The primary immunodeficiency network on European and national levels – where are we now?

Primary immunodeficiencies (PID) are rare chronic diseases. Many of the autosomal recessive forms affect less than 1 in a million individuals, whereas the X-linked recessive forms affect about one in a hundred thousand individuals or less. Thus, each disease affects only a few individuals in each country. However, due to the fact that more than 100 different disease entities are known, all PIDs considered collectively have a significant impact on public health.

PIDs, during the past decade have been much more often recognised because of dynamic developments in modern genetic and immunological techniques. Progress in molecular immunology and genetics has enabled the recognition of more defects at the DNA level. Mutation detection is the most reliable method to confirm the diagnosis. Advances in molecular genetic are challenging our classification of PIDs, which is still based on clinical and immunological grounds. It offers hope for gene therapy, which is used with success in numerous diseases, mostly in the severe form of primary immunodeficiency. Adenosine deaminase deficiency was the first hereditary disorder to be treated by gene therapy. Now gene therapy is provided for severe immunodeficiency disease (SCID) patients in a few centres in Europe: in the Institut National de la Sante et de la Recherche Medicale in Paris by Alan Fischer in gamma – chain SCID patients, and also recently by Adrian Thrascher at the Paediatric Immunology Unit at Great Ormond Street Hospital in London. Gene therapy is ongoing in some children and adults with X-linked form of chronic granulomatous diseases, and is provided among others by Reinhard Seger at the University Children's Hospital in Zurich.

PID network in Europe

The European Group for Immunodeficiencies (EGID) was established in 1983 as an informal group. The first meeting at that time was in Rome, and gathered a small group of immunologists. It was organized by Professor Fernando Aiuti at the Medical Faculty, University of Rome. The second assembly was in Fillervall, near Paris by Professor Claude Griscelli of the Necker Medical School, Paris, the first president of this Group. ESID, as the European Society for Immunodeficiencies, was formed in 1994 and replaced EGID. Polish activity in EGID was present from the beginning. It was marked as a permanent representation of the country in this Group.

ESID organize a biennial congress to facilitate international contact between primary immunodeficiency specialists. The last congress was organized in Versailles, France in October 2004. The next one will be organized for the first time in an East European country in Budapest, Hungary, 4-7 October 2006. The congress president is Professor Laszlo Marodi from the Department of Infectious and Pediatric Immunology at Debrecen.

European registry of PID

The prevalence of immunodeficiency disorders varies extensively, depending on the type of disease. Furthermore, multiple etiologies and distinct clinical subtypes exist for some diseases, where each subtype is represented by a limited number of patients in each major referral centre. Genetic and/or therapeutic studies usually involve a large number of patients. Identification and localization of patients is therefore necessary for the successful completion of these studies. Access to a sufficiently large number of patients thus constitutes the basis for clinical trials, and it is only by pooling the resources from different countries that we will solve the molecular basis of these disorders and this will be able to institute efficient therapeutic measures.

The formation of the first registry of PID patients was initiated by ESID in January 1994. Up to 2003, in total, data from about 10,000 patients from 26 countries was received. In 1995, the first locus-specific mutation database accessible through the internet was established (the BTKbase for X-linked agammaglobulinaemia – curators Mauno Vihinen and C.I. Edvard Smith). Since that time several additional locus-specific databases have been established. This registry has been useful in many ways. Analysis of the prevalence of PID from different countries has been shown major variations between geographical regions in Europe. Unfortunately, that registry suffered from incomplete registration of patient data and a lacks of follow – up information.

For these reasons, the second-generation Pan-European PID patient registry, which is integrated with a mutation database with more detailed clinical data has been initiated by ESID in 2002. The head of the new registry is Professor Bodo Grimbacher at the Department of Clinical Immunology and Rheumatology at the University of Freiburg in Germany. A home page on the internet has been constructed with information on the ESID registry: www.esid-registry.org. This is associated with more than 30 sub-registres on variety of primary immunodeficiencies. The paper on the ESID online clinical and research database by Viviane Knerr and colleagues, run in this journal has shown wonderful progress in building up the Pan- European PID patients registry. Discrepancy between the date of the update of the registry and the publishing date of the paper is caused by the delay in printing of this journal. The group of researchers led by Mauno Vihinen, from Helsinki, have published also in this journal a paper on PID mutation

databases existing on http://bioinf.uta.fi and now connected with www.esid-registry.org. A European Committee grant; EURO-POLICY-PID running project strongly supports the development of Pan-European PID patient registry. In this journal we present key objectives of this project.

National Register of Polish PID Patients is already started. In present journal Department of Immunology, CMHI is presenting there Twenty Five Years of Investigations into PID diseases. This registry updated by March 2006, due to delay in printing of this journal, is the biggest one in Poland and includes 846 patients. The large group of DNA repair disorders is presented by Ataxia telangiectasia and the biggest one in Europe, group of patients with Nijmegen Breakage Syndrome. The paper on Nijmegen Breakage Syndrome, the diagnostic difficulties of primary immunodeficiency by Aleksandra Szczawińska - Popłonyk and colleagues run in this journal.

Polish initiative for PID

During the past 50 years at least a few main clinical institutions have actively diagnosed and treated PID patients. As the first paediatric clinical immunology unit developed in Poland, the Department of Immunology at The Mother and Child Institute, Warsaw was set up by Professor Henryka Siwińska-Gołębiowska in 1968.At present, a national project with the aim of improving patient care in Poland, and raising awareness of PIDs across the country was initiated by the Polish Working Group for PIDs, which was established in March 2005. The project is supported by a grant from the Polish Ministry of Science PBZ-KBN-119/P05/04, granted for 2005 to 2008. The Group has been assembled from six main Polish centres for the diagnosis and therapy of PIDs, as follows: the Department of Immunology, The Children's Memorial Health Institute of Warsaw, led by Profesor Ewa Bernatowska, the Department of Immunology, Polish-American Institute of Paediatrics, Jagiellonian University, Medical College of Kraków, led by Professor Marek Zembala, The Department of Paediatric Propedeutics Clinic of Children, Immunology and Rheumatology , Medical University of Wroclaw, Bottom of Form led by Professor Adam Jankowski, the Department of Paediatric Pneumonology, Allergology and Clinical Immunology, Karol Marcinkowski University of Medical Sciences, Poznań, led by Professor Anna Bręborowicz, the Department of Paediatrics, Prevention Cardiology and Clinical Immunology, the Medical University of Lodz, led by Professor Krzysztow Zeman and the Clinic of Child Immunology at the Medical University of Bialystok led by Professor Danuta Jastrzębska-Piotrowska and the person responsible for PIDs patients, Bożena Mikołuć.

The main objectives of the Group's activity are: (1) to build up a Polish national registry of PID, (2) to harmonise the existing Polish diagnostic guidelines based on the ESID proposal and to develop therapeutic guidelines at a national level, (3) to improve awareness of PIDs among paediatricians and general practitioners.

(4) to achieve the development of channels for the active dissemination of information about PIDs among patient organisations, the media, and public health groups, government and non-governmental organisations in Poland.

The Polish registry is planned to be developed in co-operation with Professor Bodo Grimbacher from the University of Freiburg, the head of the European Registry online. The Registry will be located on a server in Freiburg and will automatically be a part of the Pan-European PID patient registry system online. Training concerning the introduction of individual PID patients to the Pan-European PID patient registry system online is already provided in the Department of Immunology, Children's Memorial Health Institute, Warsaw, for physicians from other Polish centres for the diagnosis and therapy of PIDs. Based on the Polish registry, demographic data on age, gender and ethnic origin will be statistically analysed, as well as disease type and method of treatment.

One of the most important parts of the plan for thedissemination of information is to build up a Website platform. The website will be developed by financial support from of EURO-POLICY-PID SP23-CT-2005-006411, an EC grant conduced by C.I.E. Smith from the Karolinska Institutet, Stockholm, which will be located on a CMHI server. The newly-created website will include the following elements: the up-to-date Polish registry of PID patients, which will include collected patient data with PIDs from the whole of Poland, periodical statistical analyses of collected data, general information about PIDs, a list detailing Polish PID diagnostic centres, information about Polish Parents of Patients Organisation, with PIDs Association and other related organisations from Poland and all over the world. The website will collect diagnostic and therapeutic guidelines for PIDs, information on Polish and major international meetings and symposiums on PIDs, helpful links to other websites related to PIDs including the ESID. Activity to build up the necessary capacity in order to increase awareness about PID in Poland will be initiated as a project for the prospective and retrospective study of PIDs, within the Department of Immunology, Children's Memorial Institute, Warsaw. It will be based on PID patients referred by physicians / paediatricians from 17 Polish provinces. The expected result of this analysis is to identify a target physician group, which could be involved in the early diagnosis of PIDs. The other parameters to be analysed are types of recurrent infection, how long it takes to make a diagnosis, etc.

The Department of Immunology, CMHI, Warsaw plans to disseminate information on PIDs to another Website platform in Poland, to make all information more available. The first objective is the Polish Society of Experimental and Clinical Immunology. Later, the website will offer information on all topics related to vaccination in immunodeficiency patients . Department of Immunology, CMHI is providing long – term co-operation with the

Department of Vaccines and Biological, WHO and the Global Advisory Committee on Vaccine Safety in WHO, Geneva, in the area of serious advice events follow vaccination in immunodeficiency patients.

Clinical immunology specialisation

Clinical Immunology has passed through extraordinary changes during the last few decades. In the field of Primary Immunodeficiencies, we have moved from a clinical era to the molecular era. Clinical immunology is a newly-created, medical sub-specialization in Poland, beginning in 2000. The programme for this specialisation was created by the Department of Immunology, CMHI , in co-operation with three other immunological centres in Poland. The programme was prepared with the purpose of taking advantage of the new understanding of either basic or clinical immunology. The clinical training covered a wide range of multi – disciplinary clinicians. To date, 20 Polish young physicians, from 12 out of 17 palatinates, have started to specialise in clinical immunology. All of them attended the Autumn/Winter School of Clinical Immunology, traditionally organised by our department. The School of Clinical Immunology is recommended by the Polish Society of Experimental and Clinical Immunology as a recommended educationalve activity, due to the programme of specialisation in clinical immunology.

International educational programme for young immunologists

ESID Summer School

The ESID Summer School has been providing study opportunities for a new generation of young clinical scientists. The ESID Summer School has been a great success so far. They are organised every two years in various attractive parts of Europe.

The Autumn/Winter School of Clinical Immunology

It is a tradition within the Department of Immunology, CMHI, to invite young immunologists and doctors interested in clinical immunology from all of Europe, to spend time together. The meeting gives opportunities to listen to lectures given by experts in immunology, from all over Europe and the world. It also creates a forum to exchange their own experiences, as well as to discuss difficult cases and diagnostic and therapeutic problems. About 60 participants from both Central/Eastern and Western European countries have attended these meetings.

The Fourth School of Clinical Immunology will be organized this year in Ruciane Nida, June 8-10. All lectures and presentations will be available on CD, as usual.

Polish PID patients organization

The Association of Friends to Children with Immunological System Deficiencies was form in 1986 in Warsaw. It organised meetings,and provided financial help for some patients. Recently two nationawide meetings of patients with children suffering from Ataxia-Telangiectasia syndrome have been held. A handbook for patients, “Diagnosis and Therapy of Primary Immunodeficiencies”, has been written and published. The Association, in co-operation with the International Patients Organization for Immunodeficiencies in Europe and the Jeffrey Modell Foundation in the US disseminate information about PIDs among primary care doctors, nurses, and parents on a national and an international level.

Summary

Efficient early diagnosis of PIDs is crucial for prognosis of the patients. Only through out close collaboration with primary care physicians, nurses, and patients organizations at a national and international level is it possible to achieve this aim. There is now a need for active dissemination of information on disease presentations, expected prevalence and consensus methods for diagnosis and treatment, not only to ESID, but to related patient, medical and public heath groups and EU agencies.

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