

EUROPEAN NETWORK OF RARE BLEEDING DISORDERS (EN-RBD)



alekos

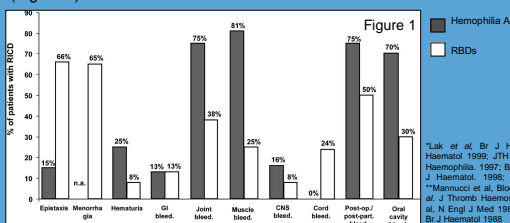
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Background

- Rare Bleeding Disorders (RBDs: fibrinogen, Factor (F)II, FV, FV+FXIII, FVII, FX, FXI, FXIII deficiencies) are autosomal recessive diseases representing 3-5% of all the inherited coagulation deficiencies
- Prevalence: approx. 1:500,000 (FVII) to 1:2,000,000 (FXIII), in general population, but in areas where consanguineous marriages are frequent (Middle-East countries and Southern Italia) RBDs are more frequent (8-10 times)
- The recent immigration toward Europe has increased the number of patients in some European countries, representing a significant clinical problem and increasing the demand for diagnosis and treatment
- The type and severity of bleeding symptoms, the underlying molecular defects and the actual management of bleeding episodes in patients affected by RBDs are not well established

However, from the data of three large National Registries (Iran*, Italy** and North America***) as well as from other relatively large cohorts# a few general considerations can be drawn on the spectrum of clinical manifestations in RBDs (Figure 1)

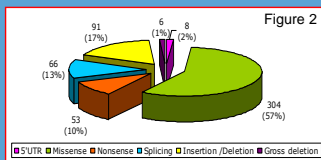


RBDs are generally less severe than hemophilia A and B:

- life and limb threatening symptoms are apparently less frequent
- varies from mild to moderate bleeding episodes to potentially serious or life threatening haemorrhages
- some deficiencies such as afibrinogenemia, FVII, FX and FXIII could be more severe and some patients require prophylaxis

Figure 2 shows the percentages of different types of 572 mutations previously published

(Zivelin A et al, Chapter 116 of Williams Hematology 7th Edition 2006, updated 2007, <http://www.med.unc.edu/wh>)

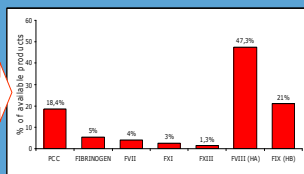


RBDs treatment is based on replacement therapy by cryoprecipitate, prothrombin complex concentrates or single factor concentrates and on non-transfusional treatment. However figure 3 shows the different availability of products for RBDs compared to hemophilias

(derived from World Federation of Hemophilia, http://www.wfh.org/2/docs/Safety_Supply/FF6_Registry_6ed2005.pdf)

Figure 3

	n° products	manufacturer
PCC	16	14
FIBRINOGEN	5	5
FVII	3	3
FXI	2	2
FXIII	1	1
FVIII (HA)	36	23
FIX (HB)	16	13



Aim

- Despite the existence of a huge amount of information on different aspects of RBDs, data are not yet sufficiently homogenous in order to indicate which course of action is needed to improve diagnosis and treatment
- This lacuna could be made up by the collection and organization of clinical, laboratory and treatment data and their statistical analysis using a unique and homogenous model

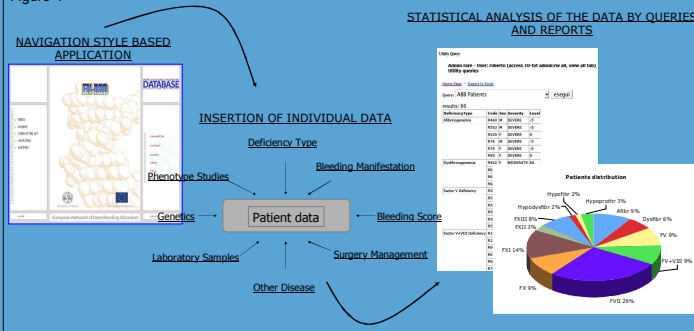
As the most readily available data come from Europe, through the EN-RBD project, we chose to create a network among European Centres dealing with RBDs, in order to develop a novel communication tool for managing, editing and viewing collected information

The project was signed and funded in the frame of the community action programme for public health, by PHEA (Public Health Executive Agency) and the University of Milan on March 2007

Methods

- The purpose of the EN-RBD web-application was to manage an on-line database storing information on patients affected by RBDs. The main focus is editing/viewing of data and extraction of data through database queries
- The technology is based on a web site, with an open-source free database engine (MySQL as RDBMS), and an open-source free web server with scripting capabilities (Apache and php). Client-side, any web browser compatible with security certificates can be used to access the web-application
- Particular attention is reserved to data security and privacy through methods of authentication, authorization, accounting (A-A-A) and all communications between the client and the server are encrypted. The application is web-based style, language is English, a help platform is available as a web page with a description of all database fields, that can be used as a contextual help, by clicking on the field name links. In order to comply with European privacy laws, personal identification data are not inserted in the database
- Administration data are managed by the database administrator and contain users and operators data, password management, queries management, and contextual on-line help guide editing
- Figure 4 shows the flow of information from the data insertion to the final report

Figure 4



EN-RBD ACCESS:

Privacy and security of the data are two of the main issues of our project, that is why we decided to use a two-level key system to access the database

- Client-Server credentials: a SSL Certificate and a SSL Certificate password will be separately sent to the partners. These credentials will be necessary to establish a communication with the EN-RBD Server and the Server will recognize the computers as authorized to connect
- User credentials: once the communication between the computer client and the EN-RBD Server is safely established, User-ID and password are necessary so that the Server will acknowledge that the user at the authorized computer is allowed to access the database application

EVALUATION OF THE PROJECT

- Each partner is asked to discuss and quantify results, to point out the arising problems and to suggest solutions during the annual meetings or periodical audio/video conferences (the first EN-RBD meeting was held on November, 16th in Milan)
- EN-RBD project results will be submitted to congresses and to scientific journals in order to verify the efficacy of the project itself, by its impact on the scientific community
- An external reviewer extraneous to the project with thorough RBDs expertise will be asked for a final evaluation

DISSEMINATION OF THE RESULTS

The results of our project will be disseminated through:

- Specific web pages and monthly newsletter at www.rbdd.eu
- Publications in scientific journals of the field, as well as data presented during National and International congresses by oral or poster presentations
- ad hoc divulgative pamphlets or CD-ROMs to be sent to patients' associations or National Health ministries in order to more directly benefit not only experts in the field but also patients and those not familiar with the web

Expected results

- The final goal will be the creation of a unique on-line tool available to all European Centres, dealing with RBDs
- Statistical results derived by all the clinical, therapeutic and genetic information will be available to clinicians and patients, as well as National and Supranational organizations and regulatory agencies (FDA, EMEA)
- Data obtained on distribution and treatment of patients could be useful to draw up guidelines to assist the clinician in patient management as well as to stimulate the interest of pharmaceutical industries in developing new products

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