Introduction on Rare Neurologic Diseases and the role of the WFN

Antonio Federico, Dept Medicine, Surgery and Neurosciences, Medical School, University of Siena, Italy

No disclosure

Rare Diseases.
Learning objective n.1: What are rare diseases?

- A disease is considered rare in USA if it affects more than 250.000 persons (1/1.200)
- In Europe, 5/10.000
- In Japan, 4/10.000
- WOH indicated in 5.000 these conditions, the majority of them having a genetic basis and affecting the nervous system togheter with other systems

- Rare diseases and orphan therapies are one of the many unacceptable inequalities of our health system.
- A patient with a rare disease is doubly unfortunate: he has a disease like many others but has troubles in finding a doctor expert in his disease.
- He has the general problem of not having readily available therapies.
- Finally, his hopes for the future are not good, as pharmaceutical companies are not interested in developing drugs that have a limited market (orphan drugs)

Common Opinions on Rare Diseases

Rare Diseases. Learning objective n.1: What are rare diseases?

Opinions	*Comments*
Diseases that are rare	They are rare if considered in singularly, but are frequent as a group
The clinical signs are difficult for the diagnosis	There may exist some guidelines for the clinical suspicion
Laboratory investigations are too sophisticated and not easily available	There exist several first level investigations
It is very hard and time consuming the investigation strategy in relationship to the therapeutic possibilities	For many rare diseases therapeutic strategies exist: they are more effective if started early. It might be useful the genetic counselling and also the development of Scientific knowledge.

Rare Diseases
Learning objective n.2: How many are rare neurologic diseases?

NEUROLOGICAL

More than 60%

NON NEUROLOGICAL

40%

The neurologist has a key role in the diagnosis and treatment of rare diseases

Learning objective n.3: Guideline for diagnosis of rare neurologic diseases?

Guidelines for Diagnosis of a rare neurological disease

- **Type of inheritance (dominant, X-linked, maternal, recessive, sporadic)**
- **Evolution**
- **Clinical symptoms**
- **Multisystem involvement**
- **Neurological involvement (central, peripheral nervous system, muscle, endocrine, etc)**

Clinical approach to a patient with a rare neurological disease

Deep family history
Personal anamnesis
General and neurological examination
Laboratory investigations (EEG, EMG, NCV, Neuroimaging, Neuropsychological tests, etc)
CSF examination
Biochemical and molecular investigations

Confirmation of the diagnosis

Biochemical investigations in urines, serum, peripheral leucocytes or cultured fibroblasts
Neurophysiological investigations
Conventional and non conventional neuroimaging investigations
Biopsy (bone marrow, skin, muscle, nerve, olfactory mucosa, tonsils, brain??, etc)
Chromosomal analysis
Molecular genetic analyses

Learning objective n.3: Guideline for diagnosis of rare neurologic diseases

Rare diseases with common symptoms

- ***Cerebrovascular diseases***: **CADASIL, Protein S deficiency, Fabry disease, Pseudoxanthoma elasticum, MELAS, etc**
- ***Leucodystrophies***: **Metachromatic leucodystrophy, Krabbe, Canavan, Vanishing white matter disease, Megalocystic leucodystrophy, Alexander d., Spastic paraparesis with leucodystrophy and atrophy of corpus callosum; Paelizaeus Merzbacker, etc**
- ***Ataxia*: Vitamin E deficiency, Bassen Kornzweig, SCAs, Ataxia-telangiectasia, Friedreich, Niemann Pick, GM2 Gangliosidosis, etc**
- ***Parkinson***: **mitochondrial diseases, adult celiac disease, pseudo-hypo-para-thyroidism, synnucleinopathies, taupathies, etc**
- ***Epilepsy*: numerous metabolic diseases, MERRF, Double cortex syndrome, facomatoses, cortical dysplasias, etc**
- ***Peripheral neuropathy*: CMT, Tomacular neuropathy, giant axonal neuropathy, Congenital hypomyelinating neuropathy, Dejerine Sottas, Refsum, Tangier, Amiloidosis, Poliglucosan syndrome, Churg-Strauss S., etc**

WHO and WFN

Learning objective n.4: WFN and Rare Neurologic Diseases

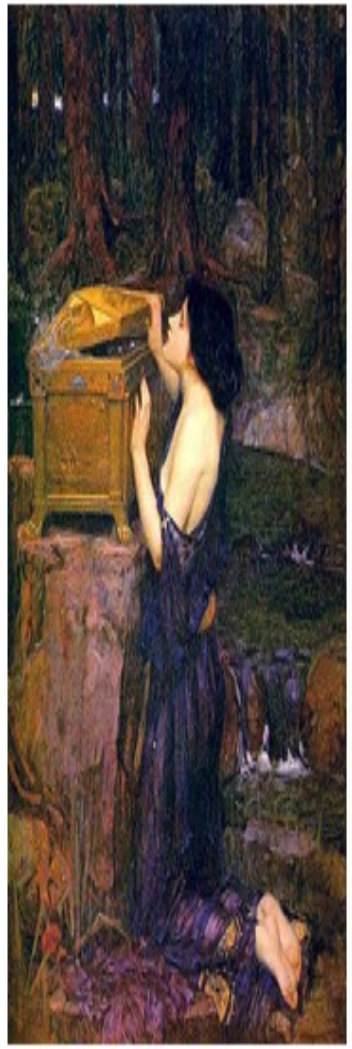
- **Advisory Group for the Revision of the ICD-10 Diseases of the Nervous System Chapter (Chair prof. R. Shakir) with the review of the Neurology Chapter also from a rare diseases perspective.**
- **Specialist Study Group on Rare Neurologic Diseases approved on 2021 chaired by prof. A. Federico with the aim to promote within the world neurology the knowledge of rare neurologic diseases, their diagnosis and care.**

Learning objective n.5: Historical and final considerations on Rare Neurologic Diseases in Clinical Neurosciences

The study of rare diseases: butterfly collecting or an entrèe to understanding common conditions?

K. Talbot

Pract. Neurol. 7: 210-211, 2007



John William Waterhouse *Pandora* (1896)

Rare Neurological Diseases:

a Pandora's box for Neurology

and

Neurosciences

Nature is nowhere accustommed more openly to display her secret mysteres than in cases where she shows traces after working apart from the beathen path; nor is there any better way to advance the proper practice of medicine than to give our minds to the discoveries of the usual law of nature by careful investigation of causes of rarer forms of diseases. For it has been found, in almost all things, that what they contain of useful or applicable is hardly preceived under we are deprived of them or they become deranged in some way.
William Harvey, 1647