ESID Newsletter

Contents

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

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

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

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

Front page: autumn colors on a wet day.

Dear ESID members,

I'm looking back at a very successful meeting of ESID, INGID, and IPOPI in 's-Hertogenbosch in October. I thank all participants for coming in such great numbers, all speakers and chair(wo)men for their contributions, and all those people who helped me organise the meeting.

Well over a thousand participants! That makes us wonder what to expect in 2010 in Istanbul. I wish Necil Kutukculer good luck in organising that meeting. I know now how much work it is … We are also looking forward already to the 2012 meeting, for which we – together with INGID and IPOPI – voted for Florence. Of course good luck to Eleonora Gambineri too, and congratulations as well.

But ESID does much more than organise biennial meetings, as you can see when you read the following pages!

Senior members, don't forget to tell your juniors about the upcoming ESID Summer School, and junior members, block the data in your agenda, and remember to apply in time for participation in that event.

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. The aims of this society are, among others, to facilitate the exchange of ideas and information among physicians, scientists and other investigators who are concerned with immunodeficiencies and to promote the research on these diseases. Anyone who is interested in primary immunodeficiency diseases can become a member of ESID. Registration is possible online at www.esid.org/members.php.

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

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

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

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

= ESID Information =

President's letter

Dear ESID members,

We have had a wonderful 2008 meeting in the Netherlands. Our society is more lively than ever and the field of primary immunodeficiency is blossoming! I would like to thank the Dutch organizers as well as the ESID board members, who together prepared a terrific scientific program. I know that many of you faced a number of logistic problems, whether related to the travel, accomodation, or venue. Despite these difficulties, the meeting turned out to be a great success. I am confident that the 2010 meeting in Istambul, organized by our friend and colleague Necil Kutukculer, will be an even greater success.

All best wishes,

Jean-Laurent CASANOVA

Secretary's report

Dear ESID members,

ESID is growing rapidly, both in size of its membership, size of its biannual congresses and also in its scientific impact. ESID is seen as the world's leading organization to foster research, management and awareness for primary immunodeficiency disorders. This change happened during the last years, and ESID had to take several measures to account for this development.

First ESID needed to become an officially registered organization with a proper legal act. This has been facilitated by the great work of Esther de Vries in 2007 and 2008. We are now registered as a charitable society under the legal governance of The Netherlands. In addition, ESID had been registered in the Dutch chamber of commerce since 1994. Please find the legal act attached to this report.

Next we had to improve our website appearance which was done by me and the help of a company called Piccobello, who designed an up-to-date content management system for ESID. Since, ESID is getting regular funding from pharmaceutical companies sponsoring our website.

The new website now also allows us to perform electronic voting, to achieve anonymous voting, vote more frequently on all sorts of question concerning the society, making ESID much more democratic, and including ESID members into the voting process who are not ale to attend the general assembly.

To account for al these changes, ESID also needed a new constitution, which was finally passed at the general assembly at 's-Hertogenbosch after initial discussions in Budapest followed by intense discussions on the ESID board and two rounds of polls over the internet. Please find the new ESID constitution attached to this report.

The next step was to contract a primary congress organizer (PCO). Our congresses are now so large and important to the field that we unfortunately can no longer accept that always during the first day, there is not enough food, as it happened in Budapest and in 's-Hertogenbosch. Other organisational issues which were obvious during our last meeting can best be addressed by having a permanent congress organizer who very well knows our needs year by year and with whom w do not need to start from scratch when organizing our biannual congresses. Following a tender, we have invited two PCOs (CPO Hanser which we knew from the ESID Weimar meeting, and Kenes who organized the Geneva ESID meeting) to present to the GA in Holland. Following these presentations and the face-to-face discussions with the company's representatives the ESID board has

decided to start contract negotiations with Kenes, which are still ongoing.

We also decided at the GA in s'Hertogenbosch that we would like to invite INGID and IPOPI to be involved in the selection of the venue for the upcoming ESID/INGID/IPOPI meeting in 2012.
We have received 3 applications to host the ESID Biennial Meeting 2012. The candidates presented the possible venues and cities during the General Assembly on October, 17th.
The two cities which received the most votes in the first ballot were London (104) and Florence (92), whereas Prague received 53 votes. The second ballot between Florence and London resulted in a narrow margin for Florence (160 vs. 144 votes).
Thus the 2012 ESID Biennial Meeting will be in Florence!
These are the detailed results of the first and second ballot.

First ballot:

Organisation	Total votes	London	Florence	Prague
ESID	135	35	60	40
IPOPI	93	65	16	12
INGID	21	4	16	1
Total result	**249**	**104**	**92**	**53**

Second (and final) ballot:

Organisation	Total votes	London	Florence
ESID	156	56	100
IPOPI	118	78	40
INGID	30	10	20
Total result	**304**	**144**	**160**

So 2012, we will meet in Florence. Congratulations to Eleonora Gambineri who put together this bid, and I sincerely hope that Prague and London will reapply for our 2014 congress.

I have realized that not all nominees for ESID posts have received >90% of your votes, but I myself have had only one Email complaint who stated that he/she was not happy that I have implemented the electronic voting and that he/she would like to go back to 'hand rising' at the GA. This wish was in stark contrast to all I have heard during the last months, so I think we will stick to the electronic voting. However, if many of our members feel the same, I will only learn this if you tell me! So please, if you have any concerns of how the ESID board runs your society, please Email to: b.grimbacher@ucl.ac.uk. I will take your concerns seriously.

Bodo GRIMBACHER

Minutes of the General assembly
17.10.2008; Start 14:45; End 16:45.

1. Approval of minutes
Approval of minutes of the last GA in Budapest 2006 as published in the ESID newsletter. No questions were asked. minutes were approved by acclamation.

2. Presidential report
JL points out that there have been three very important improvements during the last 2 years: Firstly that ESID now is registered as a legal entity; secondly that he is very happy about the outcome of the new constitution with ESID being a Society with its roots in Europe but open to the world;
and thirdly that he appreciates the possibility of electronic voting.

3. Report of the Treasurer
Some questions on the future financing of the ESID registry WP were answered and some were deferred to the registry WP report. JL Casanova thanks Esther de Vries for her outstanding work and asks the GA to release Esther from her duties serving as the ESID treasurer for the last eight years. She is released by the GA by acclamation.

4. Report of the Working Parties

see respective sections of the ESID website.
In brief Andrew Cant reported of a successful Summer School in Malaga in 2007 with 60 applicants but only 30 could be accommodated.
Bobby Gaspar reported of the activities of the clinical WP and announces that the next survey will be on the long term outcome of XLP.
Eleonora GAmbineri reported the achievements of the WP over the past 2 years: 1) Improvement of the network: a) implementation of the ESID*juniors* section on ESID website, with new topics and links. b) ESID Spring School in Prague as platform for ESID*juniors* to follow up learning progress and to create interactions 2) Take active part in ESID activities: a) some junior members involved in the editorial board of the ESID Newsletter, b) ESID junior representative as part of the faculty of the ESID Summer School in 2007 c) First ESID*juniors* Corner within the 2008 ESID meeting 3) Develop exchange programs: a) 1000 Euro Scholarship for Short term programs (2-4 weeks to learn diagnostic/therapeutic procedures or lab techniques in other countries) awarded to 2 juniors this year b) Travel grants to attend the 2008 ESID Spring School in Prague, the 2008 CIS/FOCIS meeting in Boston and the 2008 ESID meeting.
Gerhard Kindle gave a presentation on the novel reporting features of the ESID registry and that the numbers tripled since 2006, i.e. there are now more than 7250 PID patients registered. Registration, however varies considerably in countries.
Laszlo Marodi gave a presentation of the enormous recent success of his WP with PID meetings all-over Eastern and Central Europe and now also selected cities in Western Europe. There are even more to come in 2008 and a list of meetings planned for 2009 (see attachement).
Naomi Taylor pointed out that recent questions which were addressed were the question of reversions in PID genes, esp in WAS.

5. Report of the Secretary and The new ESID constitution
Bodo Grimbacher asks if there are any comments on the new ESID constitution. The new constitution is ratified by the GA by acclamation.
Bodo explains the difficulties to collect ESID membership fees separate to the ESID congress. Bodo asks the GA to approve that the ESID membership fees 2010/2012 can be collected with the registration of the upcoming ESID meetings. ESID members who cannot come to the biennial meeting can still pay via the ESID website.
Necil Kutukculer accepts to collect the membership fees in 2010 with the registration to the meeting.
A few questions were answered and the GA approves the request with 3 no and 12 abstains.
Bodo also reports to the GA that IPOPI and INGID would be very pleased if they also had a vote in deciding for the upcoming venues for the combined meetings starting 2012. It was clarified that for the upcoming votes, each member shall have one vote. In the end votes will be simply added. The GA approved this request with 0 no and 4 abstains.

6. Presentations of Primary Congress Organizations
Mr. Dan Rivlin form Kenes international, an Israelian company based in Geneva, delivered his presentation and an evaluation of the current three proposed venues for 2012.
He was asked how much Kenes will charge for their services: Association management will be 15.000 per yr. Kenes will get 10% of the ESID congress turnaround, reimbursement of their cost, and an additional profit share if any future congress makes more than 150.000 EUR profit.
Mrs Hanser from CPO Hanser, a German company delivered her presentation. Due to

the limitation of time no questions could be asked.

7. Results of Board elections
President JL Casanova; President elect Amos Etzioni; Secretary Bodo Grimbacher; Treasurer Eleonora Gambineri; Registry WP Gerhard Kindle; Education WP Andrew Cant; Clinical WP Klaus Warnatz; SCT-BMT WP Bobby Gaspar; PID care in development WP Laszlo Marodi; Genetics WP Naomi Taylor; ESIDjuniors Crina Samarigetean.

Candidate	Yes	No	Abstain	total valid votes
László (143)	106	13	24	143
Andrew (142)	127	4	11	142
Naomi (134)	104	7	23	134
Gerhard (135)	110	7	18	135
Bodo (141)	116	13	12	141
Jean-Laurent (138)	101	26	11	138
Crina (136)	114	8	14	136
Bobby (143)	134	5	4	143
Klaus (139)	121	4	14	139
Eleonora (142)	128	4	10	142
Amos (142)	111	15	16	142

Additional members:
Esther deVries (past meeting president); Necil Kutukculer (current meeting president)

8. Varia
Election of two auditors:
Esther de Vries and Anna-Rosa Soresina were elected by acclamation. In the interest of time, any other concerns should be addressed to b.grimbacher@ucl.ac.uk.

ESID Constitution

(approved 2008-10-17 by ESID General Assembly)

ESID Constitution

The forerunner of the European Society for Immunodeficiencies, (hereafter referred to as ESID), was established in September 1983 in Rome, Italy, as an informal group (EGID) interested in sharing experience and developing co-operative studies in the field of immunodeficiency diseases. In the 1990's the number of co-operative teams has risen substantially and this expansion has been commensurate with a growth in the complexity of the organisation, necessitating a clearer definition of its purpose and activities. At the Biennial Meeting in Sitges in 1994 the first constitution of ESID was approved. In 2000 the constitution was revised in Geneva in order to better reflect the evolution of this organisation. In 2008 the Constitution was adapted when official Articles were made up by drawing up a Dutch notarial deed.

§1

THE EXECUTIVE BOARD

The Board consists of the President, the Secretary, the Treasurer, the chairpersons of all Working Parties. Each term of office is 2 years for the President, Secretary and chairpersons of all Working Parties, renewable at the next Biennial meeting, but limited to 2 terms (4 years) only. The Treasurer can serve 4 terms (8 years). The President-Elect is elected at the General Assembly two years prior to office, the President of a Biennial Meeting is elected at the General Assembly during the Biennial Meeting four years before the Biennial Meeting he/she will organise. The Past-President is part of the Board for two years after his/her presidency, the President-Elect for two years before his/her presidency, the president of the Biennial Meeting from the two years

before to the two years after the Biennial meeting that he/she is organising.

Decisions are taken by a majority vote. The President has the deciding vote, if the vote is otherwise tied. The Board should meet at least once a year.

ESID Board members must be full members of ESID. They may be citizens from any country, but need to work in Europe for the time of his/her service.

All ESID Board members shall declare any financial or other possible conflict of interest to the ESID board in writing.

§2

THE GENERAL ASSEMBLY

The General Assembly is open to all members of ESID and to the President and the Board of the International Patient Organization for Primary Immunodeficiencies (IPOPI) and the International Nursing Group for Immunodeficiencies (INGID). It normally takes place at the time of the Biennial ESID Meeting. It is chaired by the President and includes the Presidential report, the Secretary´s report, the Treasurer´s report and any other business. The agenda for the meeting is made available over the internet, mailed, and/or published in the ESID Newsletter at least one month in advance.

All ESID officers will be elected by electronic voting on the protected part of the ESID website. Votes may only be casted by electronic voting. The poll will open one month prior to the General Assembly and will close at the day preceeding the day of the General Assembly at 12:00 noon (Central European Time). To facititate this, at least three months prior to the poll, the Board will encourage ESID members to consider their candidature for available posts. This is primarily the responsibility of the Secretary. At least one month prior to the meeting, available candidates will present themselves to the ESID members in the ESID Newsletter and/or on the ESID website.

Either during the General Assembly or by electronic voting the ESID full members also have the following obligations: To elect the president and the location of the Biennial Meeting; To decide on the biennial fee for membership of ESID as proposed by the Board; To either agree or disagree with policy decisions as proposed by the Board; To make proposals as to starting/discontinuing activities of the Society; To decide about amendments to the Articles, the Constitution and dissolution of the Society (see also §13).

§3

ESID MEMBERS

ESID members may be citizens of any country, working anywhere in the world, however, they shall be MDs, PhDs (biology), Veterinarians, Pharmacists, Dentists, or graduate students in any of these fields, or PhDs of other fields and corresponding graduate students. ESID full and associate members can participate in co-operative ESID and ESID related EU/Biomedicine studies; they can enter reports on immunodeficiency diseases and patients into the ESID registries; they are entitled to a password to enable them to enter the restricted part of the ESID website. All members are entitled to receive ESID Newsletters and regular information about meetings, co-operative studies and results of ESID research projects, ESID summer schools etc.;

The ESID Board has the right to expel an ESID member (e.g. due to malpractice in science) by a two-thirds majority vote.

§4

WORKING PARTIES

The Board takes the initiative to establish and close Working Parties. Each Working Party is headed by a chairperson who becomes a member of the Board. Seven Working Parties (Clinical, Genetics, Registries, SC Transplantation&Gene Therapy, Juniors, Education and PID care in development) are presently operating within ESID, but more can be established if and when required. The Chairperson of each Working Party is elected by electronic voting by all ESID full members every two years and may stand for one re-election. The Chairpersons of the Working Parties must be full members of ESID. They may be citizens from any country, but need to work in Europe for time of his/her service. The substructure of the Working Party is determined by the Chairperson. The Working Party Chairpersons give an annual report to the Board on Working Party activities and publications and a biennial report to the General Assembly. The Chairpersons of the Working Parties shall declare any financial or other possible conflict of interest to the ESID board in writing.

§5

DEFINITION OF EUROPE

For the ESID Europe shall be defined as: all countries of the European Union plus Iceland, Norway, Switzerland, Serbia, Bosnia, Montenegro, Croatia, Albania, Macedonia, Andorra, Monaco, Lichtenstein, Ukraine, Belarus, Russia, Moldavia, Turkey, and Israel.

§6

THE PRESIDENT

The President shall be a full member of ESID of at least two years standing. He/she may be a citizen from any country, but needs to work in Europe for time of his/her service. He/she is elected by electronic voting by all ESID full members, and serves for two years. The President may stand for one re-election. He/she may thus serve for a maximum period of 4 years. The President serves as President-Elect for two years before becoming President. The President promotes the activities of ESID. These include fund raising, co-ordination of Working Party activities, giving guidelines to the organisers of the Biennial Meeting, and in negotiations with other organisations.

§7

THE SECRETARY

The secretary is elected for two years. He/she must be a full member of ESID. He/she may be a citizen from any country, but needs to work in Europe for time of his/her service. He/she may stand for one re-election. The secretary writes the annual business plan with the executive officers, organises board meetings, agendas, keeps and circulates the minutes, chases up the reports for the General Assembly meetings, writes the agenda and minutes and circulates these to the members through the ESID Newsletter and ESID website.

§8

THE TREASURER

The Treasurer is elected for a period of two years which is renewable three times. He/she must be a full member of ESID. He/she may be a citizen from any country, but needs to work in Europe for time of his/her service. He/she may thus serve for a maximum period of 8 years. He/she collects the two-yearly membership fee and accounts for the use of the funds for ESID purposes. He/she is also responsible for fundraising and maintaining the finances to support the infrastructure of ESID.

§9

INFORMAL NETWORKS

ESID encourages the formation of informal national networks among its members to locally promote the aims of ESID. The chairman/ co-ordinator of such a network (presumably elected for a limited time period) would have an advisory function to the Board. They will promote the interaction between ESID and National Immunology and Clinical Immunology Societies or Groups.

§10

MEMBERSHIP FEE

Each member pays a two-yearly membership fee to ESID which is fixed by electronic voting of all ESID full members during the month preceeding the General Assembly after proposal by the Board. The fee can be reduced by the Board in particular circumstances on request. In addition, the Board has the discretionary power to identify exceptional circumstances and modify the fee for some countries. Members under 35years of age pay a reduced membership fee (50% of the full fee).

§11

BIENNIAL MEETING

Meetings of ESID take place once every two years. The President and the location of the Biennial Meeting is decided by electronic voting of all ESID full members during the month preceeding the General Assembly upon proposal by the Board or members. The local host must be a full member of ESID. The ESID meeting is organized by a local steering committee in close collaboration with a congress organizing company. The scientific content of the meeting is proposed by a scientific committee. This scientific committee is suggested by the congress president but approved by the ESID board. The ESID board needs to approve the scientific content of the meeting. In case of a dispute, the ESID board will have the final say.

§12

USE OF ESID FUNDS

ESID funds consist of subscription fees and of funds raised from public organisations, charities and pharmaceutical companies.

ESID funds can be used for the following purposes:

1. Funding studies on co-operative European data of immunodeficiency diseases.
2. Funding activities of the Working Parties, e.g. reasonable travel expenses to Working Party meetings taking place outside the Biennial Meeting.
3. Funding the dissemination of information by the Secretary to members of the Group.
4. Funding of other administrative costs considered necessary by the Board.
5. Maintaining the ESID online Registry.
6. Maintaining the ESID website.
7. Organising the biennial ESID Summer Schools, and biennial ESID Educational Days.
8. Publication of the ESID Newsletter and Supplements.

§13

CHANGING THE CONSTITUTION

Amendments to and changes of the Constitution are made by electronic voting by all ESID full members with a two-thirds majority vote. Notice of the intention to change the Constitution shall be made available to all members at least 4 weeks before the relevant business meeting of the General Assembly.

News & Views

"BCG infection in SCID patients Interest Group: Post-vaccinal BCG infection in SCID patients/ International survey diagnosis and treatment policies"

Dear Colleagues,

Even though BCG vaccination is strongly discouraged in most PID patients, almost 5-out-of-6 newborns worldwide are still BCG-vaccinated shortly after birth* (*data based on worldwide SCID incidence, WHO immunization coverage with BCG at birth, and WHO worldwide fertility rates). This preventable complication is the usual picture most immunologists working away from North America, Western Europe and Australia have to face at SCID diagnosis. On the other hand, the lack of information and standardization regarding Diagnosis, Treatment, Risk factors, and Outcome of this preventable complication makes the management of these patients more difficult.

The aim of this questionnaire is to gather all the available information and experience regarding post-vaccinal Bacille Calmette-Guérin (BCG) infection in SCID patients.

Please, download the questionnaire from:http://www.garrahan.gov.ar/docs/SCID%20BCG%20survey%20Sept%202008.xls and send your responses to: bcg.scid@yahoo.com. If you have any doubts or comments, please do not hesitate to contact us. Thanks a lot for your cooperation!

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J Project Meetings in 2008 (No. 23 to 27)

- Ukraine (Odessa); Lyudmila Chernyshova; Apr 12-13; chernyshova@ukr.net.
- Bulgaria (Sunny Beach); Elissaveta Naumova; May 22-23; immun@sun.medun.acad.bg. Guergana Stoyanova; gal_ps@yahoo.co.uk.
- Bosnia-Herzegovina (Sarajevo); Velma Mulaosmanovic; Oct 10-11. velmamulaosmanovic@hotmail.com
- Republic of Moldova (Chisinau); Lyudmila Cerempei; Oct 31-Nov 1; lcerempei@rambler.ru
- Latvia (Riga); Tatjana Prokofjeva; Nov 27-28; monja@balticom.lv

Early diagnosis and therapy for Primary immunodeficiency diseases. J-project meeting Oct 10-11, 2008, Sarajevo, Bosnia and Herzegovina

On October 10-11, 2008, the J Project Primary Immunodeficiency Diseases (PID) awareness meeting was held in Sarajevo, Bosnia and Herzegovina. The meeting was organised by the recently founded Department of Allergology, Rheumatology and Clinical Immunology of the Children's Hospital, University Clinical Center Sarajevo in collaboration with the East-Central-European Infectious and Paediatric Immunology (ECE-IPI) Center for Training and Research and PID Care in Development Working Party of the European Society for Immunodeficiencies. For the first time, to my best knowledge, we had PID meeting in B&H. The meeting was attended by participants from several countries Slovenia, Switzerland, Hungary, Serbia and Bosnia and Herzegovina.

The J Project Meeting in Sarajevo, was entitled like the previous one held in November 2007 in Ljubljana, Slovenia:

„Early Diagnosis and Treatment of Primary Immunodeficiency Diseases". The keynote speaker was Prof. Dr Reinhard Seger from the University Children's Hospital Zürich, Switzerland who presented an excellent overview of current progress in bone marrow transplantation and gene therapy for PID. Prof. L. Marodi (Hungary) gave interesting overview of J Project achievements and current concepts. In addition, a number of invited and local speakers presented and discussed specific aspects of PID. So, we would like to thank our distinguished invited speakers, including Prof. L. Marodi (Hungary), Dr T.Avčin (Slovenia) and Dr S.Pašić (Serbia). The official language of the J Project Meeting in Sarajevo was English and Bosnian/Croatian/Serbian in order to foster discussions among participants from different countries and local ones.

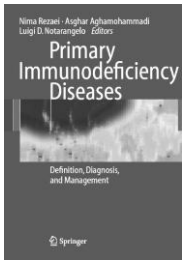
Scientific programme was divided in sessions as follows :1) Early recognition of PID; 2)Assesment of PID, 3) Treatment of PID; 4) PID syndromes I, 5) PID syndromes II. Aims of meeting were to increase public awareness, to increase and broaden knowledge of PID, to establish professional collaboration with other centers, to facilitate early diagnosis and treatment, to incourage establishement of patient suport group and the main aim was to improve patient care. Desired concept of the meeting was completelly fullfiled - collegial discussion in friendly athomsphere about certain and suspected diagnosis of PID patients and best therapy, emphasising Education, Sociability and Interaction for all. Main problems that we in B&H are facing with, were well and easily defined : proffesional education (all levels), underdiagnosed PID patients and laboratory facilities. In particular, the J project Meeting provided an initiative to establish the B&H multidisciplinary team for PID. Moreover, the J project Meeting in Sarajevo provided and excellent opportunity to promote international collaboration in the field of PID among Central and South-Eastern European countries.

The scientific and social program of the meeting was rated as highly sucessful and we would like to thank all participants for their contribution as well as our sponsors ECE-IPI, Alkaloid, Roche, Unifarm, Medis, Pfizer for their support. In addition, we would like to thank Prof. Senka Dinarević, Director of the Children's Hospital Sarajevo, Prof. Laszlo Marodi, Chair of the ECE-IPI Center for Training and Research for their continuous support and help with the organisation of the meeting. Special thanks to Doc Dr Tadej Avčin, Children's Hospital Ljubljana for all his support, for making us scientifically impressed with Primary Immunodeficiency Disease World and for sharing knowledge with us.

There is clear hope and best wishes that patients with PID will have brighter future.

Velma MULAOSMANOVIC

New Text in Primary Immunodeficiency Diseases



Primary Immunodeficiency Diseases: Definition, Diagnosis, and Management. Rezaei, Nima; Aghamohammadi, Asghar; Notarangelo, Luigi D. (Eds.). Springer-Verlag Berlin and Heidelberg GmbH & Co. K. August 2008, XXVIII, 358 p. 55 illus., 41 in color., Softcover. ISBN: 978-3-540-78537-8 http://www.springer.com/978-3-540-78537-8

We are pleased to introduce the new text in primary immunodeficiency diseases (PID), which has recently been published by Springer.

As all ESID members know, more than 150 different forms of PID are now known. Our understanding about PID is rapidly improving, and this may facilitate the accuracy of diagnosis and efficiency of management.

This book is an attempt to gather the most recent advances in this field, and tries to provide a concise and structured review of hitherto known PID. Although the ultimate orientation of the book is toward practical diagnosis and management, the pathophysiology of diseases is also discussed. For this purpose, this book consists of 11 chapters as follow:

- Chapter 1: An introduction on primary immunodeficiency diseases. Nima Rezaei, Francisco A. Bonilla, Kathleen E. Sullivan, Esther de Vries, and Jordan S. Orange
- Chapter 2: Combined T- and B-cell immunodeficiencies. Françoise Le Deist, Despina Moshous, Steven J. Howe, Amit Nahum, Fotini D. Kavadas, Elana Lavine, Chaim M. Roifman, and Alain Fischer
- Chapter 3: Predominantly antibody deficiencies. Asghar Aghamohammadi, Vassilios Lougaris, Alessandro Plebani, Toshio Miyawaki, Anne Durandy, and Lennart Hammarström
- Chapter 4: Phagocytes Defects. Uwe Wintergerst, Sergio D. Rosenzweig, Mario Abinun, Harry L. Malech, Steven M. Holland, and Nima Rezaei
- Chapter 5: Genetic Disorders of Immune Regulation. Carsten Speckmann, Jan Rohr, and Stephan Ehl
- Chapter 6: Defects in innate immunity: receptors and signaling components. Nima Parvaneh, Joachim Roesler, Steven M. Holland, and Tim Niehues
- Chapter 7: Autoinflammatory disorders. Stephan Berg and Anders Fasth
- Chapter 8: Complement deficiencies. Maryam Mahmoudi, Tom Eirik Mollnes, Taco W. Kuijpers, and Dirk Roos
- Chapter 9: Other well-defined immunodeficiencies. Mehdi Yeganeh, Eleonora Gambineri, Kamran Abolmaali, Banafshe Tamizifar, and Teresa Español
- Chapter 10: Syndromic Immunodeficiencies. Jeffrey E. Ming and E. Richard Stiehm
- Chapter 11: Treatment of primary immunodeficiency diseases. Hale Yarmohammadi and Charlotte Cunningham-Rundles

The first chapter gives an overview on PID and presents a classification of these disorders.

In chapters 2-9, definition, etiology, clinical manifestations, diagnosis, and management of each disease are discussed separately. Syndromic immunodeficiencies are briefly presented in chapter 10, whilst some of them are explained in greater detail in other chapters. Although management of the various forms of PID is discussed in chapters 2-9, the global therapeutic approach to common PID represents the focus of discussion in chapter 11.

The book is the result of valuable contributions from more than 40 senior and junior scientists in this field from more than 30 universities worldwide. We would like to acknowledge the expertise of all contributors, for generously giving their time and considerable effort in preparing their respective chapters. We are also grateful to Springer for giving us the opportunity to publish this book.

We hope that this book will be comprehensible, cogent, and manageable for physicians and nurses, who wish to learn more about primary immunodeficiency diseases. Moreover, it is our hope that the book will represent a useful resource for doctors in training as well as for specialists in clinical decision-making and treatment planning.

Nima REZAEI
Asghar AGHAMOHAMMADI
Luigi NOTARANGELO

ESID Junior Educational Grant

I am a Paediatric Immunologist from Russia and am writing to thank ESID for their kind support in giving me the Educational Grant to support my time in Newcastle, for which I am very grateful.

My interest in immunology started in 1997, when I was a third year student at the Russian Medical University in Moscow; I read immunology books, which kindled my interest in primary immunodeficiency.

In 1999, when I was a final year student, I visited the children's immunology department in the Institute of immunology, and took part in a European research project about the randomized use of steroids in treating young children with asthma. In that department I spent my first year of postgraduate education, treating patients with primary immunodeficiency and allergy.

In 2001 I started my training in the Clinical immunology department, at the Russian Clinical Children's Hospital. As a scientist and later as a doctor. During this time I treated patients with a different form of primary immunodeficiency, SLE and JRA. My main interest is in the treatment of patients with SCID. In 2003 I was a Participant of the ESID Summer School in Portugal and I have also attended the ESID spring meeting in Prague. Several times I have attended several Russian immunology conferences. I have published in Russian journals.

At the end of 2007 year I decided my main interest was in BMT for primary immunodeficiency. I would like to continue my work in this field in Russia. To gain wider experience, I sought training at the BMT unit in Newcastle upon Tyne, UK.

From January - July 2008 I had a clinical attachment with Professor Andrew Cant and his clinical team on the Peadiatric immunology and infection disease unit. I had the opportunity to see many unique patients, and manage complex SCID and other primary immunodeficiency patients as well as patients with complex autoimmunity undergoing HSCT, including mismatched HSCT and umbilical cord blood stem cell transplantation. I was involved in selecting appropriate chemotherapy conditioning regimens for PID patients and managing complications post HSCT such as graft versus host disease, pneumonitis, and severe viral re-activation.

I have also gained experience in the pre-transplant management and discharge planning of these patients, and saw them in the follow up clinic. An important part of the training involves a weekly multidisciplinary ward round with BMT physicians, nurses, a gastroenterologist, virologist and microbiologist as well as the social worker. I have also been involved in multidisciplinary training rounds discussing diagnosis and management of these complex patients.

I was able to perform an audit of outcome of ADA-SCID patients post HSCT, and helped in a study analyzing the nutritional requiment of BMT patients.

I was able to attend the inaugral symposium of the Centre for Immunodeficiency in London in May 2008, and learnt about the pathogenesis of Crohn's disease, the genetic causes of the HyperIgE syndrome and HLH. (I also had the opportunity to see some of the beautiful countryside in the North East of England.)

This training was extremely important for me to take back to Russia. I hope to implement some of the things I have learnt, to improve care for these patients in a country with an emerging PID practice. I am so thankful to professor Andrew Cant and his medical team, and other staff in the BMT unit, who taught me, helped me in my training and made me very welcome.

Anna YURASOVA

Working Party reports

Registries Working Party

The ESID Meeting in 's-Hertogenbosch was a good opportunity for us to meet many of the researchers and study nurses participating in the ESID Database project. In addition, we exchanged ideas with representatives from other registries (e.g. Japan, Australia, "Eurofever" registry). We also held a workshop on the opportunities that the ESID Database offers to PID researchers and would like to thank all those who attended for the lively discussion.

The meeting has certainly given the project fresh impetus and we have received loads of emails following the meeting. For example, we received specifications for autoinflammatory syndromes which is a disease field added to PID only recently. We are also currently setting up additional subregistries for primary antibody deficiencies as part of the EURO-PADnet project. Any researcher who is interested in conducting research on cohorts in the ESID Database is welcome to contact us at registry@esid.org

The total number of patients in the ESID Database as of the editorial deadline for this newsletter (November 14th, 2008) is 7'401, which means an increase of almost 1'000 patients since the last newsletter (June 2008: 6'422). Of these, France by far contributes the largest share with 2'804 patients, followed by Turkey with 1'146 and the United Kingdom with 932 patients.

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

Gerhard KINDLE

SCT and GT Working Party

Dear Friends and Colleagues, thank you for supporting my application as Chair of the BMT and GT working party. I am extremely grateful for your support and hope that over the next few years we can continue to increase research and education in the field of transplant and gene therapy for severe immunodeficiencies. I am also Ghair of the Inborn Errors Working Party of EBMT and this now allows the activities of both working parties to be combined, which to many of us in the field makes a lot of sense.

First let me say that I would really encourage you to be as active as possible in the working party. There are many questions that need to be answered and many studies that need to be done and we need enthusiastic individuals to coordinate and run these studies. We have within the ESID BMT community an enormous opportunity to lead and inform the field as indeed we have done so over the last two decades. The collaborative instinct within ESID is very strong and there remains a desire to answer questions on transplant outcome by pooling our data together. Over the years many papers have been published but as our experience and insight into these conditions grows, we come across more questions that need to be answered! So I would really encourage you to come with ideas for future studies and I will see whether we can effectively take these forward.

As a start to this, I will remind you of a study that I talked of previously that originated when I was head of the Clinical WP. We wanted to look at the outcome of XLP including the mode of presentation and outcome after HSCT. This study is ongoing and you can find an electronic version of the questionnaire on the BMT and GT WP section of the ESID website. This rare disease presents in many ways and we have little data on the outcome after transplant. If you have treated a patient, I would urge you to fill in and send us the questionnaire

and all authors will be acknowledged as authors in any eventual publication.

One important event in the working party calendar is the annual Inborn Errors WP meeting which is held in the autumn and is held in a different country each year. This year Fulvio Porta hosted a wonderful meeting in the beautiful town of Sirmione on the shores of Lake Garda. Italian hospitality was at its very best and the meeting wasn't bad either! Amongst other things we revisited the EBMT guidelines on conditioning protocols and we are working on revised protocols which will eventually be made available on both EBMT and ESID websites in the near future.

Finally, I would like to highlight a couple of dates for next year's diary. The annual EBMT meeting will be held in Goteborg Sweden on 29th March to 1st April with the Inborn Errors WP being held on Monday 30th March. We are also finalising arrangements for next year's autumn meeting of the Inborn Errors WP. Sirmione will be a difficult act to follow but Paul Veys and I will be hosting the meeting next year at Clare College Cambridge. This is again a truly beautiful location although on this occasion quintessentially English! I will give you more details in further newsletters.

Bobby GASPAR

PID-care in development WP

The second PID-care in Development WP Meeting (the first was in Bari, Italy, on September 20) was organized by Anna Sediva. The Meeting was part of the XXV. Congress of the Czech Society for Allergy and Clinical Immunology, and the Congress of the Slovakian Immunology Society. The motto of these conferences was "from experiment to clinic". This motto was also reflected in the session on Primary immunodeficicences. The program was open by an invited lecture given by Hermann Wolf, who, together with prof.Martha Eibl, visited from Vienna, Austria. The talks covered wide fields of hypogamma globulinemia. The lectures then continued by a series of presentations by Anna Sediva and Jiri Litzman, who also chaired the session. They covered areas of innate immunity and its deficiences, bringing to the audience news in this expanding field. The session was than concluded with the overview of stem cell transplantation in PIDs in Czech Republic, with the historical overview and report of three cases of BMTs for chronic granulomatous disease last year. And lastly, the report on XLA molecular diagnostics in Czech Republic by Tomas Freiberger concluded the oral presentations. Session was also complemented by poster presentations. Best poster was awarded to the work on the transcription events in hereditary angioedema due to the mutations in C1 inhibitor genes and goes to the PID center in Brno. Overall, this was a very successful event that further fostered the knowledge on PIDs in Czech Republic and Slovakia.

Anna SEDIVA

ESIDjuniors Working Party

Dear all, first of all, I want to thank all of you for your trust and support, for giving me the opportunity to chair the ESID juniors Working Party for the next two years. It is a great honor and such an amazing and unique chance! I also want to congratulate Eleonora Gambinieri for her new position as ESID treasurer and for her great job she has done for ESID junior WP.

Looking back, I can say that we succeed to realize many of our wishes. We have been able to play an active role not only in our party, but also in many ESID activities. We have an improved network, we have a dedicated 'ESID Juniors section' on the ESID website (http://www.esid.org/workingparty.php?party=6), with new topics

and links. Please, have a look on it and used it. And if you have recent fotos from the Educational day please send them to Benjamin Gathman at benjamin.gathmann @uniklinik-freiburg.de.

We developed and participated actively in different exchange programs. We had for the first time a junior representative as part of the faculty of ESID Summer School in 2007 and for the first time we had a dedicated ESID Junior Corner within the 2008 ESID meeting. This was an amazing chance to get to know us better, to learn and interact.

During these years we also have been involved in the editorial board of ESID Newsletter. For example, Ales Janda was promoting clinical discussions among young and experienced physicians, during his 'Interesting cases' corner, Lucia Bianchi presented different laboratory protocols and methods in the field of PIDs. Finally, I was excited to look for the most interesting papers in the field and present them to you. Now, we are looking for more volunteers to join the Editorial Board of the ESID newsletter. It is such a unique way to learn new things and interact. Don't loose it!

It was great to see so many of you in ESID meeting, being so active in the Educational Day, in the poster session and then in the evening at gala dinner. After the ESID meeting we have been busy exchanging thoughts and suggestions through emails. Briefly, here is a short summary of the things we discussed.

Develop exchange and training programs:

1. Trying to organize more 'summer/winter schools' each year, one in winter and one in summer one focused more on clinical part an one on laboratory part.
2. In the 'summer school' should be focused more on how to care for patients, mechanism of disease, and overview of different techniques.
3. Have more experimental/interactive session in clinical part.
4. Have more cooperation/collaboration between ESIDjuniors and between ESIDjuniors and other ESID parties, between West and East, between the countries which are more developed and countries which are less developed in PIDs services.

Be more active within ESID activities:

1. Improve the Educational Day. A web survey form has been created with the help of IMT Bioinformatics group from Tampere. Please provide your feedback at: http://bioinf.uta.fi/courses/ESID_poll_2008.shtml The form will be online until the end of the year.
2. Have better electronic communication (mailing list to work better, receive the mail and give the link to the webpage).
3. Joining the juniors with seniors in research activities and also in writing the papers (for e.g review articles). The example of Nima Rezaei who succeed to use innovation and energy of juniors as well as science and experience of seniors to recently publish a book on PID, is worth mentioning and followed.

Increase the motivation and participation in the working party/ESID activities:

1. Have motivations for those involved (incentives, such as 'electronic points' for those who submit cases, write in ESID newsletter, submit patient cases for ESID registry, submit data for IDdiagnostics, IDbases, act as validators for IDR, get involved in the development of PIDexpert), have discounts on books, reduced registration fee in ESID meetings. These electronic points gathered to be taken into consideration also when we select the winners for participation in summer/winter school, different travel awards.
2. Have a proper award ceremony for 'the best poster', 'the best presentation' , 'the best mentor', and other 'achievements in PIDs' in the end of the 'Educational Day' or 'ESID meeting'.
3. The funds should be split for summer/winter school, short lab visits, incentives.

4. Publish the clinical cases in ESID newsletter and the best selected cases to be published in peer review journals. The clinical cases should be discussed between the students, and with senior experts.
5. Case studies should be also in web format, notification should be automatically, to get people more involved.
6. Selecting best junior researchers in field of immunodeficiencies each year (quantity and quality of the published papers should be considered) and awarding some small prizes (e.g. at least free membership of ESID for two periods).

Increase the services:

1. Have a database with pictures of clinical case and techniques used in PIDs.
2. Have a database on activities of ESID juniors, where the electronic points can be gathered.
3. IDdiagnostics (a project previous funded by ESID and EU, need to be maintained), to be better used (for e.g. once the people submit the data for ESID registry to submit also for IDdiagnostic, the same as for IDbases), to be better integrated within ESID registry and to have better funding.
4. IDR-factfile (the core of the system, http://bioinf.uta.fi/xml/idr/factfiles.xml) to be better integrated within ESID disease registry (it has been done already in Asian PID registry, http://rapid.rcai.riken.jp: 8080/sites/RAPID /index_html and in ORPHANET, an European rare disease database). In this way, we can have even stronger the link between genotype and phenotype and between clinics and bioinformatics tools, exactly, what Prof. Alain Fisher was encouraging us to do in his inaugural speech at ESID 2008. We have already the tools, we just have to used them fully! IDR to be better used and supported by ESID and other funding organizations. These valuable services for PIDs community needs your attention!

So, be brave and step forward, give your input and help to shape the future of our party!

Let's keep the spirit of 'Education, Sociability, Interaction and Discussion= ESID juniors', alive!

Crina SAMARGHITEAN

Clinical Working Party

First of all I would like to thank you for entrusting me with the task to head the clinical working party. I also would like to thank Bobby Gaspar for his previous work and introducing me into my new position.

As I had stated before I see my primary task in the identification of the most burning tasks in the different clinical aspects of PID. Therefore I would very much encourage you to define burning questions in the care of patients with PID. In order to collect your ideas I posted a short questionnaire (see also below) on the ESID website (go to clinical WP). Please return completed questionnaires to Klaus.warnatz@uniklinik-freiburg.de. After having collected some of your ideas I will post these on the Web so that further interaction between centers will become possible in order to raise enough interest and support for these projects.

A first start has been undertaken already on the last day of the ESID meeting in s'Hertogenbosch when the clinical working party met for the first time. I thank S. Rosenzweig, M. Carneiro, M. Kanariou, T. Avcin, A.Aghamohammadi, CT Lozaro and R. Sherkat for staying for this meeting and for the lively discussion we had.

Within this meeting following questions were identified:

1) A world wide survey on BCGitis (suggested and prepared by S. Rosenzweig). Since in many countries BCG vaccination is an obligatory vaccination usually scheduled during the first few days of life PID patients with susceptibility to mycobacterial infection have the risk of BCGitis. Since this often has a fatal outcome, this survey will collect the case history, applied treatments,

outcomes. The survey has become already accessible through the ESID webpage (see Clinical WP).

2) The establishment of an Email forum for PID .

The question was raised whether the current ESID forum would benefit by changing to an Email based forum. A Questionnaire is in preparation in order to evaluate the pro and con and the acceptance of an Email forum? Several members of PAGID report a positive experience with the Emailforum of PAGID. As always this will depend on the participation of a critical number of people to be worthwhile.

3) PID warning signs for Newborns.

M. Carneiro suggested a further development /improvement of age specific PID warning signs esp. for early infanthood. Several parameters were suggested. There was a consensus that improved new born screening is needed.

4) Survey on treatment and outcome of autoimmune and inflammatory disorders in CVID.

My own interest as I have already mentioned before is the treatment and outcome of secondary complications in CVID. In order to develop new therapeutic recommendations we will collect the existing experience in the different centers treating patients with autoimmune or inflammatory CVID.

The project 1) serves as a nice example (prepared already before my time) how to carry your most burning question into the ESID community and hopefully find the right answers. We all will benefit from these surveys and trials. Therefore I ask you to get involved in the clinical working party, develop project ideas and support the activities of others in order to improve patient care.

Klaus WARNATZ

Questionnaire "burning questions in PID"

What is the burning question?

Why is this question burning? (short summary of background)

What is the patient group of interest? (cohort of interest)

How shall this question be addressed? (Outline of suggested activity)

What is needed to answer this question? (required support, etc)

Any other comments you like to include?

Who is the contact person for this project? (name, e-mail, address)

Please fill in the blank spaces and return by fax (+49-761-2703306) or email (klaus.warnatz@uniklinik-freiburg.de) to Klaus Warnatz in Freiburg.

Interesting Papers

The MyD88-dependent TLRs and IL-1Rs are essential for protective immunity to a small number of pyogenic bacteria. Nine childrens with AR- MyD88 deficiency, recently described, suffered from life-threatening, often recurrent pyogenic bacterial infections, including invasive pneumococcal disease. Their clinical status improved with age, but not due to any cellular leakiness in MyD88 deficiency. (von Bernuth et al, Science 321, 691, 2008)

HIES is characterized by high susceptibility to infections with S. aureus and C. albicans. Despite the identification of the genetic cause of HIES, the mechanisms underlying the pathological features of the disease is not clearly understood. The authors explain here the pattern of infection susceptibility and the importance of Th17 responses in normal host defense against S.aureus and C.albicans. (Ma C. S. et.al. JExpMed 2008:205:1551-1557; Milner JD et al. Nature 2008; 452: 773–776). The findings of both Milner et al. and Ma et al. alert to the potential infectious risk associated with prolonged neutralization of Th17 cells or of their mediators. These findings may be useful also for the treatment of chronic inflammatory conditions such as psoriasis or multiple sclerosis. (Fischer A. Immunol Cell Biol. 2008, 86(7): 549-51)

A comprehensive review about congenital neutropenia syndromes gives a new light on the diagnosis, molecular genetics, treatment and prognosis of these diseases. This article also shows different congenital neutropenia diseases with or without hypopigmentation, and a unifying disease model for severe congenital neutropenia. (Boztug et al. Immunol Allergy Clin North Am. 2008 May; 28(2):259-75)

Another interesting review gives a broad understanding on formation and function of the lytic NK-cell immunological synapse. There are seven known human genetic diseases that are characterized by defects in specific steps in the formation and function of the NK-cell synapse. Owing to their known molecular pathogenesis, studies of these diseases provide insight into the cell biological processes that facilitate NK-cell lytic-synapse formation. Additional mechanistic understanding of the pathogenesis of the associated clinical phenotype, haematophagocytic lymphohistiocytosis, can also be gained from studying these diseases. (Orange JS, Nat Rev Immunol. 2008, Aug 18)

A novel in silico method for disease gene identification and prioritization has been developed. The authors combine information about protein interaction networks and gene ontology terms. The method was applied to PIDs and human immunome data to suggest new genes which might have relevance to primary immunodeficiencies. (Ortutay C, Vihinen M, Nucleic Acids Res. 2008, in press)

It has been exciting this time again to search for interesting papers and it would be even more exciting receiving your feedback. So, if you have other interesting papers and want to draw attention on them send and email to Crina.Samarghitean@uta.fi. Anyone interrested in joining editorial board of ESID newsletter is welcome!

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

Crina SAMARGHITEAN

Interesting Cases

Case#7: Burkitt-like lymphoma and subsequent aplastic anemia in a EBV negative 17-years old boy with X-linked lymphoproliferative disease.

X-linked lymphoproliferative disease (XLP) is an uncommon primary immunodeficiency characterized by Epstein-Barr virus (EBV) infection typically

presenting with fulminant infectious mononucleosis, dysgammaglobulinaemia (typically decrease of IgG, normal to increased IgM) and non-Hodgkin lymphoma, mainly of mature B cell origin. Seventy percent of affected boys die before reaching age of 10 1. XLP is a very rare disease with incidence 1 to 3 patients per million males 2. Other rare manifestations of XLP are aplastic anemia and lymphocytic vasculitis 3,4.

Case: Here we present a 17 years old patient who was admitted in September 2007 to our department initially presenting with high grade Burkitt-like lymphoma (stage III – st. Jude, generalized lymphadenopathy, fluidothorax, ascites. In early childhood (till 6 year of age) the patient suffered from frequent middle ear infections (paracentesis performed approx. 20 times), he had varicella infection when he was 5. Since 2005 he was followed by endocrinologist for enlarged thyroid gland with normal function and for growth retardation, he had several impetigo infections between 2005 and 2007 treated with antibiotics. Immunological investigations at diagnosis of Burkitt lymphoma showed normal levels of immunoglobulins including subclasses (IgG 7.15, IgA 0.95, IgM 2.09, IgG1 4.35, IgG2 2.05, IgG3 0.24, IgG4 0.04 g/L), negative antibodies against EBV (EBNA, VCA IgM, VCA IgG) and CMV, no significant changes in a percentage of basic lymphocytic subpopulations (CD3, CD19, NK, CD4, CD8), normal CD4/CD8 ratio, mild activation of T cells of observed (CD3+DR+ out of lymphocytes was 15%, HLADR+ out of CD3+ T cells was 20%). Patient has healthy older brother and healthy older male cousins. Patient started treatment according BFM B NHL 2004 protocol, initially complicated with recurrent pleural effusions, resulting in a treatment delay, therefore 2 doses of rituximab where administered. Patient finished the protocol in January 2008, complete remission on PET/CT scan was confirmed in March 2008. In April 2008 patient was readmitted with pancytopaenia (WBC 1.6 x 10^9/L, Hb 46 g/L, platelets 55 x 10^9/L), relapse of primary lymphoma was excluded. Diagnosis of severe aplastic anemia was done according to findings in aspirate and biopsy of the bone marrow. Serology due to anti-CD20 treatment and substitutions was not informative, EBV, CMV and HHV6 by PCR was negative in peripheral blood and bone marrow. Only very low load of parvovirus B19 was found in the bone marrow. Coincidence of Burkitt-like lymphoma and aplastic anemia led us to analysis of SH2D1a gene and deletion of the 1st exon was found. Of note mother´s brother died at the age of 5 in 1966 under the picture of acute liver failure, probably it was a fatal infectious mononucleosis.

Discussion: Majority of clinical presentations of XLP (severe often fatal infectious mononucleosis, hemophagocytic syndrome, malignant lymphoma, dysgammaglobulinaemia) are based on impossibility to develop a normal response to EBV infection 5-9. Less common is an aplastic anemia, lymphocytic vasculitis or lymphoid granulomatosis as the first presentations. Unexplained deaths of affected boys in the family are also an important part of the picture.

All these possible manifestations can be also present in a patient without previous exposure to EBV infection 4,10,11.

Overall prognosis is poor, the only curative approach is an allogeneic transplantation of stem cells; better prognosis is associated with EBV negativity.

David SUMEREAUER
Ester MEJSTRIKOVA
University Hospital Motol, Prague, Czech Republic

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Some impressions from the ESID meeting in 's-Hertogenbosch: