Introduction: The history of the Alpha One International Registry (A.I.R.)

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At the beginning of the new Millennium, it will be 37 years since the first cases of z1-antitrypsin deficiency (AATD) were described. Since then a great deal of progress in many aspects of this condition has been accomplished, including better understanding of the pathophysiological mechanisms leading to development of pulmonary emphysema related to AATD, the creation of biochemical and molecular diagnostic tools to screen for the condition, the recognition of the broad spectrum of associated pulmonary and extrapulmonary manifestations, a growing interest in the world-wide epidemiology of the condition, and the development of therapeutic strategies, with special emphasis on AAT replacement therapy. One example of the increasing awareness about AATD is the largest European national registry for this condition, located in Sweden where the condition was first recognized in 1963 (1), which stores information on more than 900 AAT-deficient subjects enrolled since then. Records on other large series of patients are available in Denmark (700 subjects, starting from 1976), Germany (more than 400 individuals, the national registry having been set up in the 1980s), and The Netherlands (more than 400 subjects, recruited during the last 10 years). More recently established European registries, each with more than 150 subjects enrolled, exist in Spain, Italy, and the United Kingdom. A large enrolment programme sponsored by the National Institutes of Health has led to the recruitment of 1129 AATD individuals in North America (U.S.A. and Canada).

Replacement therapy with human plasma-derived AAT was first licensed in the U.S.A. and is reserved for individuals with severe AATD (AAT serum level < 11 μM) (2), but is currently available in only a few countries, including Germany, Spain and Italy.

Despite such tangible advances in the understanding and management of AATD, many questions related to the condition still wait for definitive answers. To address these issues, a meeting was organized in spring 1996 in Geneva, under the auspices of the World Health Organization. The resulting document (3) recommended development of standards of care for AATD subjects, improvement of case-finding strategies in order to address the discrepancy between expected and diagnosed cases (based on gene frequency data, only 10–50% of cases of AATD are diagnosed in developed countries), and implementation of randomized, placebo-controlled clinical trials to determine the efficacy of intravenous AAT replacement therapy, about which evidence is so far lacking.

Central to these recommendations was the suggestion that an international registry of AATD be established. This was considered a major winning strategy, since only the collection of as large as possible a series of patients can allow better understanding of the natural history of a rare genetic disorder such as is AATD.

To comply with this recommendation, delegates from some National Registries for AATD first met in Stockholm, during the European Respiratory Society annual meeting in September 1996. A general agreement to proceed in this direction having been reached, a series of meetings, with the invaluable support of Bayer, was arranged throughout 1997 and 1998 (Lisbon, March 1997; Berlin, September 1997; Milan, February 1998). During these meetings, a temporary coordinating committee was established, under the chairmanship of Prof. Nikolaus Konietzko, and several issues were extensively discussed. First of all, based on individual experiences from countries already with running registries, criteria to characterize AATD subjects in as standardized a way as possible were identified in order to create a common database for inclusion and follow-up of patients in the International Registry. Among other topics, data confidentiality issues, updating of independent research, plans for future common studies, and sources for funding the Registry, including application to European Union projects, were discussed.

Two years after the first, informal, exploratory meeting in Stockholm, the recommendation from the WHO about an International Registry became reality:

- In September 1998, during a meeting in Geneva, the name, acronym and logo of the Registry were approved (Alpha One International Registry, A.I.R.). It currently includes 12 founding countries (Australia, Canada, Denmark, Germany, Italy, New Zealand, South Africa, Spain, Sweden, Switzerland, The Netherlands and the United Kingdom), with the prospect of broadening to other countries shortly. In addition, the final draft of the questionnaire was approved and its electronic version presented. Finally,
a draft of the statutes of the A.I.R., as a Scientific Society, was discussed.

- Effective from January 1999, the central database located in Malmö (Sweden) began to collect data on AATD subjects electronically transferred by each national registry.
- During a meeting in April 1999 in San Diego (CA, U.S.A.), a new coordinating committee was elected, and the statutes approved.
- The first open Scientific Meeting of the A.I.R. was held in Cernobbio-Como (Italy) in June 1999; it was attended by 120 delegates.
- In October 1999, the A.I.R. made its first public appearance in a meeting of an International Scientific Society, by organizing a crowded symposium during the ERS Annual Meeting in Madrid.

Prof. Robert Stockley, the new chairman of the A.I.R., who has committed himself to taking the A.I.R. into the 21st century, hopes that over the next 5–10 years the society will be able to identify as many AATD subjects as possible, design and implement appropriate clinical trials, advise AATD individuals on how to improve their overall survival and, perhaps, work towards new therapies. He closed the 1st Scientific Meeting of the A.I.R. stating that the registry is now on its way to making a difference. I cannot imagine a better acknowledgement of the work done.

References