at the current low rate.

Please, don't forget that you need to have to pay your membership fee **in time** to profit from the **discount** on the registration fee for the Budapest meeting !!

There are still several members in the database with incomplete or incorrect addresses, email addresses, etc. I once

again **ask for your help** to correct their details in the ESID database. Who can help me finding the addresses and/or email addresses of the following people :

Al-Herz Waleed
Amini Peyman
Carneiro-Sampaio Magda
Cucuruz Maria
Dos Santos Guedes Maria
Dupuis Sophie
Freihorst Joachim
Gordins Pavel
Helbert Matthew
Mori Luigi
Nieto Diaz Antonio
Nothers Gundula
Oksenhendler Eric
Panisi Cristina
Pellier Isabelle C A Anjou Maine
Renella Raffaele
Samargitean Crina
Sargur Ravishankar
Schmidt Reinhold E
Schmidt Sigune
Schütz Catharina
Strobel Stephan

Esther DE VRIES

Secretary's report

The ESID Board will meet on February 2, 2006, in Frankfurt. You will find more about this in the next issue of the ESID Newsletter !

Hermann WOLFF

News & Views

Poland's second nation-wide meeting of parents with children suffering from ataxia-telangiectasia syndrome.

On April 30, 2005, the 2nd Nationwide Meeting of Parents and Children with AT-syndrome was held at the Children's Memorial Health Institute in Warsaw. The meeting was organised by the Association of Friends to Children with Immunological System Deficiencies and the Clinical Department of Immunology at the Children's Memorial Health Institute in Warsaw.



There were thirteen families present from all over the country. The parents had another opportunity (such a meeting had been organised before) to share their experiences and express their anxiety on everyday care and treatment of their children as well to attend the lectures of the specialists on neurology, rehabilitation and oncology. During the meeting, a specialist on social care for disabled children answered the parents' inquiries. In the meantime, the children accompanied by a group of volunteers took part in a sightseeing tour round Warsaw, watched a film at the IMAX cinema, and listened to the concert of The BOHEMA held in the afternoon.

The parents were really grateful for the opportunity to participate in the meeting. They realised that they were not alone with their problems, and that they

had the possibility to learn more about their children's disease. Insisting on continuing the tradition of such meetings, the parents put forward a proposal to establish the Association of Families with AT Children. The idea is worth considering since the treatment of AT patients has many aspects and requires clinical research based on co-operation of clinical specialists, immunologists, paediatricians, neurologists, rehabilitation specialists and many others. Such an association would certainly help parents to solve their everyday problems.

We are very much obliged to the main sponsor of the meeting, The Modell Foundation, and to the remaining sponsors: Baxter, Grifols, Mead Johnson and Nutricia. We are also grateful for sweets donated by Wedel. The organisers would like to plan further meetings and hope that sponsors will be found to make it possible.

I appreciate very much the commitment of Ms Maria Bukaty, the President of the Association of Friends to Children with Immunological System Deficiencies as well as the enthusiastic contribution from two nurses, Ms Bożena Kuśmirek and Ms Maryla Podemska. I would like to give my special thanks to Professor Ewa Bernatowska for her professional guidance and support during the organisation of the meeting.



Barbara PIETRUCHA

The 3rd Autumn - Winter School of Clinical Immunology: Progress in Education in Clinical Immunology, September 23 - 24, 2005, Gdansk, Poland.

The third Autumn - Winter School of Clinical Immunology was organized in Gdansk - the town lying on the Bay of Gdansk and the southern coast of the Baltic Sea. Gdansk was

first mentioned as a Polish city in 997. Under the rule of the Polish Crown, the city became a wealthy member of the Hanseatic League. The meeting took place close to the Old Town, which is situated on the banks of the Motlawa river.



Now, about the meeting, which was the first one organized as a part of a new EU project entitled 'Policy oriented and harmonizing research activities in the field of primary immunodeficiency diseases' - EURO-POLICY-PID. The initiator and coordinator of this project is C. I. Edward Smith, from Carolinska Institutet, the leader of the former EU project called EURO-PID-NAS. The objectives of the new project are to build up the necessary research capacity at a European level in order to: increase the understanding of PIDs' ethiology and identify novel mutations, to carry out epidemiological studies in order to determine the prevalence of PIDs in Europe, to establish harmonized guidelines for diagnostics and treatment of PIDs and to improve the awareness of PID among the European population.

The first session included the state of the objectives of the project. Anna Berglöf - the project manager from Carolinska Institutet, presented the objectives, deliverables, milestones and expected results of that project and the description of work to be accomplished by individual partners. Her presentation was followed by remarks of other partners involved in that project; they presented the

updated results of their activities.

Next, Bodo Grimbacher from Freiburg gave a lecture on the Paneuropean PID patients registry, which is successfully growing and has already gathered 1,084 patients from all over Europe. The biggest numbers of registered patients come from Italy, Turkey and Poland.

Mauno Vihinen from Helsinki presented PID mutation databases existing on <http://bioinf.uta.fi> and now connected with www.esid-registry.org.

Helen Chapel from Oxford shared the British experience concerning the increase of awareness about PIDs in national public health groups, government and non-government organizations.

Esther de Vries from 's-Hertogenbosch presented the diagnostic protocol for suspected immunodeficiency from the Clinical Working Party of ESID. This manuscript will be published soon.

The national Polish project with the aim to improve patients' care and to raise the awareness of PID across the country was presented by Ewa Bernatowska from Warsaw.

An excellent review on advances in molecular diagnosis and clinical correlation of PID was the topic of the next lectures. C. I. Edward Smith presented the genotype - phenotype correlation in X-linked agammaglobulinaemia. Recent advances in diagnostics and classification of CVID were presented by Bodo Grimbacher. Christine Kinnon spoke about updated genetic diagnostics in PIDs. Krystyna Chrzanowska gave a talk on Nijmegen breakage syndrome (NBS) linking DNA damage with immunodeficiency and cancer predisposition, basing on 90 NBS patients already registered in Poland. Wide spectrum of HIGM syndromes was shown by Anne Durandy. Allison Jones shared with her experience on longterm follow-up of different PIDs after bone marrow transplantation. Amos Etzioni gave an excellent and practical review on ethiology and clinical aspects of neutropenia.

After a long and busy day, altogether - speakers and participants enjoyed themselves listening to classical music and eating Polish food. Later in the evening, the international

group consisted of some participants spontaneously initiated singing songs in a tavern located in the Old Town of Gdansk.

The next day of the meeting was created as a case report session, with Teresa Español and Amos Etzioni chairing. Some interesting PID cases and patients with unusual features suspected of PIDs were presented by young immunologists from Central and Eastern Europe.

More than sixty participants attended the meeting. The list of young immunologists is still growing. For the first time, young colleagues from new EU countries such as Lithuania, Estonia and Latvia came to the meeting. The group of 29 young Polish physicians specializing in clinical immunology was also present.

The 4th School of Clinical Immunology is going to be sponsored by two EU grants: EURO-POLICY-PID SP23-CT-2005-006411 and PERFECT QLG1-CT-2002-90358. The next meeting will be organized in Ruciane Nida - a little town situated in the very heart of the Mazurian Lake district, among forests, in the middle of the Old Continent, in the Northern - Eastern part of Poland. The symposium will be held from 9 to 10 of June, 2006. For more information please contact us at immuno@czd.waw.pl!



Ewa BERNATOWSKA

J-project meetings

In November, two meetings of the ongoing J-project took place, one in Debrecen (Melinda Erdos, November 4-5), and the other in Lviv (Larysa Kostyuchenko, Western Ukraine). Genetic diagnostics and management of primary immunodeficiency disorders in East-Central-Europe, and PID patient care and treatment in West-Ukraine were discussed at the respective meetings.

Laszlo MARODI

Dear ESID Members,

I was asked to represent ESID at the Plasma Protein Users Group, following the removal of human immunoglobulin therapeutic products from the WHO's list of essential medicines. ESID wrote to support their continuation on the list in 2001, as did many others including IPOPI, but we failed to prevent their removal. Now we have a chance to re-instate these therapies onto this important list, since WHO's Global Collaboration on Blood Safety (GCBS), an international collaboration of concerned stakeholders, agreed at their recent meeting to provide support for the reinstatement of IVIG on the WHO's List of Essential Medicines. So it is time to take action!

It was agreed that letters from patient groups in developing countries would be an important contribution when requesting the Ig products be re-instated on the WHO essential medicines list. However the formal application forms in line with the WHO's bureaucratic requirements, should also be completed by physicians, their world-wide professional organisations, PID networks, immunological societies and all those interested in PIDs and other immunological diseases. This will be a prerequisite to a valid application and to the eventual success. As a professional organisation, ESID is sending a letter to Dr. Hans Hogerzeil, hogerzeilh@who.int, at the WHO. The Board has expressed disappointment

at the decision by the WHO not to reinstate IVIG on the list of Essential Medicines, and stating their intention to apply for reinstatement of IVIG in the 2007 review. It would be helpful if you feel that you can take action now to write a letter to Hans Hogerzeil as well. Letters from individuals and country organisations will help - this is politics!

Very many thanks!

Helen CHAPEL

Important 'Descartes prize' won by famous European PID scientists!

ESID scientists won the famous Descartes prize. This is the text of the speech Alain Fischer gave in London on Friday, 2 December at the occasion of the reception of the Descartes prize:

On behalf of our « Europid » team, I would like to express my thanks to the Commission and the Descartes Jury for considering our work for the attribution of the Descartes prize. I guess, this is not only explained by the fact that 2 out of the 7 groups*, parts of the Europid team are located at Universite Rene Descartes in Paris ! In any case, we feel very proud since it actually recognizes a 20-year long

endeavour of a few hundred of clinicians and scientists from 4 countries France, Italy, Sweden and UK, in order to decipher genetic defects of the immune system.

To our opinion, this prize has a 3-fold meaning in terms of recognition. It acknowledges 1 / the role of our 7 groups, 2/ research on genetic defects of the immune system and 3/ overall research on rare diseases. I think it can be viewed by the many groups working on rare diseases in Europe as an encouragement.

To work on genetic defects of the immune system is rewarding because the many inherited diseases of the immune system provide as many unique models to study how our immune system is organized to fight the microorganisms from our environment and how its disturbances cause immunological diseases such as allergy or autoimmunity. In spite of many advances in understanding the molecular bases of these diseases , much remains to be done ! Very importantly, this is a field in which research is rapidly profiting patients and their families by providing more accurate diagnostic tools and hopes for new therapeutics. Our chance has been to work at the right time, i.e to take advantage of the advances in human and animal genomics. However, we want to take this opportunity to acknowledge that the scientific discoveries we have achieved would not have been possible without the contribution of many



clinicians from all over Europe, who have developed excellent clinical skills that have allowed early recognition of these rare disorders from the symptoms and clinical history of their patients. They have realized that progress in rare diseases is very much dependent on research, and this can only be fostered by sharing data meticulously, day after day, from cohorts of patients, recruited from across Europe, and by making biological specimens available. This has in turn requested a great deal of collaboration from the patients themselves, who have also understood the importance to be aside of researchers and clinicians in the struggle against disease. This is how ultimately research projects were launched leading to understand the mechanism of more than 20 of these diseases.

If one looks back, it has really been a fruitful and rewarding experience. It started about 20 years ago in informal chats sometimes taking place in remote areas in the Alps or Northern England and has now led to an efficient networking system. Fortunately, we have been strong enough to resist so far to the inevitable centrifuge forces.

We did get support from the European community through the FP4, 5 and 6 programmes although, I have to say the financial contribution remained limited and the amount of administrative work ever increasing. I understand that these problems have been appreciated by the Commission and hopefully are going to be addressed.

I would certainly suggest that the European community very significantly increases its contribution to research effort for rare diseases. This is worthwhile in several respects.

Firstly, there are 5000 to 6000 rare diseases, accounting thus for about 20-30 millions of patients throughout Europe.

These diseases are often severe and chronic in nature, whereas understanding, therapy and even social consideration are too often limited. There is thus a legitimate social demand to do more for this one facet of the spectrum of neglected diseases. The European dimension is particularly appropriate since, none of the European countries can build, on its own successful research projects because of the scarcity of patients afflicted by a given condition. Research on rare diseases is not only socially commanded, it also provides wonderful examples where a number of professional from the health medical and research world located in many countries and with different culture background can work together. An effort of communication, and the Descartes prize initiative is one, should be placed on such networks to promote the concept of European citizenship.

Scientifically speaking, high quality research on rare diseases can deeply impact on basic science as discussed above. It also has a direct return to improving care of these patients and importantly, as now understood by a number of biotechnology companies and even by some "big pharmas", they can provide proof of concepts for new therapeutics aimed at treating more frequent diseases. Thus, the European community can do a lot for patients with rare diseases by promoting research activity not only through the allocation of more funds (which I think is justified) but also through the elaboration with scientists in the field and patients' groups of new forms of organization.

Let's hope that the 7th FP programme will take this strong opportunity.

Having said that, I would not leave the impression that the Research directorate of the European commission should govern from top how research should be funded and organized at the European level! Far from that, for instance, we certainly applaude the initiative of an European Research Council aiming at significantly supporting the best

projects in Europe with a limited amount of administrative load. Let's hope it will be granted enough money !

*European Health Forum Gastein,
5-8 October, 2005*

We strongly feel that research should stand ahead in the road toward European integration. To publicize successful collaborative research efforts is certainly a worthwhile initiative and we are very honoured to be part of it. Let me express my gratitude to the members of our 7 groups of the European team who have contributed so much and again to the jury and the commission.

Thank you.

* Groups involved :

JL Casanova - Université René Descartes - Paris; A Fischer - Université René Descartes - Paris; L Hammarström - Karolinska Institutet - Stockholm; L Notarangelo - Università Degli Studi di Brescia - Brescia; CIE Smit - Karolinska Institutet - Stockholm; A Thrasher - University College, London; A Villa - CNR Istituto di Technologie Biomedecine - Milan.

About 600 experts took part in the 8th European Health Forum Gastein, which has increasingly established itself as the leading health policy event in the European Union. This year's programme included a breakfast session on biosimilar medicines on 6 October 2005. Dr. Pfister provided an overview of biosimilar medicines and the current scientific and regulatory issues surrounding them. Dr. Pfister illustrated how biopharmaceuticals differ from traditional chemical medicines. He emphasized the following points: the manufacturing process in fact makes the biological product; any change in the production may change the product; any change in the product may change the efficacy and safety of the product. As the patents for the first biotechnologically produced medications expire, the market is open for the introduction of biosimilar drugs. Unlike conventional generic drugs, small differences in molecular composition and quality can have dramatic biological consequences and possible adverse reactions for patients. Concerns that biosimilars might differ from the reference product raises considerations for patient safety and efficacy. The regulatory bodies have so far maintained a cautious approach to biosimilars. The European Union is the first region in the world to have established a regulatory and legislative pathway for the approval of biosimilar medicines. It takes effect on 20 November 2005 and sets out the general parameters to be followed by the EU's regulator, the European Agency for the Evaluation of Medicinal Products (EMA) in the production of its guidelines for the industry on biosimilars. EMA is currently finalizing a number of guidelines on the process of bringing different biosimilars to the market. If you are interested in getting more information, please contact: Kurt Pfister at kurt.pfister@pfc.ch.

Meetings announced by

Molecular Farming - production of recombinant medicines by plant biotechnology. Tuesday, January 24, 2006. Birkbeck College, London. "Modern biopharmaceuticals are needed in ever-increasing amounts, and are becoming more and more complex to produce. Transgenic plants offer a eukaryotic expression system that is highly scalable, and which may help to address many of the production problems that will be faced in the future. In the last 20 years, proof of concept for a number of plant-derived pharmaceuticals has been obtained and several candidate products are now poised to enter human clinical trials" - Professor Julian Ma - Meetings Chair. Deadline for early registration is November 20th 2005, after which the registration doubles. The Deadline for abstract submissions is December 20th 2005. This meeting has CPD accreditation.

New Anabolics in Bone Research. Friday, January 27, 2006. Birkbeck College. Deadline for early registration is November 10th 2005, after which the registration doubles. Deadline for abstract submissions is October 20th 2005.

Applications of Reverse Genetics of Viruses. Friday, February 03, 2006. Birkbeck College. Deadline for early registration is November 20th 2005 after which the registration doubles. Deadline for abstract submissions is December 20th 2005.

Comparative immunology in the post-genomic era - mapping disease resistance/susceptibility genes. Tuesday, February 21, 2006. Birkbeck College. "The availability of genome sequences for the major agricultural species and companion animals has revolutionised our ability to understand host-pathogen interactions in these species, and gives us the realistic opportunity to

identify disease resistance genes. This is of particular interest in agricultural species, as the use of prophylactic and therapeutic drugs is reduced, and we move to more extensive rearing systems". Dr P Kaiser- Head of the Avian Genomics group at the Institute for Animal Health - Meetings Chair. Deadline for early registration is January 20th 2006, after which the registration doubles. Deadline for abstract submissions is December 20th 2005.

Inga BIMBIRYTE, EuroSciCon

JMF to Develop Newborn Screening Test. Collaboration with NIH and Affymetrix will focus on early detection of PI

The Jeffrey Modell Foundation (JMF), the National Human Genome Research Institute (NHGRI) at the National Institutes of Health, and Affymetrix Inc. (Nasdaq: AFFX) announced a joint research project to develop two molecular DNA tests that could ultimately help save the lives of children born with Severe Combined Immunodeficiency (SCID) and other PI disorders.

The joint research collaboration aims to demonstrate the feasibility of using a pair of molecular DNA tests to detect PI in newborns and children with recurrent opportunistic infections. The first test, which will be developed by NHGRI, will look for expression of a gene found only in children with normal immune systems. If the first test is negative, a secondary test that is based on Affymetrix GeneChip® technology will be used to screen for defects in the specific genes associated with PI.

According to Fred Modell, Co-Founder of JMF, "Over the past 20 years, we have met with too many grieving parents whose infants or very young children were lost because their underlying condition had not been diagnosed in an accurate and timely manner. We have discussed this tragic problem with government agencies, with other non-profits and with

industry. We believe it is essential that we 'jumpstart' the development of newborn screening for SCID, and we have taken the initiative to make this happen now. This collaboration with Affymetrix and NHGRI will give doctors the tools they need to help save these children."

Jennifer Puck, M.D., Chief of the Genetics and Molecular Biology Branch and Head of the Immunologic Disease Section at NHGRI added that, "Primary Immunodeficiencies are treatable, but to be treated optimally they must be recognized early in life before severe infections occur. This project will combine a simple 'yes or no' screening test with advanced technology that may help scientists and ultimately physicians identify infants who need urgent medical attention for Primary Immunodeficiency. The collaboration demonstrates how public, private, and non-profit entities can partner to apply the benefits of the human genome sequence to improving health outcomes."

"The Jeffrey Modell Foundation sets the standard in advocating for and promoting advanced newborn screening that could save the lives of children with Primary Immunodeficiencies," said Janet A. Warrington, Ph.D., Vice President, Emerging Markets and Molecular Diagnostics Research and Development at Affymetrix. "We are honored to be working with the JMF and NHGRI on this important project and believe our GeneChip technology can accelerate more comprehensive detection and treatment of Primary Immunodeficiencies and other genetic conditions."



Don't forget to register in time for the Budapest meeting in October this year !



This is where the meeting will take place.

Main topics of the meeting:

- Deficiencies of innate immunity
 - Complement deficiencies
 - T- and B-cell deficiencies
- Deficiencies of immunoregulations
 - Immunoglobulin substitution
 - Cytokine therapy
 - Gene therapy

See you all in Budapest in October !

Organised by Laszlo MARODI



The Jeffrey Modell Foundation can be found at www.jmfworld.com .

Working Party reports

Clinical Working Party

On behalf of the ESID Clinical working party and the ESID/EBMT working party, we would like to gather data on the outcome of treatment for ADA deficiency following PEG-ADA therapy and BMT. Detailed gene therapy outcome is not included in this questionnaire due to the small number of patients treated.

I would be really grateful if you could take the time to fill in this form (you find it on the last pages of this issue of the ESID Newsletter). As a priority I would be grateful if you could first complete forms for patients who have been treated with PEG-ADA either alone or subsequently by BMT or GT. At present there is no formal outcome for PEG-ADA treatment and this gives us an opportunity to gather some important data from the European centres. We are hoping to present this data at a symposium at EBMT in March 2005 so I would urge your attention to this group of patients first. Forms for patients who have received BMT alone should be completed as a second priority. These forms will also form the basis of entry onto the online ESID registry and so gathering the data now will allow easy access onto the online version. Many thanks and I am look forward to receiving your forms.

Kind regards,

Bobby GASPAR

Educational Working Party

The Educational Working Party has several activities to comment on. First of all, the again very successfull Summer School, of course, which took place in October 2005 in Palma de Mallorca. Furthermore, the upcoming Educational Day

in Budapest in October 2006, and the contribution to the Lagid meeting in November 2005.

ESID Summer School 2005

The ESID Summer School is held every other year, and last year the School took place at Palma de Mallorca, October 19 - 23. This was the 5th Summer School and the first one organised outside Portugal. Among close to 50 applicants, 26 were chosen to participate. As previously, the majority comes from Europe but not exclusively. One important goal of the Summer School is to spread the knowledge of primary immunodeficiency also to less fortunate countries and to help young doctors living in areas with no Summer Schools to improve their skills in immunology. So, among the participants we had young colleagues from Sudan, Cyprus, Egypt, Costa Rica, Brazil, New Zealand and Australia.

This created quite a mixture of background knowledge and was a challenge to the teachers. But more important, we all, teachers and students, learned a lot from this heterogeneity and it was impressive to see the strong friendship that developed during these few days and the dedication of the teachers, who included night lectures (!) on technical subjects such as how to interpret and perform flow cytometry as extra activities.

The faculty included the following senior ESID members: Professor Andrew Cant, Newcastle, UK, Professor Jean-Laurent Casanova, Paris, France, Professor Jacques van Dongen, Rotterdam, the Netherlands, Dr Teresa Español, Barcelona, Spain, Professor Anders Fasth, Göteborg, Sweden, Professor Georges Holländer, Basel, Switzerland, Professor Gavin Spickett, Newcastle, UK, and Dr Esther de Vries, 's-Hertogenbosch, the Netherlands.

During the course from Wednesday afternoon to Sunday lunch 35 hours of lectures were given so you can easily imagine that the days were intense. The following areas were covered: the patient with recurrent infections and differential diagnosis; innate immunity and

its deficiencies; the molecular and cellular basis of primary immunodeficiencies; the clinical presentation, diagnosis and treatment (including hematopoietic stem cell transplantation and immunoglobulin substitution) of primary immunodeficiencies. As for previous Summer Schools, the participants own cases were very important. They give the opportunity to discuss the clinical everyday, the many differential diagnostic alternatives, how to investigate a case of suspected immunodeficiency and the treatment.

The Summer School is of one of the most successful activities of ESID. The praise given by the students is embarrassingly good. "The days were so full and yet we did not feel tiredness!" "The faculty members had the gift to spread their enthusiasm onto us." "I can honestly say this was one of the best courses I have ever attended" The formal evaluation included visual analogue scales from 0 - 100 and the average for content as well as

presentation were above 95!

The Summer School is sponsored by the plasma industry and without the generous support from Baxter Bioscience, Bayer, Grifolds, Octapharma and ZLB Behring this event would not be possible. The course and accommodation are both free to the participants and we even had the possibility to give some students a travel grant. The next Summer School will take place 2007.

Anders FASTH

Impressions from a participant, Gustavo Lazo, from Costa Rica:

I am very grateful with ESID because they gave me the golden opportunity of learning about PID from every faculty member. The Summer School was incredible. I learned a lot not only from the faculty members, but also from my colleagues.

I was anxious to see how the immunologists are



working on PID in Europe, and the Summer School allowed me to hear wonderful lectures and to interact with people with different points of view, different expertise and other cultures.

Now I know that I can help my patients a lot, even if we don't have many resources. I know that immunology is always changing and we are forced to read, and to share knowledge in order to do our best for the patients who are our main motivation.

I thought that I was going to learn about PID, but I was wrong, because we talked about basic immunology, diagnostic tools, genetics, etc. Of course the Summer School wasn't only to study. We had time enough to socialize and now I am glad to have many friends all around the world.

I need to thank ESID, the faculty members, and the sponsors for such a wonderful experience !

ESID Educational Day 2006

As with the last two ESID Biennial meetings, an Educational Day will be held at the opening day of the Budapest meeting. This year the educational day will focus on B cell development and B cell defects.

LAGID meeting November 5 - 7, 2005

During three days the Latin American Group for Immunodeficiency met in the lovely colonial city of San Miguel Allende, Mexico. The Educational WP sponsored the travel of three representatives of ESID, who lectured at the meeting, Jean-Laurent Casanova, Bodo Grimbacher and Anders Fasth.

Also to my great joy, many students from previous ESID Summer Schools from different countries in Latin America participated in the meeting.

LAGID is moving towards the formation of a society and will also change to biannual meetings. This means that there will be no competition with the ESID biannual meetings. At the meeting the creation of a LAGID School on Primary Immunodeficiency was announced. The first LAGID School will be arranged by Beatriz Carvalho in Sao Paolo, Brazil some time in late August or September 2006.

LAGID is moving towards the formation of a society and will also change to biannual meetings. This means that there will be no competition with the ESID biannual meetings. At the meeting the creation of a LAGID School on Primary Immunodeficiency was announced. The first LAGID School will be arranged by Beatriz Carvalho in Sao Paolo, Brazil some time in late August or September 2006.



Anders FASTH

*Registry Working Party,
the ESID online registry*

The year 2005 has been a successful year for the ESID registry. Since the last ESID Newsletter, there has still been an increase in the number of entries in the database. By October, the number of patients had reached 1105. The ESID registry working group has organised two workshops in the autumn for ESID members from centres that were either preparing to start documentation soon, or had just recently started. In a theoretical and a practical part we tried to familiarize the participants with the ESID registry, starting with the preliminary procedure of signing an agreement with ESID and applying for a password. We talked about ethics approvals and how to obtain them

and had a hands-on session in the afternoon where the participants had the opportunity to document a fictitious patient in our Test system. Apart from that, we had a common dinner with lively conversations in relaxed atmosphere. The Workshop was closed the next day with a guided walk through the Old Town of Freiburg and lots of information about its history and particularities.

In retrospect both workshops were a confirmation of what we already presumed: Obtaining the obligatory ethics approval is time-consuming and requires different amounts of work in different countries. Therefore, we have started preparing some kind of "ethics starter kit" in English, containing helpful documents in an English translation which can be presented to the local committees. For all of you who might need these documents as a reference, please contact us (frisch@medizin.ukl.uni-freiburg.de).

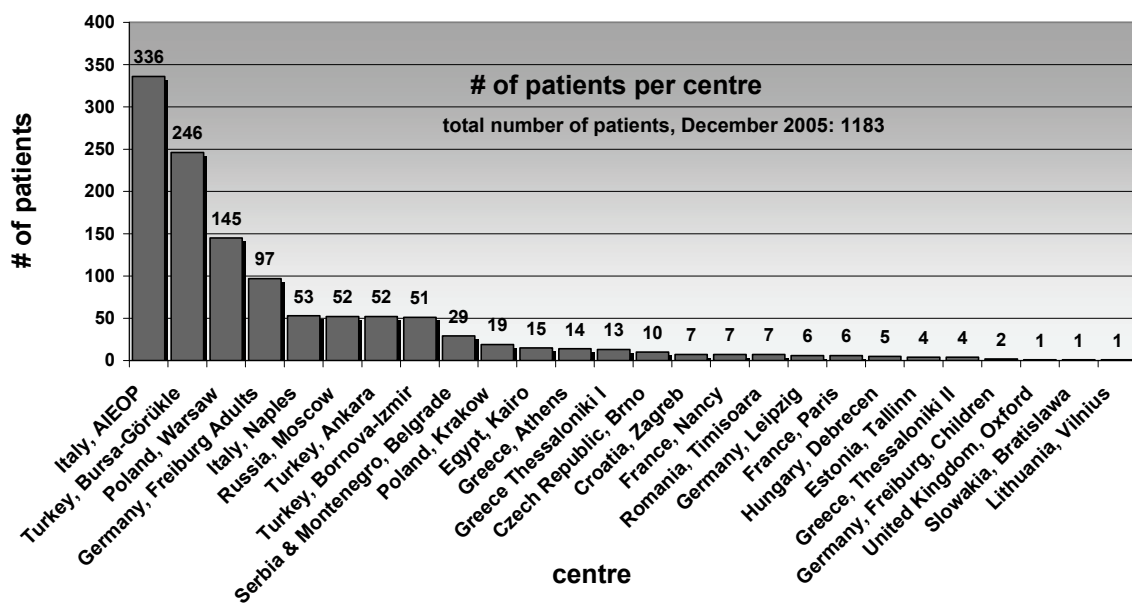
Another important topic during the workshop was the personalized 3-server-solution which is meant to be available next year. Instead of a coded identification number, this solution allows the documenting physician to view the patient's name and personal data on the screen. Hence you will no longer need to run a separate list linking the IDs to the respective patient. How is this possible without running the risk of having personal patient data available for trespassers/hackers? The solution is the deployment of a personalized system using three servers. Our modified and improved solution uses three servers: One for the patient's personal data and one for therapeutic data. The third server is called the gateway-server and brings the information together. All three will be run and maintained in Freiburg. What makes the system so secure is the fact that the servers run behind different certified firewalls: the university firewall and the hospital firewall. This solution has already been proved and tested in routine use in other institutions and systems. The immense advantage for all users is that they can work with a personalized version without additional costs for a local server. Just like today, the complete system runs on the internet. There

will even be the possibility to enlarge the system with features like automated report generation on the base of patient and laboratory data you entered into the database. During the deployment of this solution the online database needs to be shut down for a few days around Christmas. All members with passwords will be informed in time via Email.

The previous ESID Newsletters have given you regular updates about the progress that has been made and the projects we are working on. As you may have noticed, in the passed year 2005 the focus of the database team lay mostly on the acquisition of new documenting centres and on the increase of patient numbers in the registry. With 1.173 patients in November 2005, the database already offers a considerable cohort of patients (see charts for more details), so that in 2006 we will concentrate more on the output-features. Physicians in our documenting centres ask for queries on their own patients and on larger cohorts. Therefore, we have collected a number of frequently asked questions to the database which will be programmed as pre-defined queries that can be run by the physicians themselves. Also the users will

find interesting and important data in the database, for example on therapy (drug groups, route of administration, compliance, side effects) or on the quality of life (days missed at school/work, days in hospital). The ESID database is meant to be a research platform for both documenting centres and sponsors, and all of you are kindly invited to use it as such. As the CVID subregistry has been the first with an extended disease-specific dataset and therefore contains the largest number of patient datasets, a number of fields out of all fields in the subregistry has been defined in order to answer the "10 most burning questions on CVID" in a survey. So far, we received study goals on CD3-deficiency, FOX N1, Nijmegen Breakage syndromes, Wiskott-Aldrich Syndrome, ADA-SCID and CVID. However, we will be happy to receive more study goals on various ADA-SCID and to answer your questions on the preparation of such.

Although the ESID database has made considerable progresses in 2005, we still need to work on the development of further extended subregistries next year. In this respect we would like to remind the members of steering committees to send us their proposals for disease-specific data models. This can be in form of a simple document

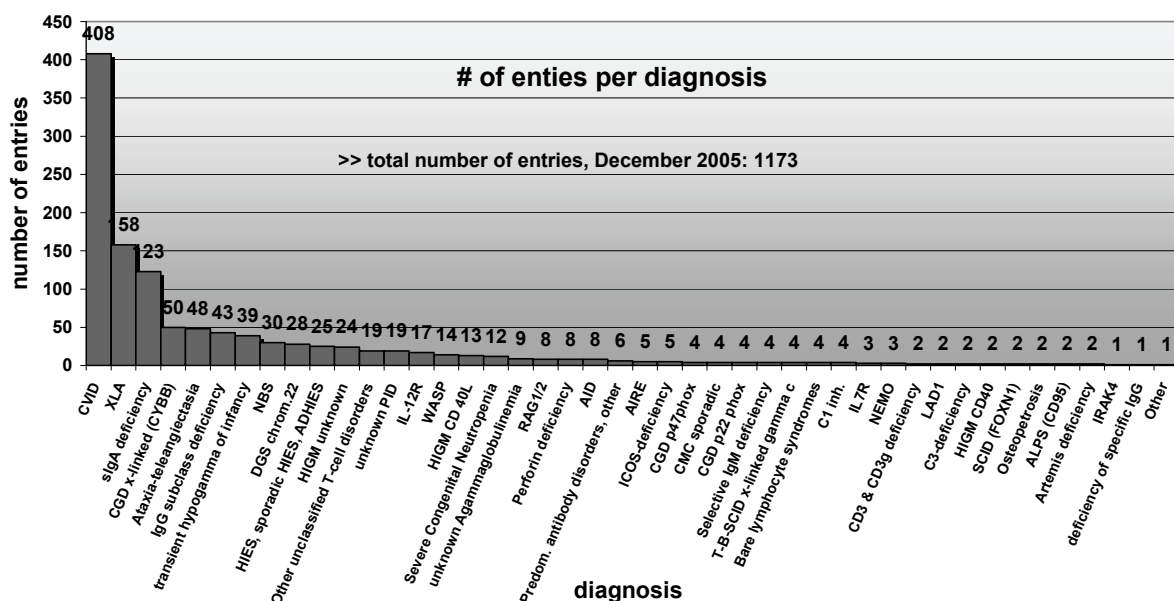


containing all questions you would like the database to answer. Also other ESID members who wish to contribute to the development of the database are invited to contact us. We can put you in touch with existing steering committees and are looking forward to receiving your input which will be of great value for all database users. Just recently the groups working on ADA deficiency and ataxia teleangiectatica (AT) have submitted their data models. Those will be programmed next.

Since the last ESID Newsletter, there has still been a slight increase in the number of entries in the database. By November 2005, the number of patients has reached 1.173. The increase in patient numbers in 2005 has also been achieved thanks to the excellent offer of the sponsoring PPTA member companies to pay a 2000 Euro incentive for the first 10 centres to enter 50 complete core datasets. This stimulated the data entry a lot. Please have a look at the latest charts below. The total number of registered documenting centres is now 50, situated in 27 different countries. Some countries are planning to establish National Registries within the ESID system. The first country to do so was

Italy. The Italian AIEOP data has been transported into the ESID online database in the summer, which increased the number of patients by 336 all at once. There will be imports once a year. Since AIEOP collects data on five Primary Immuno deficiencies, the Italian documenting centres are asked to enter all patients with other diseases, which are not included in the AIEOP network, directly into the ESID database. Those centres will also need to sign an individual agreement with ESID and collect consent forms from their patients.

A very positive achievement is the vote of centres in the United Kingdom at the recent UKPIN meeting, to build up a National Registry in collaboration with ESID. The UK delegates liked the ESID system because of its good compliance with the UK requirements: The system is easy to handle for physicians, the IT-support is provided by Freiburg, there are already MREC-approvals (ethics and data protection) for adults and infants on hand, etc. All these advantages have led to five centre agreements being finalised in order to start documentation as soon as possible. Other centres are being encouraged to participate though a decision to fund the proposal for a peripatetic data entry person is not yet finalised. All British centres are now requested



to contact Mary Gray in Oxford (mary.gray@orh.nhs.uk) and ask for all necessary documents for the next step, which is the application at the centre internal committees.

France has also built up a National Documenting centre which resides in Paris. Since November, Dr. Romain Micol has been employed by Prof. Fischer's department exclusively for this purpose. He is responsible for the organisational work and for the documentation of all French patients into the registry. In October he also attended one of our ESID-database-workshops in Freiburg, where he learnt not only about the features of the database, but also about the preliminary requirements like ethics and data protection approval and patient consents. Back in Paris he has already started preparing for the documentation of French patients. Interested centres in France may address themselves to him for further information (romain.micol@nck.aphp.fr).

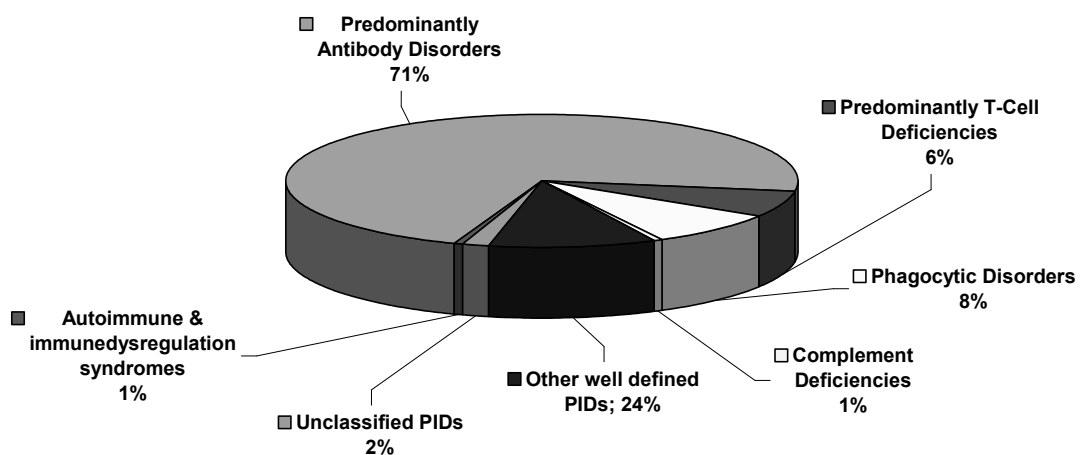
The new Spanish REDIP online registry is now available for the documentation of the Spanish patients. Spain maintains a National Register with a one time registration since 1993. Today

more than 2000 patients are incorporated. Spain decided to maintain its system as an online database from which a data export to the ESID online database is intended on a regularly basis. We will now have to wait for the Spanish centres to document into the new REDIP registry before Spanish data can be made available in our system.

Poland also opted for a National Registry within ESID and will start preparing for this in January 2006. The head centre will be in Warsaw, one of the biggest Polish centres for PID and one of our best contributors to the database in 2005.

Several additional countries like the Netherlands, Belgium and Portugal are discussing this option, but the considerations are still going on. The great advantage for all countries which do not have a National registry yet, is that they can use the ESID system exactly like an independent system, but without any costs for programming and support. The country elects one head of National Registry which will be the only contractor with ESID. All other centres refer to this direct contact partner in their own country. The degree of sharing data within the National Registry is completely customisable and can be decided upon internally. These criteria can be taken into

Distribution per PID-category



account while discussing the topic. Should you have any questions, we'll be happy to send you information.

*Registry Working Party,
the new ESID website*

The new ESID website will be online in February 2006. Lots of attractive new features will be presented in a more appealing way. Please have a look at it - you will certainly find it much more worthwhile to visit the site now and then, because there will be publications in the field of primary immunodeficiency, ongoing study protocols, and information about upcoming meetings. You will also be able to chat in the new discussion forums on PID-related topics. The Working Party sections will be updated continually. Are you looking for diagnostic criteria? A lab which is specialised on specific topics? An ESID centre in another country? Information about the ESID Juniors? All this can be found on the new website. Last but not least there will be a password protected area for ESID members only where you can manage your personal details, pay your membership fee and submit texts. These will then be validated by the web administrator and posted on the website.

We hope that the ESID members will benefit from the new opportunities and will contribute to the websites' content.

We wish our database users and ESID members all the best and are looking forward to a good cooperation and a successful year 2006!

Bodo GRIMBACHER and team

PID-care in development:

Can you give me some information about your background and can you tell me something about your career history?

I will give you some information about our Immunology Department's Staff. Each individual member will present him/herself to you here:

I'm Oscar Porras-Madrigal, 53 years old.



I studied Medicine at the University of Costa Rica, Paediatrics at the University of Costa Rica and Clinical Immunology at the Clinical Immunology Institute in Göteborg, Sweden. I obtained my PhD at the University of Göteborg, Sweden. I did my PhD thesis studying bacterial adhesion and *Haemophilus influenzae*, my tutor was Prof. Catherina Svanborg-Eden, my tutor in Immunology was Prof. Lars A. Hanson and my tutor in paediatric rheumatology, BMT and immunodeficiencies is Prof. Anders Fasth. My wife is an Agricultural Engineer and we have three daughters (22, 20-20 years old). I did my clinical training in paediatrics at the National Children s Hospital in Costa Rica, and my clinical training in Immunology and Paediatric Rheumatology at the East Hospital in Göteborg.

My name is Arturo Abdelnour. I was born April 20th, 1962 in Bogota, Colombia. My father is Costa Rican so after a few years of living in Colombia we moved to Costa Rica where I went to Medical School from 1978-1983. After obtaining my MD, I did my paediatric training at the National Children's Hospital in San Jose, Costa Rica, and then I travelled to Göteborg, Sweden, where I did my PhD in Clinical Immunology. Since the year 1994, I have been working at the Department of Immunology & Pediatric Rheumatology at the National Children's Hospital in San Jose, with a 2 year interruption (2003-2004) when I worked as Medical Manager at GlaxoSmithKline in the Department of Clinical Research.

My name is Iris Leiva. I was born August 6th, 1962 in San Jose, Costa Rica. I got my degree in Medicine in 1985 and I did my training in pediatrics at the National Children's Hospital in San Jose, Costa Rica from 1987-1989, after that I went to Paris where I got my degree in Clinical Immunology and Rheumatology. I have been working at the Department of Immunology and Pediatric Rheumatology since 1993.

Dr. Olga Arguedas is not in Costa Rica in this moment (she is in Genova with a PRINTO scholarship in pediatric rheumatology) but is a very important part of the team as PhD in Clinical Immunology since 1989.

Can you give me some information about health care in your country?

Costa Rica is a very small country in Central America where it is possible to find not only beautiful places for tourists, but also a very high incidence of some PIDs (for example osteopetrosis and ataxia telangiectasia). Costa Rica is 51100 Km², with a population of 4178755, the population density is 56/Km². Poverty is 25.6%, birth rate is 17.01/1000, mortality rate is 3.75/1000, infant mortality is 9.25/1000, life expectancy is 78.73 years.

Costa Rica is a country that abolished the army in 1948, and divided the defence budget between education and health. We have a socialized health system based on solidarity. The system is organized into public (90%-95%) and private medicine (5-10%), and the public one provides health care to pregnant women and children independently of their insurance status. The Social Security System uses most of the available human health resources, and is designed to provide equal health opportunities for all Costa Ricans, independently of their economic contribution and independently of the place where they live. The public system is organized into different levels of attention - primary, secondary and tertiary - the complexity being higher as the level increases. Usually, people consult in the primary level first and they are referred to a secondary or tertiary level as required. Costa Rica's Health Indexes are among the best of Latin America, reflecting the excellence of the Health Care System in our country.

Can you give me some information about PID-care in your country?

The Immunology and Rheumatology Department at the National Children's Hospital in San José, Costa Rica started in 1985 under the leadership of Oscar Porras MD, PhD. Actually there are 4 full time Clinical Immunologist, a fellow in Clinical Immunology & Rheumatology, a resident in paediatrics and an intern. The facilities are divided into two main areas; inpatient and outpatient, which also include an area with facilities for IVIG-substitution. A program of Bone Marrow Transplantation is also working where basically patients with Primary Immunodeficiency's and occasionally patients with Haematology Diseases are transplanted (using allogenic BMT with HLA-identical related donors).

We have registered 283 IDP; the most frequent IDP is Ataxia-Telangiectasia (82 cases). A founder effect has been described in A-T, one mutation explains more than 80% of the cases. The infection treatment usually is

teamwork with the paediatric infectologist. We don't have a patient organization.

How did you all become interested in immunodeficiencies?

It was Oscar Porras who has offered us the opportunity to be trained in Clinical Immunology and our interest has been growing since we want to offer the best to our patients.

Dr. Porras became interested in PID, after his experience in Sweden, and after he started studying the epidemiology of Ataxia-Telangiectasia in Costa Rica in collaboration with Dr. RA Gatti.

What has been your role in PID-care in your country until now?

We started the facilities for diagnosis and treatment in 1985, the facilities for evaluation of children with recurrent infections in 1986, and BMT in 1985 with the collaboration of Dr. Anders Fasth. We already started with a PID national registry in 1986 !

What do you hope to achieve in the future?

I think we have achieved expertise approaching the patient in which we suspect a Primary Immunodeficiency, being able to make a good initial evaluation and in many cases a diagnosis. But we don't have the facility to look for genetic defects, thus I think we have to enter into the molecular area to be able to offer the best to our patients. Also we have to improve our Bone Marrow Transplantation Program.

So, our goals are:

- to develop a PID adult clinic
- to develop PID molecular diagnosis
- to develop T-cell depleted BMT

- to decrease the age at diagnosis of PID by 50%
- to develop an interdisciplinary clinic for A-T
- to organize one of the ESID meetings in Costa Rica !

How could ESID help to achieve these goals?

ESID can help us basically in two ways; one, making collaborative projects to train people and help people to assist to courses or short visits to different Clinical Immunology Departments and second, coordinating multicenter studies in which "less developed countries" can participate.

Some specific topics we could develop together are:

- Developing a visiting professor scholarship that will allow us to invite a specialist to share knowledge and discuss cases. That will also develop collaboration with European centres
- Encouraging Alfa projects on PID from the European community, that is a very effective way to have European centers and Latin American centers to work on a project that produces exchange of doctors and improvement in PID care

Gustavo LAZO



**QUESTIONNAIRE Outcome of treatment for Adenosine Deaminase Deficiency
On behalf of ESID/EBMT inborn errors WP**

Centre: **Patient identifier:**

Sex: **Date of birth:**

1. PRESENTATION DETAILS

Age at referral/diagnosis:

Clinical History at diagnosis (please tick more than one if necessary):

Failure to thrive: Chronic diarrhoea:
Pneumonitis (+ organism if known):
Bacterial pneumonias ((+ organism if known):
Other respiratory problems:
Candidiasis:

Bone defects: Neurological problems:
.....
Eczema: Other bacterial infections:
.....
Autoimmune manifestations: Haematological abnormalities:
Hearing impairment:

Immunology (at presentation)

Absolute lymphocyte count: Neutrophil count:
CD3+ :
CD4+ : CD8+ :
CD19+ or CD20+ : CD16+/CD56+ :

PHA stim (SI - if possible) :
Other mitogen responses (specify) :

IgG:
IgM:
IgA:

Antibody responses - Tet: Y/N..... Hib: Y/N..... Other (specify):
TRECs (if available):

Diagnosis (please indicate reference units)

Erythrocyte dATP level:
RBC ADA activity: Lymphocyte ADA activity:
Plasma ADA activity : SAHH level:

2. TREATMENT WITH PEG-ADA: Y/N.....

Date started: **Age when started :**

Dose 1 (units/kg): Duration (mths):
Dose 2 (units/kg): Duration (mths):

Prophylactic Medication on PEG-ADA

Antibiotic prophylaxis: Y/N..... Discontinued: Y/N.....
 Fungal prophylaxis: Y/N Discontinued: Y/N.....
 Viral prophylaxis: Y/N..... Discontinued: Y/N.....

Cellular immune reconstitution on PEG-ADA

	1 mth post PEG-ADA	3 mths post PEG-ADA	6 mths post PEG-ADA	12 mths post PEG-ADA	24 mths post PEG-ADA	Most recent
If diff time specify						
ALC						
CD3+						
CD4+						
CD8+						
CD19+ or CD20						
CD16+/CD56+						
TRECs (if available)						

Time to normal PHA response:
 Time to normal antigen specific response:

Humoral immune reconstitution on PEG-ADA

Ig replacement discontinued: Y/N.....
 IgG prodn: Y/N.....IgM prodn: Y/N.....IgA prodn: Y/N.....
 Antibody responses - Tet: Y/N.....Hib: Y/N.....Other (specify):

Metabolic recovery on PEG-ADA (please indicate reference units)

	1 mth post PEG-ADA	3 mths post PEG-ADA	6 mths post PEG-ADA	12 mths post PEG-ADA	24 mths post PEG-ADA	Most recent
If diff time specify						
dATP						
RBC ADA						
Plasma ADA						
Lymph ADA						
SAHH						

Side effects on PEG-ADA

Autoimmune cytopaenia: Y/N.....(specify)
 Thrombocytosis: Y/N.....
 Other (please specify):

Improvements noted on PEG-ADA

Weight gain: Y/N.....
Infection frequency: Y/N.....
Development: Y/N.....
Gut symptoms: Y/N.....
Other (specify):.....

Outcome on PEG-ADA

Remains on PEG-ADA: Y/N.....Time of last f/u.....

Death on PEG-ADA: Y/N.....
(if Y - age of death: cause of death:.....)

Proceed to HSCT: Y/N.....
(if Y - outcome of HSCT: alive/dead.....)

Proceed to Gene therapy + PEG-ADA: Y/N.....
(if Y- outcome of GT +PEG-ADA: alive/dead.....)

Proceed to GT alone: Y/N.....
(if Y- outcome of GT alone: alive/dead.....)

Non-immunological outcome on PEG-ADA

Audiology

Hearing loss: Y / N / not done..... if Y – date of assessment.....
If Y specify degree of loss:
Hearing aids: Y / N

Neuropsychological

Assessment done Y / N if Y – date of assessment.....
Assessment type: Bayleys / WPPSI / WISC / Other (specify).....
Full scale score.....Verbal scale.....Performance scale.....

3. TREATMENT BY HSCT: Y/N.....

No. of transplants:

Date of 1st transplant:.....Age at 1st transplant:.....
Donor Type: MSD / MFD / mMFD / MUD / mMUD/ Parental Haplo
Stem cell source: BM / PBSC / Cord / other (specify)
Donor compatibility: 12/12, 11/12, 10/10, 9/10, 6/6, 5/6, 5/10, other (specify).....

Conditioning regime

Specify (drug+dose) :
.....
.....
.....
.....
Serotherapy (drug+dose):
.....
GvHD prophylaxis(drug + dose)
.....

GvHD Y/N.....

Grade:
 Skin: Y/N.....
 GI: Y/N.....
 Liver: Y/N.....

Donor engraftment ...Y/N.....

(give most recent result)
 PBMC engraftment: % donor.....
 Myeloid engraftment: % donor.....
 T cell engraftment: % donor.....
 B cell engraftment % donor.....

Date of 2nd transplant:.....Age at 2nd transplant:.....

Donor Type: MSD / MFD / mMFD / MUD / mMUD/ Parental Haplo
 Stem cell source: BM / PBSC / Cord / other (specify)
 Donor compatibility: 12/12, 11/12, 10/10, 9/10, 6/6, 5/6, 5/10, other (specify).....

Conditioning regime

Specify (drug+dose) :

 Serotherapy (drug+dose):

 GvHD prophylaxis(drug + dose)

Outcome of HSCT

Deceased: Y/N.....
 If Y – cause of death:..... time after HSCT:.....
 If alive – time of last f/u.....

Cellular immune reconstitution after HSCT

	6 mths post HSCT	12 mths post HSCT	24 mths post HSCT	Most recent
If diff time specify				
ALC				
CD3+				
CD4+				
CD8+				
CD19+ or CD20				
CD16+/CD56+				
TRECs (if available)				

Time to normal PHA response:
 Time to normal antigen specific response:

Humoral immune reconstitution after HSCT

Ig replacement discontinued: Y/N.....
 IgG prodn: Y/N.....IgM prodn: Y/N.....IgA prodn: Y/N.....
 Antibody responses - Tet: Y/N.....Hib: Y/N.....Other (specify):

Metabolic recovery after HSCT (please indicate reference units)

	6 mths post HSCT	12 mths post HSCT	24 mths post HSCT	Most re-cent
If diff time specify				
dATP				
RBC ADA				
Plasma ADA				
Lymph ADA				

Non-immunological outcome post HSCT

Audiology

Hearing loss: Y / N / not done..... if Y – date of assessment.....
 If Y specify degree of loss:
 Hearing aids: Y / N

Neuropsychological

Assessment done Y / N if Y – date of assessment.....
 Assessment type: Bayleys / WPPSI / WISC / Other (specify).....
 Full scale score.....Verbal scale.....Performance scale.....

Please send forms back by:

- 1) e-mail to: h.gaspar@ich.ucl.ac.uk
- 2) Fax to: +44 207 905 2810
- 3) post to: **Dr Bobby Gaspar**
Molecular Immunology Unit
Institute of Child Health
30, Guilford Street
London WC1N 1EH

Tel no: +44 207 905 2319/2289 (if required)