The ESID online clinical and research database

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Abstract

The ESID online database has been set up by the European Society for Immunodeficiencies in order to provide detailed long term documentation of data about patients with primary immunodeficiencies. Its aim is to improve diagnosis, therapy and prognosis of PID patients by enabling large genetic and therapeutic trials. The database is capable of collecting therapy and laboratory data on almost 180 different primary immunodeficiencies with a common core dataset and additionally offers large disease-specific data models for a number of diseases which expands constantly. The project involves numerous documenting centres throughout Europe and is being supported by the European Union and pharmaceutical companies. One of the advantages of the system is the easy handling which does not require technical premises on site. The database can be accessed online and is password protected.

Key words: *primary immunodeficiency, database, online, research, European, clinical.*

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Introduction

The European Society for Immunodeficiencies (ESID) is a non-profit organisation which seeks to facilitate the exchange between people concerned with Primary Immunodeficiencies (PID) such as physicians, nurses, biomedical investigators, patients and their families. For all these different groups of people ESID provides professional information and useful help. ESID also supports the research on causes, mechanisms and treatment of PIDs and brings doctors up-to-date in regard of diagnosis, pathogenesis and therapy. For this purpose, summer schools, scientific meetings and trainings are organized regularly.

Another aim is to intensify the overall awareness of Primary Immunodeficiencies. A joint working group of ESID-board members and delegates from important organisations like EFIS (European Federation of Immunological Societies), IPOPI (International Patient Organisation for Primary Immunodeficiencies), JMF (Jeffrey Modell Foundation) and INGID (International Nursing Group for Immunodeficiencies) have been successfully carrying out a series of campaigns in order to increase the interest of EU health policy in PID. These activities led to the support of the ESID online clinical and research database within the 6th framework program of the EU. This project called EU-POLICY-PID was launched in February 2005 and has four key objectives: To increase the understanding of the aetiology of PID and identify novel mutations and new disease genes (1), to carry out epidemiological studies in order to determine the prevalence of PID in Europe (2), furthermore the project wants to establish and evaluate harmonised guidelines for the diagnosis and treatment of PID (3) and to improve the awareness of PID among the European population (4). The ESID online database is a secure, internet-based patient registry, which will help to achieve these aims by bringing together clinical and laboratory data of PID patients. Diagnosis, classification, prognosis and therapy will be improved by making the data of different centres more easily accessible to others and assuring detailed long-term documentation and facilitating large genetic and therapeutic trials by obtaining follow-up data. The database will form a platform for studies of demographics, the harmonisation and development of new diagnostic and treatment studies and the identification of novel disease genes. It is also the basis for EU-POLICY-PID to establish standard European guidelines and procedures for setting up clinical patient and research databases.

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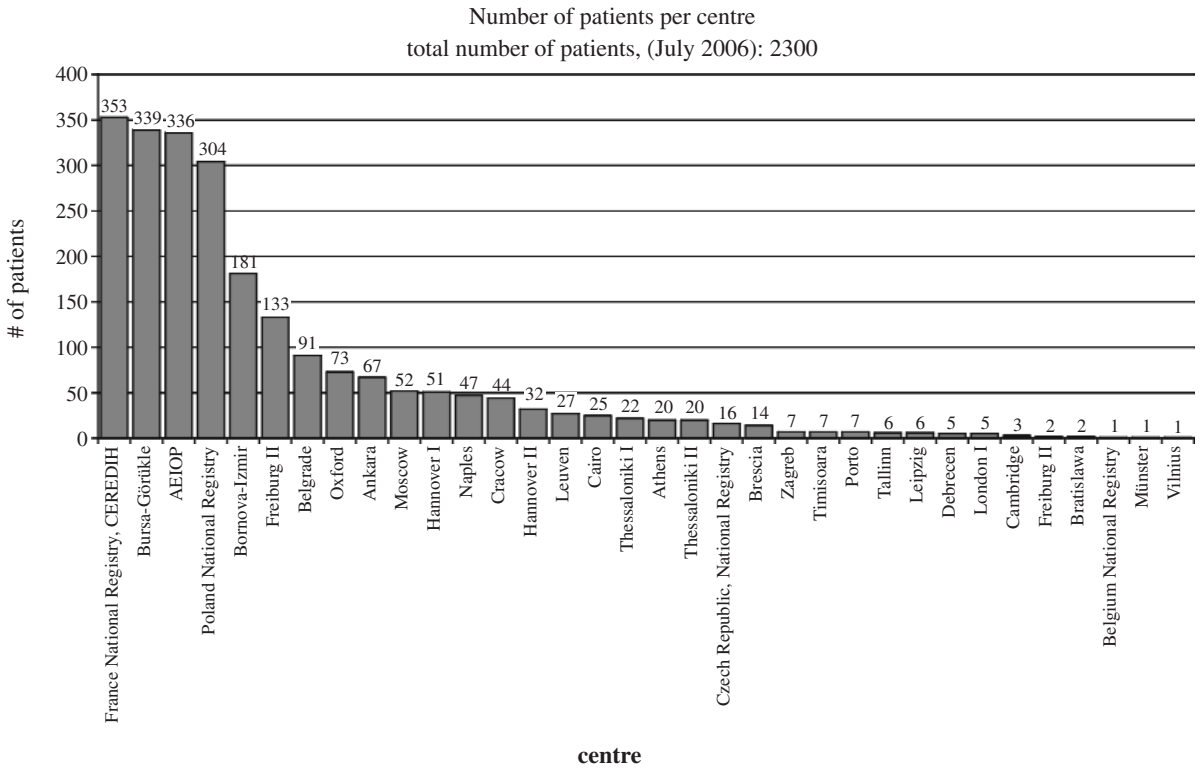

Fig. 1. Number of patients registered in the ESID online database by July 2006

How does the database work, what does it offer to the user?

The ESID online database allows the documentation of patients with any primary immunodeficiency into an online system that provides a common dataset for 168 primary immunodeficiencies. In this so-called core dataset, the diagnosis, therapy and laboratory data, leukocytes, thrombocytes, erythrocytes, lymphocytes, granulocytes, hemoglobin, eosinophils, basophils, macrophages, IgG, IgA, IgM, CD3, CD4, CD8, CD19 or CD20 and CD56 is stored. Certain fields of the core dataset are subject to an annual reimbursement of 10 Euro provided by the PPTA (Plasma Protein Therapeutics Association)[1], another sponsor of the project. This payment is meant to compensate for the secretarial work of entering the data and will also be paid for follow-up documentation. The documenting centres can only see their own data, though they can easily agree on cooperation with others. In that case, the partners can be given access to each others data.

On the website www.esid.org, the user is invited to benefit from the information provided by ESID. By accessing the registry working party section and clicking on the button "ESID online registry", a tree of PID diagnosis becomes visible and the user is asked to select the respective sub-registry in which he/she wants to document a new patient. The PID are grouped in seven categories which are:

- predominantly antibody disorders,
- predominantly T-cell deficiencies,
- phagocytic disorders,
- complement deficiencies
- other well defined PIDs,
- autoimmune and immunedysregulation syndromes,
- unclassified immunodeficiencies.

By selecting the categories, the tree expands and more defined subclasses appear. Some are marked in blue, which means that an extended disease-specific data model is available. Experts from all over Europe work in more than 40 steering committees on the creation of data models which reflect the characteristics of the various PIDs. So far, ten sub-registries feature an extended dataset: common variable immunodeficiency (CVID), DiGeorge syndrome, Nijmegan breakage syndrome, centromere instability and facial abnormality syndrome (ICF), Hyper IgE-syndromes, ICOS deficiency, immune dysregulation polyendocrinopathy X-link syndrome (IPEX), secondary hypogammaglobulinemia, X-linked agammaglobulinemia and TACI deficiency) and eleven more are presently being programmed and will be

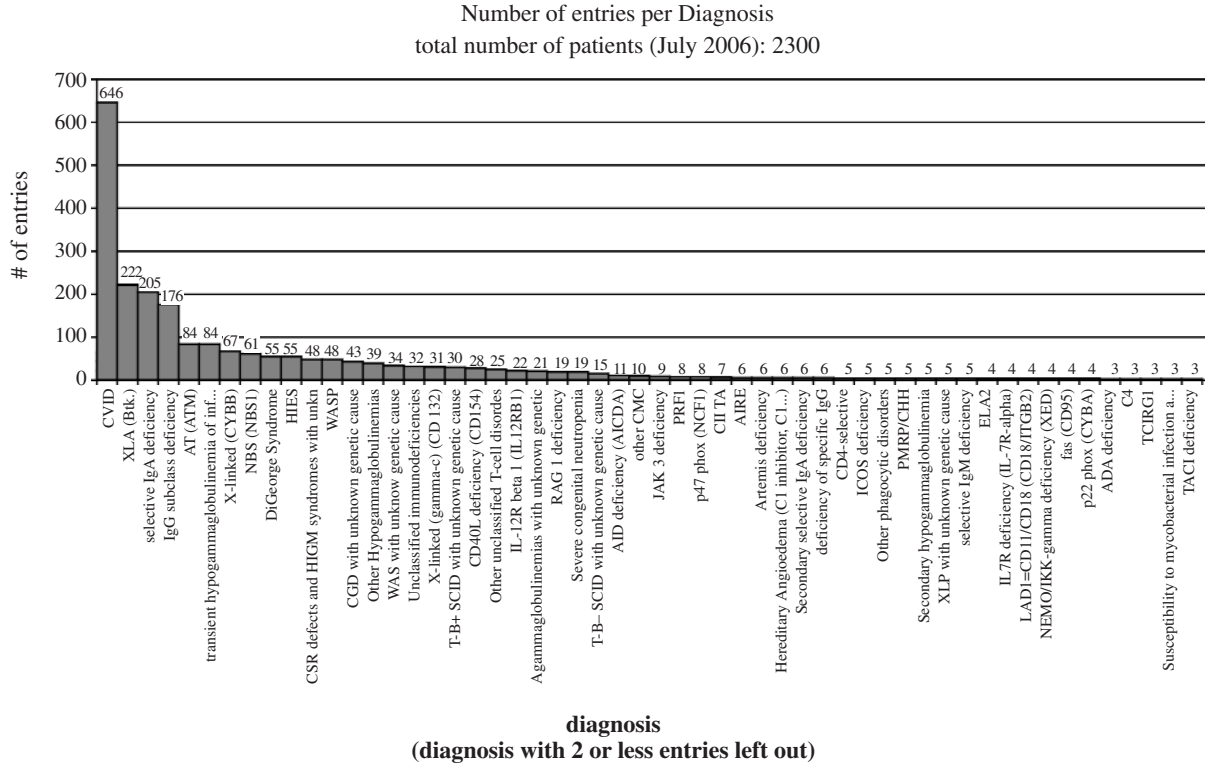

Fig. 2. Number of entries per diagnosis in the ESID Online Database by July 2006

online soon (severe combined immunodeficiency (SCID), Hyper IgM syndromes, IgA deficiency, osteopetrosis, ataxia teleangiectatica (AT), CD40 ligand deficiency, BAFF receptor deficiency, Comel Netherton syndrome, deficiency of specific IgG, IgG subclass deficiency, selective IgM deficiency).

One of the goals of the system is to be user-friendly. In this respect, the database is available online, which implies that a standard browser is sufficient to access the ESID database and the user will neither have to invest in any technical equipment nor download additional software. Apart from that, the handling of the database is kept as clear and simple as possible. For this purpose, a great number of "Tool tips" have been implemented. These buttons clarify the function of individual fields and explain what the user is asked to enter in the respective fields. The database also offers the opportunity to edit the drop-down-menus of certain fields. Thus the user can add specifications considered to be relevant, which will then be visible for all users.

Another novelty is the ESID Mutation Detection Tool, which is a multicomponent system for the deposition of genetic mutation data. It directs the user via an SSL-encrypted connection to the "IDbases" in the Institute of Medical Technology in Tampere, Finland. There, the gene mutation event is deposited and validated with bioinformatics-tools and automatically submitted back to the ESID Mutation Web Service, which matches the validated data with the ESID online database. The exchanged data is coded and contains no personal patient information, thus the data received in Finland is anonymous. Currently, this tool works with genomic DNA and cDNA and includes information related to the number of affected alleles where applicable. This tool support is planned to be extended to approximately 90 sub-registries.

The ESID database is meant to be the basis for all kinds of surveys on primary immunodeficiencies. The fields that are considered relevant to such a survey are currently being defined in the respective steering committees and highlighted on the user interface. Therefore a colour coding scheme has been applied: The fields will be tinted in a pre-assigned colour and are thus clearly recognizable for the user. A first study on CVID has already been started.

Different easy-to-use query tools that will enable the users to run queries themselves will also be implemented in the near future.

At the moment it is essential to attract documenting centres for the project, so that data on as many patients as possible can be deposited in the database. Currently 71

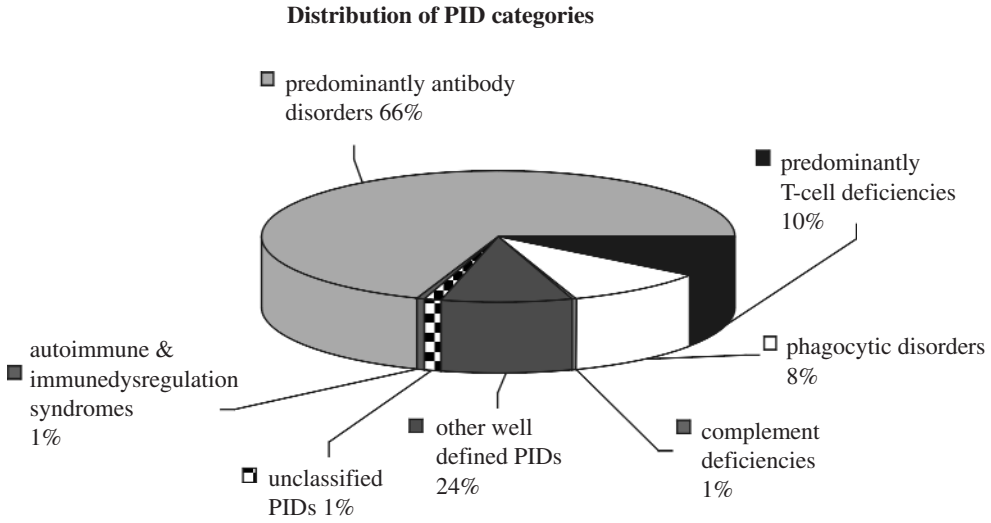

Fig. 3. Distribution of entries in the main PID categories

documenting centres in 27 countries have obtained passwords for the online documentation. Not all of them have started entering their patients yet, but so far a total number of 2295 patients have been documented by July 2006. Approximately 350 patients have been imported electronically from the Italian National PID Register (AIEOP) into the ESID database. Another international CVID-register compiled by Dr. Lennart Hammarström in Stockholm, Sweden, with 519 patients will be integrated successively in the ESID-CVID sub-registry once patients consented. For some centres the import of their data in Hammarström's database into ESID has already taken place or started.

For the state of the database by July 2006, please see the Figures 1-3.

Security and data protection

Due to the lack of a centralized European data protection and ethics board, the concept of this European Online Database is to pass the local ethics and data protection committees. All necessary security facilities have been provided. The data is stored on a password-protected internet server which runs within a secure server network in Freiburg, protected by an audited firewall system. All patient data is coded, i.e. the identification of an individual patient is impossible, except for the treating physician. Only patient data relevant to the medical condition (age, laboratory and examination results) is stored and processed automatically. ESID offers a coded version of the database system, which records no personal patient data. In order to make the work with the database even more comfortable, ESID has developed a personalised version in May 2006. This multi-server-solution enables the attending and documenting physician to see not only an identification number, but also the patient's name, address, etc. on the screen. Data security is guaranteed through the separation of identifying patient data on one server and diagnostic data on another, separate server. The information from both servers can only be combined on the physician's screen by using the correct password. This solution has previously been tested on other projects and offers the highest security standards. At the same time, the coded system remains available as before. Genetic data relevant to the medical condition is stored anonymously in the long-established mutation database (Mutbase), created for the documentation and analysis of mutations involved in immunodeficiencies. All data transmission is SSL-encrypted. Not all database users are authorized to see all fields. The system of user roles assigns different access rights to different users: During the login process the profile of the respective user and his rights within the web application are determined. This means that a specific user will only see those fields for which he has been authorized. This authorization process takes place within the ESID board. The financial supporters of the database are, apart from the European Union, five pharmaceutical companies producing immunoglobulins. Members of these companies have the right to see the core dataset of all patients but without knowing, where the patient comes from. It is impossible for these users to trace an entry back to the documenting centre.

Before patient data can be entered into the database, the patient has to be informed and consented. Informed patient consents in 17 different languages are provided on the ESID-website (www.esid.org).

Future perspective

We are working on more output features for the database. Currently a tool for pre-defined queries is being programmed. The users will thus be able to do instant queries on their own patients by using this tool. For more complex queries or queries in cooperation with other centres, they can contact the database coordinators in Freiburg, Germany.

Test-database

For all those who are interested in this system, the test-database gives a first impression of how this clinical and research database works. One can try out all features and even create new fictitious patients. The URL for the TEST-database is http://www.esid.org/esid_testregistry.php

First choose one sub-registry, then enter the test usernames: *test* and the password *start*. Please do not change this password, otherwise the next user will not be able to test the system. In case you should be asked to change the password, please ignore this request and simply close the pop-up window. One can either have a look at existing (fictitious) patients by clicking on "Show all patients" (top menu) and then selecting one. Then the user can view the different categories by clicking on the left menu (core dataset, core laboratory etc.). It is also possible to create new (fictitious) patients (top menu).

The ESID database will provide the platform for future awareness programs, diagnostic and therapeutic trials, drug surveillance programs and quality of life assessments in the field of primary immunodeficiencies. To achieve this ambitious goal, the ESID registry working party is constantly improving and enhancing the functions of the database that provide a mature instrument for the documentation of patients. However, for the benefit of all users and that of the patients, the ESID online database needs to be filled with patient data. 71 documenting centres are already contributing to the success of this European project and ESID is confident that more participants will sign up in the near future since many centres all over Europe have already signalled interest.

Footnote

[1]Plasma Protein Therapeutics Association (PPTA): Five member companies producing immunoglobulins support the ESID database as sponsors. These are: Baxter, Biotest, Grifols, Kedrion and Octapharma.