Italy

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The health care of rare diseases in Italy is organised around the Istituto Superiore di Sanità with regional and interregional centres of reference.

The Italian legislation in the field of rare diseases is directed by the Decree n° 279 of 18/05/2001. A disease is said to be rare if, according to the requirements of the European Union, its prevalence is less than 1:2.000. The list established in Italy includes 284 rare diseases and syndroms (estimated around 5.000). This decree plans on creating a national network of regional and interregional centres of reference for diagnosis and health care of rare diseases. This decree also defines the role of the Istituto Superiore di Sanità in the field of rare diseases. This decree was supposed to be updated every 3 years, which has not been made for now.

• Regional centres of reference

Regional centres of reference are in charge of:

- Establishing the diagnosis, including biochemical and molecular, of specific diseases and communicating a certificate.
- Providing adapted care and follow up to the patients, also through a collaboration with general practitioners.
- Keeping patients' files and communicating each new case to the national register.

The regional requirements for the recognition of centres are not homogeneous. There is no follow up of the activities of centres and they don't benefit from any specific financing.

Every Italian region has spotted a regional centre of reference for rare diseases and has initiated a register for rare diseases. The list of the centres of reference is available on the website of the National Centre for Rare Diseases (http://www.iss.it/cnmr/), and for some regions on their regional website (as for example the website of the region of Emilia Romagna - http://www.saluter.it/malattierare/). The first epidemiological data should be available at the National Centre for Rare Diseases during the fall of 2009.

• Interregional centres of reference

Interregional centres of reference are in charge of:

- Coordinating the activities of regional centres and making sure the recommendations for diagnosis and therapeutic care, when available, are followed,
- Supporting general practitioner on rare diseases and available drugs,
- Participating in health personnel training and prevention of rare diseases,
- Spreading information and raising general public awareness on rare diseases and having links with patients' organisations,

To date, no interregional genodermatoses centre has been identified.

• The national centre for rare diseases of the Istituto Superiore di Sanità (ISS)

The national centre for rare diseases aims at:

- Coordinating epidemiological, clinical and research activities in the field of rare diseases,
- Gathering data of national registers for rare diseases and organising them into a national register,
- Establishing recommendations for the health care of rare diseases,
- Coordinating and granting research projects.

• The Italian Agency of Drugs: Agenzia Italiana del Farmaco

L'Agenzia Italiana del Farmaco is in charge of promoting investments in the field of research and development and to guarantee, through the simplification of drugs registration procedures, a fast access to innovating medical products and to orphan drugs for rare diseases.

• The reimbursment of rare diseases patients' care

The national care system reimburses:

- All the costs of the examinations performed to establish a diagnosis including molecular and antenatal diagnosis,

- The costs of laboratory examinations, consultations with specialists and hospitalizations
- The costs of drugs, medical devices and in some regions emollients, antiseptics, (nutritional supplements), sun screens, dressings and bandages.

Transportation is not reimbursed.

• National recommendations for health care of rare diseases patients

The national centre for rare diseases of the Istituto Superiore di Sanità is in charge of establishing recommendations for diagnosis, follow up and treatment of rare diseases. These recommendations are prepared by a group of experts following the Delphi method.

Genodermatoses recognised by the health system in Italy

• The genodermatoses targeted by the partners of the TAG project managed by the Italian health system

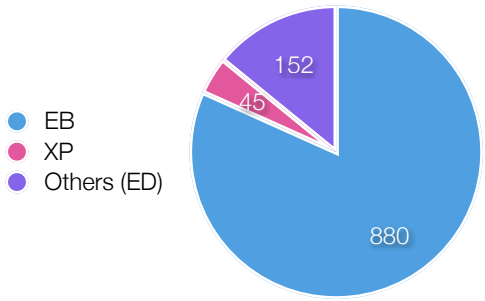
The following genodermatoses, targeted by the partners of the TAG project, are managed by the Italian national care system:

- Congenital ichthyosis (including X-linked ichthyosis, Netherton Syndrome, all the types of Lamellar Ichtyosis as well as congenital nonbullous ichtyosiform erythroderma, Harlequin syndrome, ichthyosis hystrix)
- Epidermolytic hyperkeratosis
- Progressive symmetric erythrokeratodermia
- Erythrokeratodermia variabilis
- KID Syndrome
- Sjögren-Larsson Syndrome
- Refsum Disease
- Conradi-Hunermann Syndrome
- Inherited Epidermolysis bullosa
- Xeroderma pigmentosum
- Incontinentia pigmenti
- Neurofibromatosis

• The genodermatoses targeted by the partners of the TAG project not managed by the Italian care system

Hypohydrotic Ectodermal Dysplasia and Palmoplantar Keratoderma patients cannot get free diagnosis and care (only Epidermolytic Hyperkeratose (including Epidermolytic Palmoplantar Keratoderma) and Erythrokeratoderma are managed). There is no centre of reference officially recognised and there is no data collected for these diseases.

Italian registers for Epidermolysis bullosa, Ectodermal dysplasia and Xeroderma Pigmentosum



Number of cases of Epidermolysis Bullosa (EB), Xeroderma Pigmentosum (XP) and Ectodermal Dysplasia patients (others - ED)

• The Italian register for epidermolysis bullosa and the Italian register for ectodermal dysplasia

Gianluca Tadini (Centre for Inherited Cutaneous Diseases at the Institute of Dermatological Sciences of Milano University) is in charge of the national register for inherited epidermolysis bullosa and the national register of ectodermal dysplasia. These registers have been updated in 2009.

• The Italian register for epidermolysis bullosa: 880 cases

Period	Number of cases
1991-2002	706
2003-2007	116
2008-2009	58
Total	**880**

Type	Frequency	%
Epidermolytic Epidermolysis Bullosa	258	29,3
Junctional Epidermolysis Bullosa	82	9,3
Dermolytic Epidermolysis Bullosa	524	59,5
Epidermolysis Bullosa (others)	16	1,9
Total	880	100

Italian register of epidermolysis bulllosa 1991-2009 (880 cases)

• The Italian register for ectodermal dysplasia: 152 cases

152 cases are registered including 40% confirmed by molecular diagnosis.

• The Italian register for xeroderma pigmentosum : 45 cases

Kleijer WJ, Laugel V, Berneburg M, Nardo T., Fawcett H, Gratchev A, Jaspers NGJ, Sarasin A, Stefanini M, Lehmann AR (2008) DNA Repair, 7: 744-750. Incidence of DNA repair deficiency disorders in Western-Europe: Xeroderma pigmentosum, Cockayne syndrome and Trichothiodystrophy

The incidence of Xeroderma Pigmentosum in Western Europe has been established for the first time a 2,3 on one million of viable children

Group Xeroderma Pigmentosum (XP)	Italy 30 cases	Western Europe 89 cases including the 30 Italian patients
XP-A	17 %	15,7 %
XP-B	-	-
XP-C	43 %	60,7 %
XP-D	10 %	11,2 %
XP-E	27 %	2,2 %
XP-F	3 %	4,5 %
XP-G	-	5,6 %
XP-variant	14,6 %	10,6 %

Xeroderma Pigmentosum: frequency of the NER defective complementation groups

Year of birth	Number of patients		
	Total	Autochtonic	Non autochtonic
<1940	3	3	-
1940-1959	7	7	-
1960-1969	7	7	-
1970-1979	9	8	1
1980-1989	12	11	1
1990-1999	6	5	1

Distribution in time of xeroderma pigmentosum patients living and diagnosed in Italy

Regional centres for genodermatoses health care

- Inherited Epidermolysis bullosa: 35 recognised centres
- Congenital Ichthyosis: 43 centres
- Neurofibromatosis : 62 centres
- Xeroderma pigmentosum : 31 centres
- Incontinentia pigmenti : 38 centres

‣ 2008 & 2009

Recommendations for diagnosis of inherited epidermolysis bullosa

A panel of 18 experts (dermatologists, pediatricians, geneticists, molecular biologists, ethicists and a patients' organisation's representative) has worked for 2 years on the recommendations for diagnosis of inherited epidermolysis bullosa.

The multidisciplinary health care of children affected by epidermolysis bullosa, ichthyosis, neurofibromatosis and tuberous sclerosis at the Ospedale Pediatrico Bambino Gesù, Rome

The health care of these patients is organised around a "case manager".

• Therapeutic and multidisciplinary health care of inherited epidermolysis bullosa

The case-manager is the dermatologist. The health care begins during the antenatal period. Later organ complications are infections, nutrition problems, oesophagus stenosis, dental problems, anesthesia and organ surgery: pylorus stenosis, hands, etc... In 2009, 12 patients were followed in day hospital. 45 patients were hospitalized in 2008. The hospital registered 362 admissions, 208 hospitalisations and 154 day hospital for main diagnosis and treatement of for secondary diagnosis.

Admission of EB patients	Number of admissions
Day hospital	154
Hospitalizations	208
Total	362

Number of admissions of EB patients at the Ospedale Pediatrico Bambino Gesù

Year	Number of EB patients in day hospital
2007	4
2008	11
2009	12

Number of EB patients in day hospital at the Ospedale Pediatrico Bambino Gesù

Departement	Number of EB hospitalized patients
Dermatology	19
Pediatrics	4
Intensive Care	3
Digestive Surgery	10
General Surgery	1
Infectious diseases	5
Neurology	1
Genetics	1
Plastic Surgery	1
Total	**45**

Number of EB patients hospitalisés in 2008 in Ospedale Pediatrico Bambino Gesù

• Multidisciplinary health care for neurofibromatosis patients

The case-manager is Cristina Digilio from the Department of Genetics of the Ospedale Pediatrico Bambino Gesù, Rome. She follows 20 patients per month. Involved specialists are the dermatologist, ophtalmologist, neurologist, psychologist, neurosurgeon, general surgeon, plastic surgeon, orthopedist, ENT, endocrinologist and cardiologist. The examinations performed in the follow up of the neurofibromatosis patients are the abdominal ultrasound, the blood and urine tests, the urine vanillylmandelic acid level, the mesure of the blood pressure.

The development of a national network for genodermatoses

• The working group on rare diseases of the "Associazione Dermatologi Ospedalieri Italiani"

A national network for epidermolysis bullosa has been under development for the last few years. Links are already existing for other genodermatoses but they have to be developed. The creation of a working group on rare diseases within the organisation of Italian Hospital Dermatologists (ADOI-Associazione Dermatologi Ospedalieri Italiani) should facilitate the development of networks for genodermatoses. This group is made of 27 members.

‣ 2008 & 2009

• Conventions with the Ospedale Pediatrico Bambino Gesù

- A convention between the Istituto Dermopatico dell'Immacolata (IDI) and the Ospedale Pediatrico Bambino Gesù

Since 2000, an active and close collaboration has developed between the Istituto Dermopatico dell'Immacolata (IDI) of Roma to provide a global assistance to patients without having them travelling from one centre to another. This collaboration was formalized in 2004 by a convention.

- Conventions between Debra and the Ospedale Pediatrico Bambino Gesù

In 2004, a convention was signed with DebRA Italia. In 2008, a new convention "In ospedale con Ebby" was signed to create a specific room for epidermolysis bullosa patients.

- A convention between Modena University and the Ospedale Pediatrico Bambino Gesù

In July 2008, a convention was signed with Modena University to develop gene therapy at the Ospedale Pediatrico Bambino Gesù.

Training on rare dermatological diseases and on epidermolysis bullosa

• Training on rare diseases

The next training session on rare dermatological diseases will take place in Roma, November 20-21st 2009.

• Training of specialists involved in the health care of inherited epidermolysis bullosa

The training of specialists involved in the health care of inherited epidermolysis bullosa is made thanks to a continuous collaboration between dermatologists and other specialists involved to illustrate on the job the specificity of this disease and avoid secondary complications.

Organisations for genodermatoses patients in Italy

Patients' organisations are very active and well developed:

• Organisation for epydermolysis bullosa patients

Epidermolysis bullosa are gathered within DEBRA Italy, www.debraitaliaonlus.org

• Organisation for ichthyosis patients

Ichthyosis patients are gathered within UNITI, www.ittiosi.it

• Organisations for neurofibromatosis patients

Neurofibromatosis patients are gathered within 5 organisations:

- ANANas, www.ananasonline.it
- ANF, www.neurofibromatosi.org
- IOCISONO, www.associazioneiocisono.it
- LINFA, www.associazionelinfa.it
- AMINF, www.associazioni.milano.it/itsos/aminf/index.html

• Organisation for anhidrotic ectordermal dysplasia

Anhidrotic ectodermal dysplasia patients are gathered within ASSOANDE, www.assoande.it

ZOOM >>> "In ospedale con Ebby": Debra Italy's project of equipping a room for epidermolysis bullosa patients in the Ospdale Pediatrico Bambino Gesù

Debra Italy supports epidermolysis bullosa patients through the following actions: communication of the diagnosis, organisation of consultations, participation in the development of specific recommendations, public authorities awareness raising to improve the help brought to patients, awareness raising in schools, organisation of holiday trips. Debra Italy is member of the Board of the Italian Federation of Rare Diseases - UNIAMO and of the EURORDIS board. Debra Italy signed in July 2008 a convention with the Ospedale Pediatrico Bambino Gesù: "In ospedale con Ebby". This convention will enable

the equipping of a room for the epidermolysis bullosa patients who are hospitalized or coming to the day hospital. The construction is planned for 2009.

European collaborations: the *GENESKIN* network and experience

• Rare genetic skin diseases: advancing diagnosis, management and awareness through a European network

GENESKIN is an acronyme for the Rare genetic skin diseases: advancing diagnosis, management and awareness *through a European network* project. This action is coordinated by Prof. Giovanna Zambruno of the Istituto Dermopatico dell'Immacolata - IRCCS in Rome. It was financed by the European Commission for 3 years: July 1st 2005 – June 30 2008.

• GENESKIN gathered 32 clinical centres (27 organizations), research centres and patients' organisations from 12 European countries

• GENESKIN enabled the development of a European network for 5 groups of rare skin diseases

This network, through a website, helps raising the awareness on these diseases and spreading the knowledge. This network also participates in improving diagnosis and health care. It enabled ratifying new diagnosis tools, encouraging research on rare diseases. Through this network, training activities on specific groups of diseases have been organised as well as experts meetings on specific subjects (17 meetings in 8 countries gathering 665 participants in total). Finally, this network made possible the creation of a group of ethicists and the elaboration of an ethical document on genetic counseling for genodermatoses.