ESID Newsletter

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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.

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

Front page:
ESID Summer School 2007 in Malaga.

Dear ESID members,

In this issue of the ESID Newsletter, you can find the enthousiastic reports about the ESID Summer School which was again a great success. Thanks to our generous sponsors, we were able to have a lively meeting with a lot of hard work and personal contact in wonderful surroundings.

Don't forget to prepare yourself for attending the ESID 2008 meeting in `s-Hertogenbosch, and visit the website at www.esid2008.org !

Young researchers active in PID can apply for the Educational Working Party Scholarship for €10,000. Don't hesitate to get information about this if you think about applying, and if you are no longer a junior researcher yourself, don't forget to bring this possibility to the attention of the juniors around you!

Read about the efforts of dr. Mukesh Desai in establishing an adequate PID service in India, and the interesting papers selected for you this time.

Don't hesitate to mail a reaction to the authors of the Interesting Case or Young Researchers' Corner section! These sections are meant to induce junior as well as non-junior ESID members to contact eacht other.

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 2,000 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,

As always, Esther de Vries has assembled, edited and published an outstanding issue of the ESID newsletter, which I am sure will be of great interest to you. It is a pleasure to warmly thank Esther for keeping our society lively, friendly and interactive via the Newsletter. This unique way to foster the development of the ESID community at large is much appreciated by everyone of us. Many thanks Esther!

All best wishes,

Jean-Laurent CASANOVA

Treasurer's report

We now have 433 ESID members who have paid their membership fee 2006/2007. There are also 138 people listed who have not paid. I have sent all of them an email to either pay their membership fee, or let me know they are no longer interested in being an ESID member.

With the next issue of the ESID Newsletter, you will all get the invoice for the membership fee 2008/2009. You will only be able to register to the ESID 2008 meeting as a member, and pay the reduced fee, *after* you have paid your 2008/2009 fee. So don't forget to do so when the invoice arrives with the next issue!

Esther DE VRIES

Main building of the Medical University in Iasi.

News & Views

The J-Project: Romania

The J-Project meeting series was started in 2004 in Targu Mures, Romania, and among the 21 meetings organized until now, there were those in Bucharest and Oradea in this country. The 4th Romanian J-Meeting took place in Iasi, the center of Eastern Romania, from October 12 to October 13, 2007. The meeting president was prof. Stela Gotia. This was a joint East-Romanian and Moldavian meeting and speakers/participants from Chisinov also attended this importang meeting. There were 85-90 participants. There were talks on primary and secondary immunodeficiencies, intravenous immunoglobulin therapy in pediatric patients, laser biostimulation in the immunodeficiency of the child with chronic arthritis, update on monoclonal antibodies therapy, immunotherapy in autoimmune diseases, vaccination in special situations, regulatory T cells: the implications of deficiency in the pathogenesis of allergic and autoimmune diseases, update on primary immunodeficiences, primary immunodeficiency in velocardiofacial syndrome/diGeorge, cytokine profile in digestive diseases, sarcoidosis – immunological disorders, hereditary angioedema, primary immunodeficiencies and digestive diseases, adverse reactions to intravenous immunoglobulin therapy, clinical and molecular forms of X-linked lymphoproliferative disease, immune disorders in common pediatric diseases, immunodeficiency of the premature newborn, Schimke immunoosseous spondyloepiphyseal dysplasia, transient IgA deficiency – possibility of error in celiac disease diagnose in children (a case study), severe neurogenerative disease in Wiskott Aldrich syndrome, humoral immunity perturbations in malnutrition, update of the National Primary Immunodeficiency Registry in Romania, importance of complete immunologic investigation in tuberculosis in children.

Laszlo MARODI

The fifth Winter School of Clinical Immunology: "Standardising of diagnostic and therapeutic guidelines", December 13th to 15th, 2007, Zakopane, Poland

It is a tradition within the Department of Immunology at the Children's Memorial Health Institute, to invite young immunologists interested in clinical immunology from both Central and Eastern Europe. The School of Clinical Immunology has been a great success so far. It has been organised every year since 2002, and is fully supported by the following European Union grants: PERFECT QLG1-CT-2002-90358 project, provided by as a Paediatric Research Centre of Excellence – Focusing on Effective Child Treatment, 2002-2005; EURO-PID-NAS, 2002-2004, and EURO-POLICY-PID SP23-CT- 2005-006411, 2005-2008.

It is my pleasure to invite you once more to Zakopane. The leading topics of the meeting are standardising of diagnostic and therapeutic guidelines in primary immunodeficiencies, and standardization of flow cytometric immunophenotyping methods for PID

Contributions will be given by Teresa Espanol from Institute Catala de la Salut, Barcelona, Jacques. J. van Dongen and G-J. van Driessen from Erasmus University, Rotterdam. One of the sessions will be dedicated to diagnostics and theraputics standards in chosen primary immunodeficiency diseases. Time for presentations of patients with unusual primary immunodeficiencies features will be reserved in the second session. Young immunologists are invited to present their own experiences concerning the diagnosis and treatment problems in paediatric primary immunodeficiencies.

I hope that you will be able to take advantage of your this invitation, and enjoy the magic time before Christmas with us in Zakopane, and also to find some time for skiing. More information: oddzial.immunologia@czd.pl

I am looking forward to seeing you in Zakopane,

Ewa BERNATOWSKA

Polish initiative for primary immunodeficiencies

The national project, with the aims of improving patient care, resulting in early clinical recognition and improved diagnostic and treatment strategies, and raising awareness of primary immunodeficiencies (PID) across the country, was initiated by Polish immunologists. The Polish Working Group for PID was established in March, 2005. The Group was set up In six main Polish centres for the diagnosis and therapy of PID , covering the whole of Poland. The main objectives of the Group's activity are: 1/ to build up a Polish national registry of PID, 2/ to harmonize existing Polish diagnostic guidelines based on the ESID proposal, and to develop therapeutic guidelines at a national level, 3/ to increase awareness of PID among paediatricians and general practitioners, 4/ to achieve the development of channels for the active dissemination of information about PID among patient organizations, media and public health groups, and both government and non-government organizations in Poland. The project has been supported by the European Union grant EURO-POLICY-PID SP23-CT-2005-006411 co-ordinated by Edvard Smith, Karolinska Institute, Sweden, granted for 2005 to 2008, and by grant PBZ-KBN-119/ P05/04 from the Polish Ministry of Science, granted from 2005 to 2008.

Polish National Registry of PID

The Polish National Registry has been developed in co-operation with the ESID database. To date, the Polish registry has collected data on 1 030 patients. A definitely slow introduction of patient's data into the ESID database resulted in 366 patients only. We are also responsible for the NBS1 sub-

registry, which to date contains 59 patients.

Harmonization of existing Polish diagnostic and therapeutic guidelines based on the ESID proposal, and development of therapeutic guidelines at a national level - starting point and future events

Efforts for co-operation, between our department, the Department of Immunology, Children's Memorial Health Institute, with other Polish centres involved in the diagnosis and management of PID has resulted in co-ordination, and the final establishment of a local network.

Standarising existing diagnostic and therapeutic guidelines, and in the organization and provision of training has been started. The complete set of diagnostic and therapeutic guidelines for CGD and CVID has been published in Centr Eur J Immunol, vol.32, 1, 2007, 34. (www.immunologia.termedia.pl). Take it, it's becoming easy! The next edition of the Central European Journal of Immunology will be proposed the agreed standards for SCID, HIE and Ataksia-telangiectasia syndromes and BCGitis in PID. The Central European Journal of Immunology is co-edited by fourteen central European immunological societies, which gives an opportunity for co-operation in the Region.

A proposal for newly- created diagnostic and therapeutic guidelines for disseminated BCG infection, published in Emerg Infect Dis. 2007 May;13(5): 799 has already been proposed to ESID members in this Newsletter.

Harmonising guidelines for flow cytometric diagnostics in PID

A project is under way to establish and evaluate harmonized guidelines for flow cytometric diagnostics in PID. This project has been implemented in co-operation with Professor Jacques J.M. van Dongen from Erasmus University, Rotterdam. The first meeting concerning standardization of cytometry in PID was held on May 17 –18, 2007, in Poznan, Poland. A standardized approach for diagnosis of primary immunodeficiencies was presented at the meeting. Several technical tips relating to the blood sample itself, and the method of defining cell populations, as well as a general step-by-step approach to diagnostics were presented. An article on harmonising guidelines for flow cytometric diagnostics in PID will be published this year in the Central European Journal of Immunology.

Website platform

The website http://immunologia.czd.pl, located on a server at the Children's Memorial Health Institute, Warsaw, has been set up since September 2006. A newly-created website includes the following elements: the up-to-date Polish registry of PID patients, diagnostic guidelines for PID, information on Polish and major international meetings and symposiums on PID, and helpful links to other websites related to PID, including the ESID. It also includes general information about PID, a list of information about Polish PID diagnostic centres,and information about Polish Parents of Child Sufferers with the PID Association and other related organizations from Poland and all over the world also shown. The project is supported by EURO-POLICY-PID SP23-CT-2005-006411.

Educational programme for young immunologists

The School of Clinical Immunology has been organised every year since 2002. The School of Clinical Immunology provides study opportunities for a new generation of young clinical immunologists and scientists. The meetings give a chance to listen to lectures given by experts in immunology from all over Europe. A group of young immunologists from both Central-Eastern and Western European countries traditionally take part in the meetings, including a group of young Polish immunologists, together with physicians specializing in clinical immunology. It also creates a forum to exchange their own

experiences, as well as to discuss difficult cases and diagnostic and therapeutic problems. The Schools of Clinical Immunology are supported by European Union and a national grants. Extended J-Project conducted by Laszlo Marodi, and the annual ESID Prague Spring meetings organized by Anna Sediva, there are another important forum for increasing awareness of primary immunodeficiencies, which brings young immunologists together.

Ewa BERNATOWSKA

BCG disseminated infections in primary immunodeficiencies

Most serious is the increasing number of reports of disseminated BCG disease (BCG-itis), almost always in children with immunocompromising conditions such as HIV, SCID, or with another severe form of congenital immunodeficiency. Vaccination at birth is a constant element of vaccination programmes in Central and Eastern Europe, due to the high prevalence of tuberculosis. Difficulties in the diagnosis and therapy of BCG infections in primary immunodeficiency patients, hospitalised in the Department of Immunology, Children's Memorial Health Institute in Warsaw during the last 25 years, have recently been published in Emerg Infect Dis. 2007 May;13(5): 799. Based on our experience, we would like to proposed a set of novel criteria for diagnosis and prophylaxis, and therapeutic guidelines for BCG infection.

Diagnostic criteria for BCG disseminated infections in Primary Immunodeficiencies

Definitive

A male or female patient with systemic symptoms, such as fever or subfebrile states, weight loss, or stunted growth, and at least two areas of involvement beyond the site of a BCG vaccination, such as lymph nodes, skin, soft tissues, lungs, spleen, liver or bones.

Identification by the Mycobacterium bovis BCG substrain from the patient's organs by culture and/or standard PCR, as well as typical histopathological changes with granulomatous inflammation.

Probable

Systemic symptoms such as fever or subfebrile states, weight loss or stunted growth, and at least two areas of involvement beyond the site of a BCG vaccination, such as lymph nodes, skin, soft tissues, lungs, spleen, liver or bones.

Identification of M. tuberculosis complex from the organs by PCR, without differentiation of M. bovis BCG substrain or other members of the M. tuberculosis complex and with negative mycobacterial cultures, with the presence of typical histopathological changes with granulomatous inflammation.

Possible

Systemic symptoms such as fever or subfebrile condition, weight loss or stunted growth, and at least two areas of involvement beyond the site of a BCG vaccination, such as lymph nodes, skin, soft tissues, lungs, spleen, liver or bones.

No identification of mycobacteria by PCR or culture, with the presence of typical histopathological changes with granulomatous inflammation.

Spectrum of disease

A male or female patient with severe combined immunodeficiencies, deficiency of IFN –g receptor, IL- 12 receptor deficiency, or other genetically - confirmed primary immunodeficiency with disseminated BCG infection.

Exclusion criteria

Any inflammation without typical histopathological changes, with no identification of Mycobacterium tuberculosis complex by PCR analysis in male and female with primary immunodeficiency.

Differential diagnosis

Severe, long-term inflammation with granuloma formation in primary immunodeficiency patients.

Prophylaxis and therapeutic guideline of BCG disseminated infection in severe combined immunodeficiency

No signs of local changes at the site of the BCG injection, and no signs of BCGitis

Careful observation

Local changes at the site of the BCG injection

Anti-TB treatment include IHN and RMP should be initiated and continued till complete immunological reconstitution occurs after HSCT.

BCGitis with regional lymph node involvement

Anti-tuberculosis treatment with at least triple anti-TB therapy, followed by long-term prophylactic treatment, as above.

BCGitis

Anti-tuberculosis treatment including four or more anti-TB drugs, until the patient fully recovers. Then, a prophylactic programme with two drugs should be continued, until complete immunological reconstitution after HSCT is achieved.

If you have any suggestions, questions, or requests, please feel free to contact us: oddzial.immunologia@czd.pl

Ewa BERNATOWSKA

Working in London?

University College London & Royal Free Medical School
Department of Immunology and Molecular Pathology
Marie-Curie Research Group

We are looking to recruit a postdoctoral Research Associate to join the EU funded Marie-Curie Excellence Team headed by **Prof. B. Grimbacher**, which studies the intersection of autoimmunity and primary immunodeficiencies.
The post is funded for at least 36 months.

Applicants will have an MD or PhD in biology; four to ten years relevant experience; previous experience involving cell culture, DNA sequencing, talk and manuscript preparation are all essential. Experience of work with B cells, dendritic cells or microarray analysis is desirable.

Appointment will be at Grade 7 level (£26,666 - £32,796) and the basic starting salary is likely to be £26,666. In addition, £2,572 London Allowance plus other allowances (depending on eligibility criteria) are paid.

Please refer to Prof. Grimbacher b.grimbacher@medsch.ucl.ac.uk for further information about the post or refer to
http://www.ucl.ac.uk/medicalschool/infection-immunity/vacancies/vacancies.htm
for further information about the application process

Closing date: November 30, 2007.

ESID Educational Working Party '10,000 Euros' Scholarship

The scholarship will be awarded to an ESID member, who is a physician / scientist under specialist training - interested in pursuing a research project in the field of *primary immunodeficiency.*

The scholarship should be used for laboratory or clinical research work for

at least 6 months.

The application should include a personal letter with a statement of career goals and plans on how to achieve those, a project plan, curriculum vitae, list of publications, a letter of invitation from the accepting institution, and a letter of support from the applicant's head of department or tutor.

Please send your application** not later than 1 December 2007 by e-mail to: Professor Andrew J Cant **Via e-mail: Gale.Roberts@nuth.nhs.uk

Andrew J Cant, Chairman of the ESID Educational Working Party

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The ESID meeting in `s-Hertogenbosch, the Netherlands, October 16-19, 2008

Dear ESID members,

The 2008 ESID meeting will, as you know, take place in `s-Hertogenbosch, the Netherlands. Preparations are ongoing, and the program is looking very attractive already now.

There will be 6 Sessions besides the Opening and Closing Sessions with Keynote Lectures, and 4 Workshops. The themes of the Sessions will be: The thymus, T-cell development and auto-immunity; New insights in B-cell development; The interaction between innate and adaptive immunity; Migration and regulation; The adult PID patient; Novel primary immunodeficiencies & Late breakers. The themes of the Workshops will be: The ESID Online Registry: how can we use it to the full; Other management of PID; Diagnosis of PID: protocols, guidelines and laboratory technolog; New developments in gene therapy and SCT.

We'll start with the Educational Day and Summer Schools reunion on the first day. Near the end of the day, the local initiative 'Women in PID' will discuss issues on women's career possibilities in the field of PID, and all female members are heartily invited to join this event. We intend to set up a kind of women's network if people are interested. Of course, interested male members are welcome to join the discussions too!

The ESID Working Parties will meet, and INGID and IPOPI will have their own parallel meetings.

A couple of social events will make your stay most enjoyable. So do come, and don't forget to explore the medieval alleys of `s-Hertogenbosch!

You can expect the seconde announcement and call for abstracts by the end of the year.

Esther DE VRIES

Working Party reports

Educational WP
The ESID Summer School 2007

The 29 Students and 9 Faculty Members came together in Malaga between 26 and 30 September '07 for the ESID Summer School. There were participants from 18 different countries including Australia, Argentina and Brazil. The Summer School was held in a very comfortable hotel by the sea but quite some way from the nightlife of Malaga, just in case the temptation to go "party" proved a little too strong! Anders Fasth and Teresa Espanol had, of course, done a superb job in choosing such an excellent location and hotel. Esther de Vries and Helen Chapel opened the Summer School with a session on how to recognise a patient with a primary immunodeficiency using the award winning ESID diagnostic protocol. It was a great privilege to have Helen with us, making a "guest reappearance". Helen has not been to the Summer School for several years, so people may not realise that she played a big part in setting up the ESID Summer School late in the last millennium!

The opening session soon engendered some lively interaction amongst almost all of the participants, a feature that continued throughout the Summer School. The second day started with a session on T cell immunology and immunodeficiency with Georg Holländer describing the basic immunology in his very special and memorable way. Eleonora Gambineri explained how T regulatory cells worked and what happened when they were absent. It was so good to hear about this from someone actively researching in the area. I continued by talking about clinical aspects of T cell immunodeficiency. It was great to have Eleonora as Trainee Representative involved in the planning and running of the programme. Following this Georg and I talked about the various types of SCID and interspersed in the talks the students presented cases relevant to the topics being covered. The day concluded with a session on DNA repair defects before Jacques van Dongen gave an immensely practical talk on how to interpret lab results. On the third day Steve Holland from the US described the known defects of innate immunity including completely up to date descriptions of the latest knowledge of NEMO and Hyper IgE syndrome. Steve's tremendously warm, enthusiastic questioning and gently provocative style did so much to make the Summer School the success it was. After this we covered treatment of the severe PIDs by haemopoietic stem cell transplantation, including the new European data on the success of HSCT in Wiskott Aldrich Syndrome and Chronic Granulomatous Disease. Following this Anders gave a fascinating talk about neutrophil disorders including reminiscences about Dr Kostmann! By now it was time for a relaxing afternoon, and people were either lazy (like me!) and stayed by the pool or beach, whilst the more adventurous explored the old part of Malaga with its Moorish Castle and magnificent cathedral. The fourth day was devoted to B cells. Jacques gave a superbly illustrated and very clear talk on B cell development after which Anders, Teresa, and Helen gave a series of interlinked presentations on Hypogammaglobulinaemia, CVID and immunoglobulin replacement therapy. We were then all taken for a lovely evening in a restaurant in the old part of Malaga for the "Course Dinner" after which most, but not quite all of the participants managed to make it back to the coach rather than investigate the night clubs! On the final morning there was time for many more cases, the wide range and interesting nature of cases ensured that there were far ranging discussions covering many areas, a great way for us all to learn more about an area of medicine for which we have such a shared enthusiasm.

All too quickly it was time to return

to the "real world" as we joined the crowds of holidaymakers in Malaga Airport. It seems we had all learned so much, exchanged so many new ideas, learned new ways to approach our subject and made lots of friends! For those of us on the Faculty it was so encouraging to see the calibre of the next generation of clinical immunologists which bodes well for patients with PID and for ESID in the future. So yes, it really was worth all the hard work from the Faculty and organising team, especially Anders, Teresa, Esther and my long suffering PA Gale Roberts, who ensured that so many of the practical arrangements ran so smoothly. There will not be another Summer School until 2009 (details to be announced on the ESID website in the early part of that year). However, there will be an 'Educational Day' just prior to the next ESID meeting to which all true trainees are invited to participate, whilst more senior members may be allowed to come and observe! More on this in the coming months . . .

Andrew CANT

ESID Summer School – Malaga 2007

The ESID Summer School was an excellent meeting and which enabled us to learn wide ranging key concepts in basic, clinical and laboratory aspects of immunology from experts in the field. The faculty were very friendly and we were able to interact openly and make contacts and think about future collaborations.

There was a right mix of formal lectures, case presentations and time for informal discussions with the faculty. It was as if we were taken out of time & space and put in an "Immunological bubble".

On day one we were introduced to the Patient centred screening of primary immunodeficiency which worked as a background framework for case discussions for rest of the summer school. Day two was full of T cells, how they were formed, educated, what happens when these things go wrong and provided us with a firm conceptual basis to work from first principles when faced with a diagnostic dilemma. Day three offered us fascinating insights into the complex mechanisms and the key roles played by innate immunity. B-cells and abnormalities in their generation and function were closely looked at and widely debated both on Saturday and Sunday.

All through the Summer School everyone presented clinical cases which led to informative, helpful and at times healthy debate which made basic science all the more relevant. Elenora talked about the ESID juniors and the progress that has been made so far and as everyone would agree, we should all participate more actively in the junior forum.

The venue was excellent and the Summer School dinner most enjoyable. There was a collegiate atmosphere with lot of wit and fun which made the experience so much more enjoyable. The only sad thing is one can go to the Summer School only once.

I would like to thank ESID, the

faculty members and the sponsors for providing such a wonderful opportunity to learn, discuss and debate, develop contacts and forge long lasting friendship with other Summer School participants.

Ravishankar Sargur,
Specialist Registrar – Immunology,
Sheffield, UK

Science and friends. That was the excellent combination that I found in ESID Summer School 2007. All my expectations were fulfilled.

Having the opportunity to listen to the experts in the field of Primary Immunodeficiencies and to exchange opinions with them isn't a frequent issue for me. And it was also encouraging to share the knowledge not only with the faculty members but with the students attending this meeting as well. Since everyone had a different background, it was very enriching for me, and a great chance to plan collaborative works.

It was really an honour to be part of this experience and I don't have any other word than THANKS!

Natalia BASILE

Anders Fasth and Helen Chapel preparing their talk

Registries WP

The Registry WP has recently implemented some new helpful features in the PID database: Report generation!

You can now download report sheets for individual patients from the ESID Online Database. This is useful for giving you an overview of the data documented for a given patient and can be stored in the patient's file. Physicians can also hand the report over to the patient, so he/she can see what data is being stored. The patient should be encouraged to check the information so that he or she can inform the physician about mistakes concerning the documented medication, for example.

To download a report, users have to log into the database and choose a patient. Clicking on the button "Show patient report" in the top panel initiates the report generation. This takes about 20 seconds.

The file produced is an rtf file which can be opened with Microsoft Word. It contains basic information on the patient, clinical data for the visit date chosen, current medication as well as QoL and lab data for the last four visit dates. (See Figure 1 on the next page.)

List of patients by diagnosis: In addition to the patient report, users can now also print out a list of all their patients including ID, diagnosis and the patient names (if they are using the personalized version). This can be very helpful for retrieving patients for example, if users are not sure in which subregistry they documented the patient. This can also help in identifying double registrations.

The patient list is available in the "Main Registry" which also includes the live statistics. The download just takes a few seconds. The rtf file produced can be opened with Microsoft Word. (See Figure 2 on the next page.)

We hope these new features will make working with the database easier for all users. However, please note that the

ESID Online Database **Patient Report sheet**

Date of printout: 26.09.2007

ESID Database ID: **5880**
Mr. Testpatient, Manfred

Date of birth (Year-Month-Day): 1960-7-4

Diagnosed with: Deficiency of specific IgG
Country of residency: Netherlands
Followed at ESID Center: DEVELOPMENT
Type of patient consent: Research and genetics

Date of diagnosis (Year-Month-Day):	2001	-		-		
Onset of symptoms (Year-Month-Day):	1999	-		-		

Clinical data for visit date: 2007-07-30

Body weight (kg):	78.0
Body height (cm):	185.0
Head circumference (cm):	

Quality of life data

From	until	Days missed at school or work	Days in hospital	All infections	Serious infections
2007-03-23	2007-07-30	0	10	1	0
2001-05-07	2007-03-23	10	30	2	1
one year before	2001-05-07	10	9	5	2

Current medication

Since (year)	Drug group	Generic name	Brand	route	Dose	Unit	Times	per
2004	Ig-Replacement	Human Gammaglobulin	Subcuvia	s.c.	20.0	g	1.0	week
1999	Corticosteroids	Cortison		oral	20.0	mg	1.0	day

Blood count

Date	Leukocytes	Unit	Thrombocytes	Unit	Erythrocytes	Unit	Hemoglobin	Unit
2007-07-30	5.9	10^9/L	206.0	10^9/L	4.6	10^6/µL	12.0	g/dL
2007-03-23	9.7	10^9/L	196.0	10^9/L	4.8	10^6/µL	16.0	g/dL
2001-05-07	6.8	10^9/L	198.0	10^9/L		10^6/µL		g/dL

Immunology lab values

Date	IgG	Unit	IgA	Unit	IgM	Unit	Relation to Ig replacement
2007-07-30	7.9	g/L	2.0	g/L	<0.23	g/L	trough level
2007-03-23	9.0	g/L	<0.5	g/L	<0.23	g/L	other
2001-05-07	2.1	g/L	0.5	g/L	<0.23	g/L	before any Ig repl.

Figure 1

Table 1

Disease	Entries
Common variable immunodeficiency (CVID)	1150
Isolated IgG subclass deficiency	379
Agammaglobulinemia X-linked (BTK)	368
Immunoglobulin A deficiency 1 IGAD	353
Ataxia telangiectasia (ATM)	347
Transient hypogammaglobulinemia of infancy	234
DiGeorge Syndrome	166
Wiskott-Aldrich syndrome with mutations in WASP	162
Other Hypogammaglobulinemias	119
Chronic granulomatous disease X-linked (CYBB)	106
Unclassified immunodeficiencies	102
CSR defects and HIGM syndromes with unknown genetic cause	98
Severe congenital neutropenia with unknown genetic cause	86
Cyclic neutropenia with unknown genetic cause	85
Hyper-IgE syndrome	80
Schwachman-Diamond syndrome with unknown genetic cause	78
CGD with unknown genetic cause	74
Kostmann syndrome	73
CD40 antigen ligand deficiency (CD154)	65
Nijmegen breakage syndrome (NBS1)	62
T-B+ SCID with unknown genetic cause	62
Agammaglobulinemias with unknown genetic cause	56
Severe combined immunodeficiency X-linked (SCIDX1)	48
Wiskott-Aldrich syndrome with unknown genetic cause	48
Other unclassified T-cell disorders	46
T-B- SCID with unknown genetic cause	42
Hereditary Angioedema (C1inh)	39
Deficiency of specific IgG	30
Familial mediterranean fever defect (MEFV)	30
Recombination-activating gene 1 deficiency (RAG1)	28
Familial hemophagocytic lymphohistiocytosis with unknown genetic cause	27
Secondary hypogammaglobulinemia	23
Selective IgM deficiency	20

Figure 2

ESID Online Database **Patient list**

Freiburg Development Centre 2

Date of printout: 25.09.2007

List of patients by diagnosis
Total number of patients: 10

ID	Disease	Last name	First name	Year of birth	Year of death	Sex
4391	Common variable immunodeficiency (CVID)	Bellabella	Isabella	1983		female
4361	Common variable immunodeficiency (CVID)	Bo	Stakka	1983		male
4923	Common variable immunodeficiency (CVID)	Bond	James	1983		male
4298	Common variable immunodeficiency (CVID)	Leone	Sergio	1983		male
4384	Common variable immunodeficiency (CVID)	Müller	Hans	1983		male
4379	Common variable immunodeficiency (CVID)	Parker-Bowles	Camilla	1983		female
3929	Common variable immunodeficiency (CVID)	Valerien	Harry	2000		male
5458	Deficiency of specific IgG	Skipielsko	Igor	1975		
5459	Isolated IgG subclass deficiency	Megawatti	Ohma	1900		female
3936	Nijmegen breakage syndrome (NBS1)	Nein	Ja	1985		male

patient report and patient list are first test versions. Therefore all suggestions for improvements are welcome.

New red field in the lab page: In the Core Lab page next to IgG, there is now a field "IgG measured as", which is asking whether this IgG value is a trough level (blood drawn directly before IVIG) or whether the blood was taken before the initiation of any Ig replacement at all. This question is important for all kinds of studies and is therefore now a mandatory red field.

Current figures: We reached the record number of 5000 patients this summer with the documenting centre in Munich having the honour of entering the 5000th patient although it was a close race with a couple of other centres just beaten at the post.

Please note that it is essential to document a patient completely. If for some reason you are missing some data when entering a patient into the database, please make a note of this and enter the information later. There are gaps in the data making them difficult to analyse. Any suggestions or criticisms are welcome at registry@esid.org !

Gerhard KINDLE
Benjamin GATHMANN
Anne-Marie PERNER

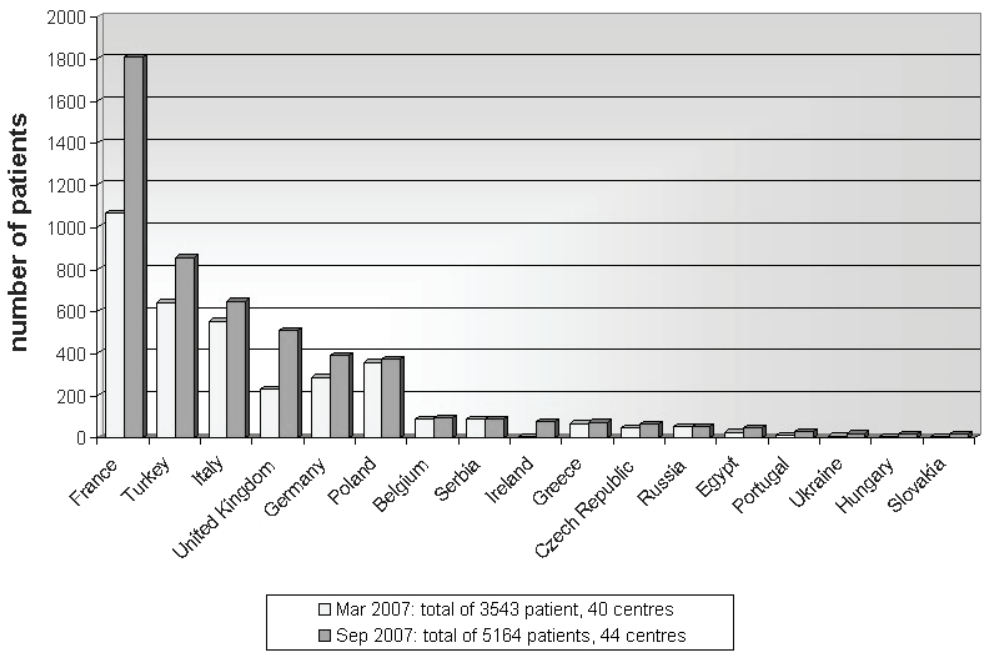

Fig. 3: Patients registered in the ESID Online Database, March and September 2007 compared. Only countries with more than 10 patients are shown.

Juniors WP

Dear all,

I hope you all spent a great summer! I just came back from the ESID Summer School where I was invited as Juniors representative. It was a memorable and great experience, I enjoyed the few days of science, teaching and fun but most of all being part of the faculty gave me the chance to interact with all the attendees and invigorate the ESID juniors' activities.

It was the first time that the head of the ESID Juniors was involved in the organization of ESID Summer School and thinking that this was one of our initial goals….I guess it is already a good achievement! I therefore want to thank you the "senior" Summer School faculty members and the ESID Board for the opportunity given.

Now coming to the main point, during the Summer School I handed out a brief questionnaire on ESID junior activities. On the next page is a summary of the keypoints taken from the results:

Are you interested in ESID Juniors working party?

26/29 people answered YES, 3/29 said not sure.

If yes, how would you like to get information?

27/29 people answered via e-mail, only 2 chose via web-site.

Would you like to participate to ESID juniors' activities?

25/29 people answered YES, 4/29 said not sure.

Do you think it is important that younger members get more influence in the ESID?

25/29 people answered YES, 4/29 said not sure.

Would you participate in the ESID Juniors' activities during ESID meetings?

29/29 people answered YES.

Have you ever visited the ESID juniors section on the ESID website?

14 people hadn't!

So in a few words, most of the people are interested in the WP and are willing to play an active role! E-mail should be the best way to communicate and keep in touch rather than ESID web-site and everyone was interested in participating in ESID Juniors section or "corner" during ESID meetings. I suppose it is already a very good outcome!

Moreover, the following suggestions and ideas were also addressed during the discussion:

Age limit: as for the Spring meeting in Prague, we all think it would be better to abolish the limit of 35 years old to join the WP. There are older people who feel to be still not "fully-grown" in the field of PID and would like to join the WP to have an opportunity to learn interacting with other trainees. This may be a reason why some people were uncertain regarding their involvement in ESID Juniors.

Web-site as a tool of interaction:

- Place on the web "Interesting cases" and "Young researchers' corner" from the ESID Newsletter and give the possibility to people to express their opinion on specific topics. A forum is already set up on the ESID website, but it is not very active. Creating a sort of "bulletin board" where every ESID member can post a case or an issue and the others get e-mail alert so that they can log on and start a discussion might be more effective.
- Have useful links for related sites (PID sources)
- Job list
- Photo-book

ESID Juniors budget: establish some funding to support our activities with particular focus on short-term stay programs (2-4 weeks) that allow young trainee to learn diagnostic/ therapeutic procedures or lab techniques in

other countries.

ESID Juniors Section/Corner within ESID meetings: a part of the meeting completely dedicated to junior members, held independently from the main sessions and symposia. It might be interesting to have a young "corner for crazy ideas" where you can present a different viewpoint or idea as well as a "corner for negative results" where you can present those interesting negative results, which can never be published.

I will work on these wonderful issues to put into practice as soon as possible. In particular I will make an effort to raise money for our budget J! But I will need the help and support of you all, so let's bring back from the Summer School the great spirit and enthusiasm and start from there!!!

I am really looking forward to hearing back from everyone soon!

Eleonora GAMBINERI

Interesting Papers

In this issue of the ESID Newsletter the papers selected focused on new genes discovered recently on some of the PIDs. They also provided the basis for the generation of new mutation databases and new factfiles for p14 deficiency (FF161), Igβ deficiency (FF159), NRAS deficiency (FF162), STAT3 deficiency (FF167/75), Tyk2 deficiency (FF163/75), UNC93B1 deficiency (FF164), RASGRP2 deficiency (FF139)) at http://bioinf.uta.fi/idr/index.shtml and http://bioinf.uta.fi/base_root/mutation_databases_list.php.

Please, have a look also on these services. Once again education and worldwide collaboration pays off.

A novel human PID syndrome caused by deficiency of the endosomal adaptor protein p14, provide evidence that the endosomal adaptor protein p14, previously characterized as confining mitogen-activated protein kinase (MAPK) signaling to late endosomes, is crucial for the function of neutrophils, B cells, cytotoxic T cells and melanocytes.
Nat Med 2007(1): 38-45, Bohn G, Allroth A, Gudrun Brandes JT, Glocker E, Schäffer AA, Rathinam C, Taub N, Teis D, Zeidler C, Dewey RA, Geffers R, Buer J, Huber LA, Welte K, Grimbacher B, Klein C.

A hypomorphic mutation in Igbeta (CD79b) in a patient with immunodeficiency and a leaky defect in B cell development, shows that minor changes in the ability of the Ig /Ig complex to bring the BCR to the cell surface have profound effects on B cell development. *J Immunol. 2007 June 15;177 (10):6889-95*. Dobbs AK, Tianyu Y, Farmer D, Kager L, Parolini O, Conley ME.

NRAS was identified as a transforming factor in neuroblastoma and other malignancies, but its principal physiological role in humans has been uncertain. This study shows that NRAS mutation causes ALPS and hematopoietic malignancies and it is an example of how gene profiling can facilitate the discovery of the molecular underpinnings of a genetic disorder. *PNAS 2007 May 22;104 (21):8953-8* Oliveira JB, Bidère N, Niemela JE, Zheng L, Sakai K, Nix CP, Danner RL, Barb J, Munson PJ, Puck JM, Dale J, Straus SE, Fleisher TA, Lenardo MJ.

The hyper-IgE syndrome (HIES) is a rare disorder of immunity and connective tissue characterized by dermatitis, boils, cyst forming pneumonias, elevated serum IgE levels, retained primary dentition, and bone abnormalities. The etiology of this disorder puzzled the investigators for a long time. Two recent articles one in *N Engl J Med 2007, Sep 19*, Holland et al and the

other one in *Nature. 2007 (7157): 1058-62,* Minegishi et al. support the role of STAT3 as the cause of the HIES.

Human tyrosine kinase2 deficiency reported in *Immunity 2006, 25, 745-755*, Minegishi et al. reveals its requisite roles in multiple cytokine signals involved in innate and acquired immunity. The articles aroused some debates in *Immunity 2007, 26, Page 536*, Woellner et al. and the question if Tyk2 deficiency might be or not a common cause of AR-HIES is still open. Further genetic analysis of HIES patients including AD and sporadic forms should clarify this issue.

Herpes simplex virus-1 (HSV-1) encephalitis (HSE) is the most common form of sporadic viral encephalitis in western countries with unclear pathology. The authors describe a genetic etiology for HSE in the intracellular protein UNC-93B. Other severe infectious disease may also reflect monogenic disorders of immunity. *Science 2006, 314(5797):308-312*, Casrouge A, Zhang SY, Eidenshenk C, Jouanguy E, Puel A, Yang K, Alcais A, Picard C, Mahfoufi N, Nicolas N, Lorenzo L, Plancoulaine S, Senechal B, Geissmann F, Tabeta K, Hoebe K, Du X, Miller RL, Heron B, Mignot C, de Villemeur TB, Lebon P, Dulac O, Rozenberg F, Beutler B, Tardieu M, Abel L, Casanova JL.

An LADIII syndrome is associated with severe defects in leukocyte and platelet integrin activation. This paper present the first human genetic adhesion disorder that is associated with defective expression of the Rap-1 activator CalDAG-GEFI in lymphocytes, neutrophils, and platelets. *JEM 2007 (204:7), 1571-1582*, Pasvolsky R, Feigelson SW, Kilic SS, Simon AJ, Tal-Lapidot G, Grabovsky V, Crittenden JR, Amariglio N, Safran M, Graybiel AM, Rechavi G, Ben-Dor S, Etzioni A, Alon R.

If you have other interesting papers and want to draw attention on them, please send and email to:
Crina.Samarghitean@uta.fi or
claire.fieschi@sls.ap-hop-paris.fr.

Crina SAMARGHITEAN
Claire FIESCHI

Interesting Cases

The clinical riddle peculiar or unresolved cases provided by ESIDJuniors

Case #4: Corticodependent severe normocytic anaemia of unknown origin, possible phagocytic defect.

We present a two year-old boy with possible immunodeficiency manifested with repeated infections, severe normocytic anaemia and in-vitro decreased superoxide production.

The boy was born from an uncomplicated pregnancy (3rd, previously one spontaneous and one planned abortion), the only remarkable information from the perinatal period is that he had purulent secretion from the umbilicus with negative cultivation and fast spontaneous resolution. He was vaccinated with BCG (obligatory in the Czech Republic), he received no other vaccines. His family history is unremarkable.

In the first month he suffered from sepsis, pyelonephritis and aseptic meningitis, one month later lymphadenopathy in his left armpit was revealed. There was repeated spontaneous purulent secretion from the affected lymph node (no infective organism found). Calcification in the spleen was detected. Antituberculotic (anti-TB) treatment was initiated and continued until he was 1 year of age; the lymphadenopathy and local reaction after vaccination resolved

and he has been without any clinical problems related to possible mycobacterial infection since.

During the first year of life persistent severe normocytic anaemia was present. He required repeated transfusions (once or twice a month). Repeated investigations of bone marrow (morphological, flow cytometry) did not reveal any malignancy or gross abnormality. He was treated with corticosteroids and erythropoetin to improve his erythrocyte count, with transient effect; further transfusions were needed once this therapy was discontinued. His clinical symptoms have not vanished completely, and he has been suffering from repeated febrile attacks, due to intermittent infections; at the age of 11 months he had severe bilateral pneumonia.

Apart from the recurrent anemia the laboratory tests have shown persistent leukopenia, intermittent neutropenia, normal proportions of lymphocyte subpopulations and mild hypogammaglobulinaemia (IgG 2,4-4.1g/l, IgM 0.25-0.32 g/l). Decreased NBT test was confirmed in repeated investigations, the values fluctuated between 3 and 8 (our reference range is above 9), as well as chemiluminiscence (196-310 cpm; control patients 956-1137), cytometric burst test with dihydrorhodamin 123 has not yet been performed. A proliferation test using phytohaemagglutinin (PHA) was normal (SI 191; control 231), however, when purified protein derivative (PPD) was applied, an increased response was noted (SI 50; control 9).

He has been treated with intravenous immunoglobulins, prophylactic treatment consistent with his possible phagocytic deficiency has been established. He has been on continuous corticosteroid treatment with a very good response regarding anaemia.

Currently, at the age of 2 years, the boy´s condition is stable, he has not required transfusion for the last 5 months, he intermitenttly suffers only from mild and infrequent infections. He has, however, a severely cushingoid habitus and mild growth retardation. The cause of his complex disease has not yet been revealed.

Questions

What do you think about the possible diagnosis of this patient? What would you suggest to investigate further?

We would like to ask you to submit a short text on your peculiar patients as well. We hope that the online submission system will be optimized soon, thus the contribution and discussion will be much easier.

Anna ŠEDIVÁ
Aleš JANDA

ESID Summer School in Malaga: working hard on mastering PIDs ...

Young Researchers' Corner

Dear ESIDJunior members,

Here we are at the third appointment with Young Researcher's Corner!

I'm quite unhappy because nobody interacts and participates to improve this novel ESID Newsletter section so far. During the 6th Prague Spring ESID Meeting in May some of the ESIDjuniors members had the possibility to meet and interact with each other: what we really appreciated was the great occasion to learn from the others!! I would like to invite all of the ESIDJuniors as well as non-Juniors to suggest an interesting lab protocol to be posted here and/or discuss about the previous or current themes: I think that this section should be developed with an active participation from all of you!

This time we're going to talk about:

CD4+CD25+FOXP3+ regulatory T cells isolation: immunodensity vs beads vs FACS sorting.

CD4+CD25+ regulatory T cells (Tregs) are considered to play a key role as suppressors of immune mediated reactions. The analysis of Treg function in patients with autoimmune, allergic or oncogenic diseases has emerged over the past years.

Ex-vivo identification of Tregs is difficult as Treg associated surface markers, e.g. the cytotoxic T lymphocyte-associated antigen-4 (CTLA-4), glucocorticoid-induced TNF receptor family related gene (GITR) and even IL2Rα (CD25) are also induced upon activation of conventional non-regulatory T cells. Recently, a transcription factor of the forkhead/winged-helix family, FoxP3, has been identified as a master control gene in the development and function of Tregs. The isolation of viable Tregs based on FOXP3 expression is technically restricted due to its intracellular localization. In the recent explosion of research reports on human CD4+CD25+ cells, although the basic functional characteristics demonstrated for these cells appear to be consistent, contradictory results have been found. One potential explanation for differences in human Treg functions may rest on the extreme variability of the culture conditions and TCR stimuli that have been used to test the functional properties of these cells in vitro. Another explanation for this variability may reside in the fact that markedly different techniques are used to isolate human CD4+CD25+ Treg cells and thus may result in the comparison of Treg populations that differ in cellular composition and/or activation state.

TREGs PURIFICATION PROTOCOLS

IMMUNODENSITY/IMMUNOMAGNETIC COMBINED SEPARATION METHOD:

Human blood mononuclear cells (PBMCs) are isolated by Ficoll density gradient centrifugation. Briefly, CD4+ T cell are indirectly isolated from whole blood by means of rosetting of unwanted haematopoietic cells (CD8, CD16, CD19, CD36 or CD56+ cells; RosetteSep™ CD4+ T cell Enrichment, StemCell Technologies, France) prior to Ficoll centrifugation. Purified CD4+ T cells are subsequently separated into a CD25+ and CD25–(CD4+) Tcell population by means of an anti-CD25 immunomagnetic beads (EasySep™ human CD25+ Selection, StemCell Technologies, France).

IMMUNOMAGNETIC PURIFICATION METHOD:

The CD4+CD25+ Regulatory T Cell Isolation Kit (Myltenyi Biotec, Germany) is developed for the isolation of CD4+CD25+ cells from PBMCs. The kit contains a cocktail of biotinylated antibodies and Anti-Biotin MicroBeads for depletion of non-CD4+ T cells from PBMCs, and CD25 MicroBeads for subsequent positive selection of the CD4+CD25+ cells. This

protocol requires MACS® Cell Separation Columns placed in a strong permanent magnet. The MACS Column matrix provides a magnetic field strong enough to retain cells labeled with minimal amounts of MACS microbeads.

FACS SORTING METHOD:

CD4+CD25+ T cells are isolated directly from PBMCs according to their CD25 high expression by means of high speed FACS-sorting (FACSaria™, BD, Belgium). The PBMCs are stained with monoclonal antibodies antiCD4PerCP, antiCD25PE, and a cocktail of FITC labeled, monocyte discriminating antibodies, antiCD14, antiCD32, and antiCD116 (all purchased from BD Pharmingen). The analysis and sort gates are restricted to the small lymphocyte gate as determined by their characteristic forward and side scatter properties.

What do you think about it?

Are the bead-isolated and the FACS-isolated CD4+CD25+ populations similar in their abilities to exhibit functional features of regulatory cells, or bead-isolated CD4+CD25+ cells are only anergic while FACS-isolated CD4+CD25high cells are both anergic and suppressive?!

Careful isolation of T-cell subsets with FACS sorting by defined surface protein expression profiles has enabled to purify and identify highly pure cell populations that consistently exhibit strong regulatory activity?!

Which other marker could be used instead of the intranuclear FOXP3 to individuate and separate Tregs subpopulation? May be CD127 a negative surface marker to isolate CD4+CD25+CD127- as pure Tregs?!

I would really appreciate your suggestions, questions and any kind of comments in the ESID FORUM on the ESID website or by e-mail. PLEASE don't hesitate to take advantage of this great opportunity!!!!

Lucia BIANCHI

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University of Florence
Dept of Pediatrics
"Anna Meyer"
Children's Hospital

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Elkord E, Hopcraft L, Burt D and Stern PL. Bead-isolated human CD4+CD25+ T regulatory cells are anergic and significantly suppress proliferation of CD4+CD25- T responder cells. Clinical Immunol. 120(2):232-3, 2006.

Baecher-Allan C. Human CD25high Tregs: Isolation by beads versus by FACS sorting. Clin Immunol. 120(2):234-5, 2006.

Baecher-Allan C, Wolf E and Hafler DA. Functional analysis of highly defined, FACS-isolated populations of human regulatory CD4+CD25+ T cells. Clinical Immunol. 115:10–18, 2005.

PID-care in development:

My name is Mukesh M Desai. I obtained an MD in Pediatrics, DCH. I am 47 years of age. I attented the Fatima Devi English Medium High School, and obtained an SSC from Poona University, an MBBS & MD from Bombay University, and a DCH (Diploma In Child Health) from the College of Physicians & Surgeons in India. My wife is Dr Durriya Desai, we have one daughter, Kashish Desai; she is 6 years old. I provide free Honorary services at Bai Jerbai Wadia Children Hospital.

During my undergraduate days I was inclined to become a surgeon and secured the highest marks in Surgery for which I was awarded the Dr A venkat Rao & Dr R L Prize in Surgery.

For inexplicable reason during the selection of the Post Graduate course I enrolled for Pediatrics which I never regretted. Call it Destiny.

After completing my MD in Pediatrics I wanted to subspecialise in Hematology and as at that time no degree (DM) course in Hematology was available in India, I became a Lecturer in Hematology at B Y L Nair Hospital Mumbai with Dr A J Desai. After 4 years, in which I was exposed to both adult & Pediatric Hematology I started Private at Sir H N Hospital a major private institute in Mumbai.

In 1994, I got an opportunity to work with Dr Zinet Currimbhoy at Bai Jerbai Wadia Hospital for Children Mumbai one of the most prominent ONLY Pediatric Institute in Mumbai and Western India. It was here that I got the opportunity to learn more about Pediatric Hematology and rediscover my roots as a Paediatrician and Pediatric Hematologist. Dr Zinet Currimbhoy pioneered the development of first paediatric Hematology Oncology Centre in India. But for her I would not have got back in to paediatric Hematology.

Over the years Dr Currimbhoy & myself realised a need to develop expertise for Primary Immunodeficiency as we were seeing increasing referrals for PID. Thus we went to Great Ormond Street Hospital London to Observe with Dr Paul Veys, Bobby Gaspar and all the others for a month and then to Hopital Enfant Malades Necker Paris with Dr Alain Fischer to learn about their primary Immunodeficiency services and learn more about their approach to a child with Primary Immunodeficiency.

Thanks to these initiatives at B J Wadia Hospital for Children we have started a Division of Immunology with in the Department of Pediatric Hematology Oncology & Immunology to exclusively cater to needs of children with PID.

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

The Health care in India is like India itself: a study in extreme contrast but there is a great sense of Optimism and Hope.

The Facilities range from the very best to plain average to outright nonexistent.

The Health care is provided by Government, Municipal Corporation of greater Mumbai, Private practitioners and Large Trust based Charitable Institute as well as Trust and Corporate based Private Hospitals and Institutions.

Our centre B J Wadia Hospital for Children is a trust based charitable institute which caters a socioeconomically deprived population and is doing a commendable job with

more than 70,000 to 80,000 patient visits per year.

In Mumbai the facilities in Private Hospitals & corporate Hospitals can match those in any developed countries in the world; predictably in great contrast facilities are basic when it comes to rural parts of India.

The government provides basic care with Primary Health centres, Community Health workers, national programmes also run through these units. The priority in rural set up is maternal child health, vaccination, Malaria control, Diarrhoea control and also there are dedicated programme to promote breast feeding.

Certainly there is a great gap if we compare rural areas with Cities in India. But this is changing very fast. Students who enrol in Medical programme are made to sign bonds and have to work in rural areas for at least 2 years after graduation.

Health care is expensive in private and majority of people who utilise these services are affluent or have medical Insurance. The government and Municipal corporation hospitals charges nominal fees for services provided which the state subsidises.

The level of care is good and appropriate.

Poor Children's health needs are catered by government, municipal corporations and trust based charitable institutes like ours. The more affluent and affording one have access to five star corporate and private trust based hospital.

It is said that health care industry in India is going to see a sea change as there are more than 100 corporate hospitals already in the offing in India.

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

PID care in India is very inadequate. There are only two places where there is a semblance of organisation for PID care.

One is our centre at B J Wadia Hospital for Children Mumbai which has just made a beginning and the other one is with Dr Surjit Singh at PGI Chandigarh.

Currently children with PID are treated by primary care paediatrician or Hematologist who may get involved in the case.

We have a lot to organise and catch up on!

IvGG substitution is a major problem due to cost and need for life long infusion. We have international as well as local brands available. The Local brand are cheaper than international brands. We have only 3 patients on regular IVGG infusions;

We have not tried SC Gamma globulin for any of our patients.

Treatment of Infections is possible as most drugs are available. The major limitations remain the cost.

Stem Cell Transplantation is available in India and the results are improving; these facilities are available in Major Metros like Mumbai, Delhi & Chennai and other cities like CMC Vellore Pune in India, There are more than 10 active transplantation centres but none of them is dedicated to Transplantation for PID. There are cases of CGD, LAD and CVID being transplanted in India but these are anecdotal examples of transplantation for PID.

Peculiarly there is mushrooming of cord blood banks in India with corporate sector getting involved in Life sciences. While Donor marrow registries are not yet developed at a National Level. TATA Memorial Centre, where transplantations are done for Hematopoietic malignancies, is next door to our institute & we have been trying to get them involved for transplantation of our babies with PID. We need trained personnel who have experience of BMT in PID as our next priority.

At the moment we are concentrating on developing Diagnostic facilities for PID at our centre. We are fortunate to have next door to us Institute of Immuno- hematology an ICMR (Indian Council of Medical Research) based organisation which will establish the investigations necessary for diagnosis of PID

cases. The director of IIH Dr K Ghosh has been very receptive to our suggestions and had sent Dr Manisha Madkaikar for training at GOSH London with Dr Bobby Gaspar. She has now joined us and we hope to establish tests necessary for diagnosis of all PID.

As mentioned before TATA Memorial Centre is next door to us & we are trying to convince & persuade them for doing BMT for our babies with PID. We are already in the process of doing that. As we are all in close proximity and there is a desire to work together this would be the fastest way of getting started with available resources.

TATA Hospital also has a very good Immunology department however their focus is largely Cancer Immunology and not PID.

Ultimately we need to develop transplantation at B J Wadia Hospital for Children as we get better organised.

We will gradually build up on this. It has been a long struggle and it has taken us more than 7 years just to get a semblance of an organised structure. Dr Zinet Currimbhoy has donated a sum of 50,000/- dollars for Immunology department and our chairman Mr Nusli Wadia has promised to match with an amount equivalent to the yearly interest generated from the donation. The donation has been called "Currimbhoy project" and an immunology fellow will be appointed from the interest funds and the appointed immunology fellow will be designated a "Currimbhoy Scholar".

We are in the process of making Immunology Division a separate division from Hematology Oncology and hope that it fructifies rapidly & we can stand all by ourselves.

PID is certainly not a priority area in India and thus the struggle for funds is perpetual. Below is a diagram of how we are organising our services with optimum utilisation of available resources.

It seems to be a long struggle for us but it is a worthwhile struggle as learning immunology will help improve over all the field of medicine in India. It is a beginning.

How did you become interested in immunodeficiencies?

I got interested in PID because of my teacher Dr Zinet Currimbhoy but it took me a while to get activated. Reading immunology has helped my hematology and I can feel the difference in my approach to a patient today. I feel that Immunology has made life very fascinating and medicine very exciting.
I cannot survive as an Immunologist in India but the desire to establish the speciality of Immunology in India is very overwhelming.

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

My Role in PID care has been to set up Immunology Division along with Dr Currimbhoy at B J Wadia Hospital for Children and to try & get on board this trilateral arrangement with the institutions I mentioned.

I am also very active in promoting PID through various talks, seminars and clinical meetings.

I have also initiated a web based group for PID in India where problem patients can be discussed and queries asked. In the beginning we have placed Normal serum Immunoglobulin levels for Indian Children for everybody to access. We have also placed information for practicing paediatrician about when to suspect immunodeficiency, where to refer in India, Role of practicing paediatrician in PID and more.

I have planned an immunology lecture series every 6 mthly for post graduate students.

We also have plans to publish a small booklet for primary immunodeficiency in India for distribution to all Paediatricians.

Presently we are working out normal immunological parameters in Indian children at different age group as our environment is

different from west.

We also have initiated to know the prevalence and incidence of EBV, parvovirus & CMV in India.

What do you hope to achieve in the future?

I am a successful Hematologist & Oncologist in Mumbai.

My personal career goal is to set up the subspeciality of Immunology in India.

Also as I missed out on formal training in subspeciality we wish to develop a structured programme for post graduate training and establish a degree course in immunology in India.

As a priority set up all possible investigative facilities at our centre in India and share this expertise to develop similar multiple centres.

Also we need to improve our care of PID and bring it to international grade.

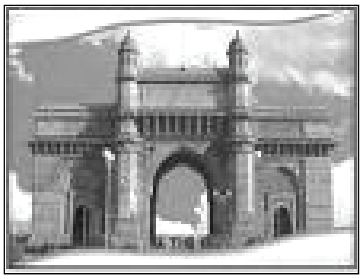
We need to initiate projects to identify & solve our problems.

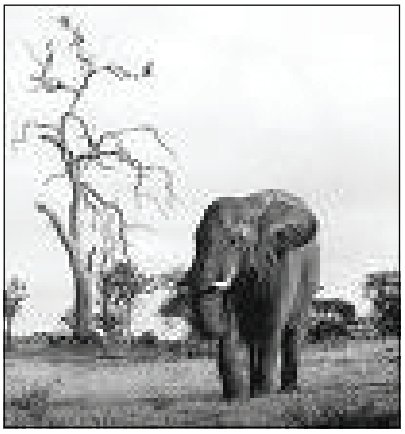
Most paediatricians ask us Okay you made a diagnosis of PID "NOW WHAT?" We have to show success by curing these babies with BMT. Seeing success at GOSH London & at Necker Paris was very important for us as that gave us the impetus to pursue our goals.

We need to show success to our paediatric colleagues for us to achieve our objective.

How could ESID help to achieve this goal?

ESID can help us in many ways! The most important way by which ESID can help is in sharing knowledge. We can initiate collaborative work though we are not ready yet. ESID can help us resolve our initial dilemmas and queries which may sound silly to the initiated one but are unresolved issues in our mind. We have often too many queries and we need answers some times to even basic issues.





India