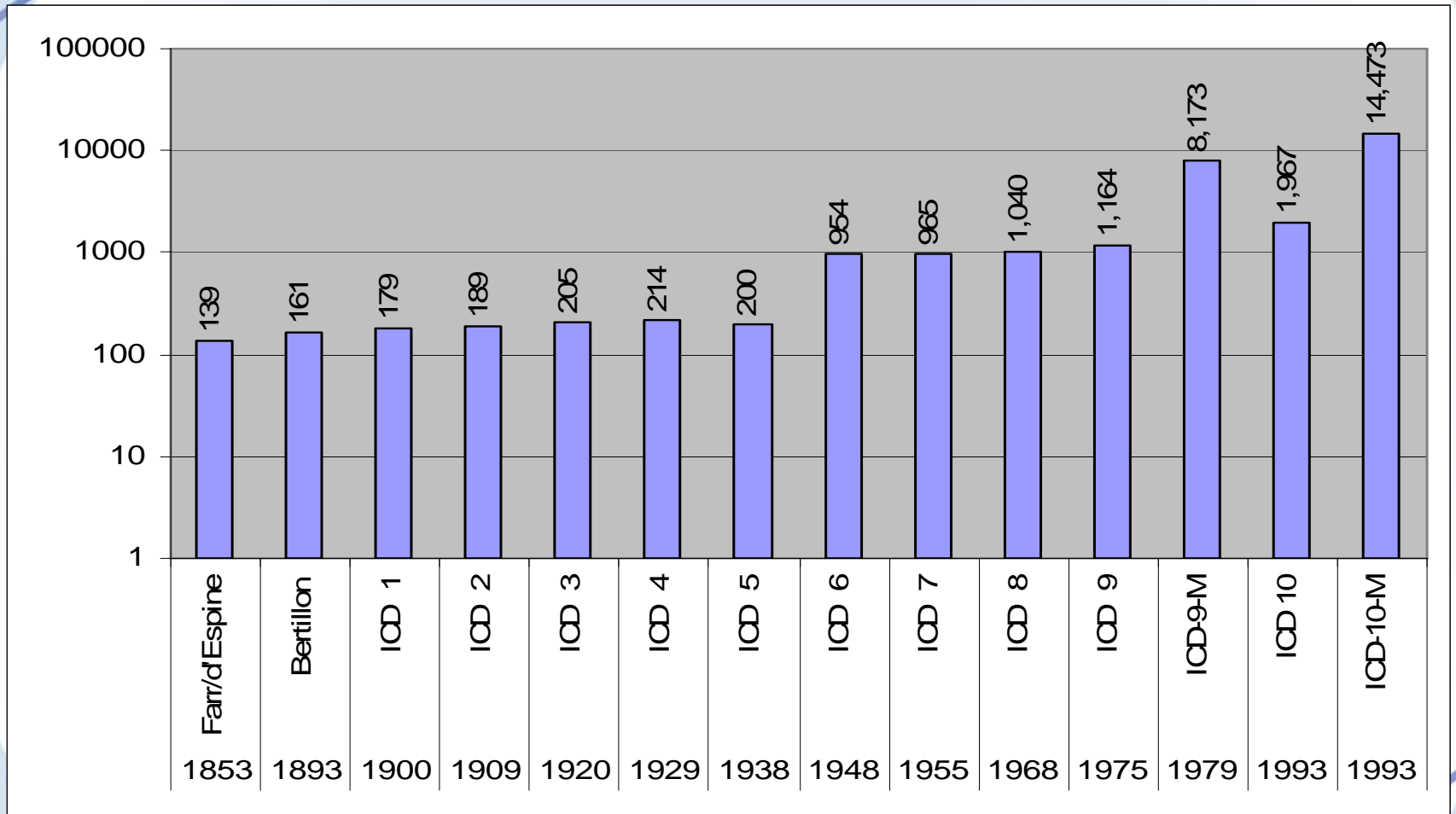


International Classification of Diseases in the field of rare diseases Revision process

Ségolène Aymé
Chair of the Topic Advisory Group
At WHO

ICD Revisions



With the courtesy of WHO

... BUILDING BLOCKS OF HEALTH
INFORMATION ...

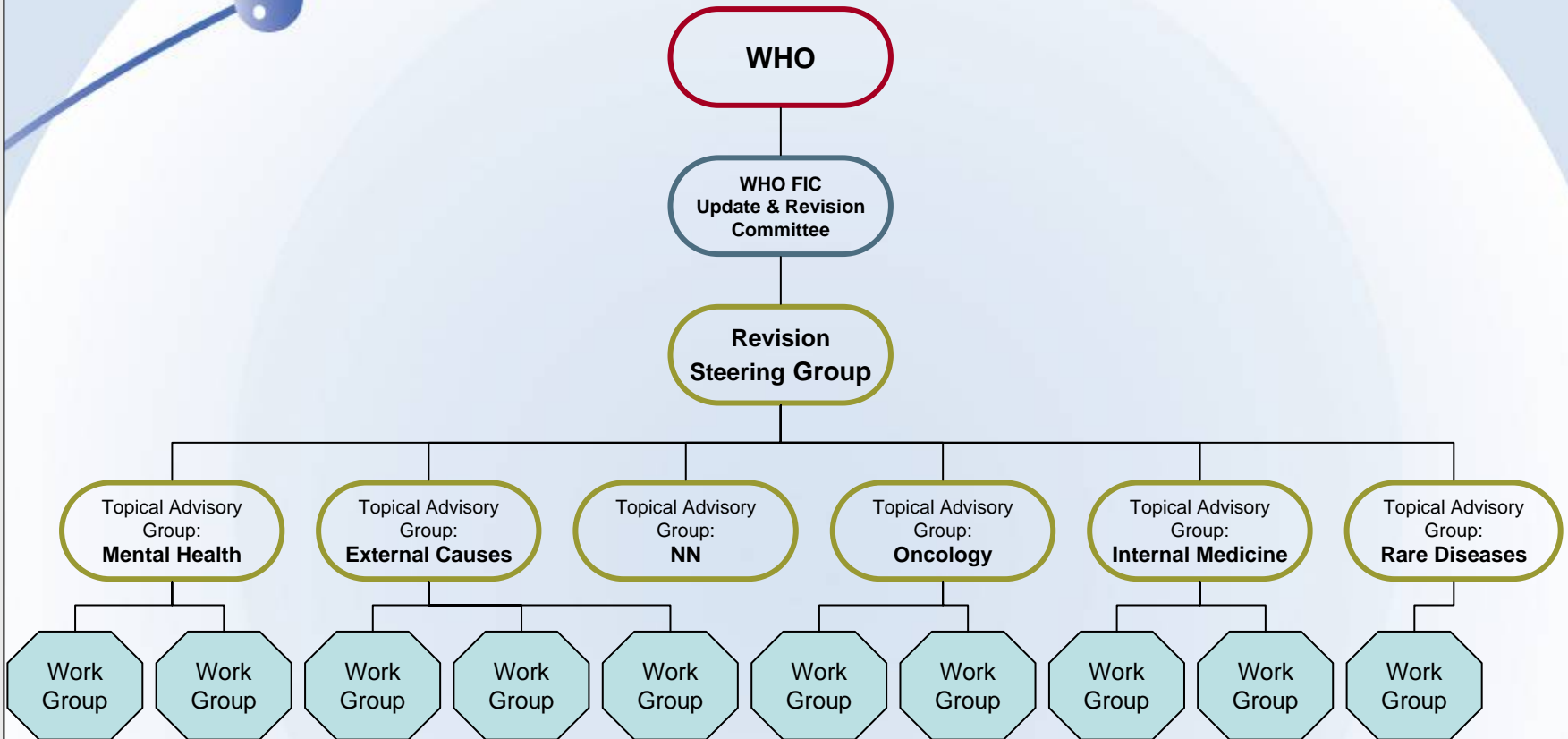
Disease: a concept linked to level of knowledge

- Recognisable pattern of signs and symptoms
 - Clinical approach
- with a unique mechanism
 - Physiopathological approach
- with unique course and prognosis
 - Clinical evolution approach
- with a unique response to intervention and treatment
- with an established cause
 - Genetic origin

ICD-10 Revision organization structure

FIELD TRIALS

K
M
S
P
O
R
T
A
L



ICD-10 Plus

ICD-11 draft

ICD Terminology

Application

ICD-10 + WEB Application

Hi-Ki
Joint-authoring Tool
WIKI like application

Protégé/OWL LEXGRID

Key Tasks

- Clinical Modification Owners enter their **CM** version Codes
- TAG and **Workgroups** enter proposals

- TAG Experts for ICD-11
- WHO editors
 - Taxonomic rules
 - Definitions
 - Diagnostic criteria

- Ontology Model
- Linkages between ICD and:
 - SNOMED
 - Other ontology & terminologies
- Clinical interface algorithms

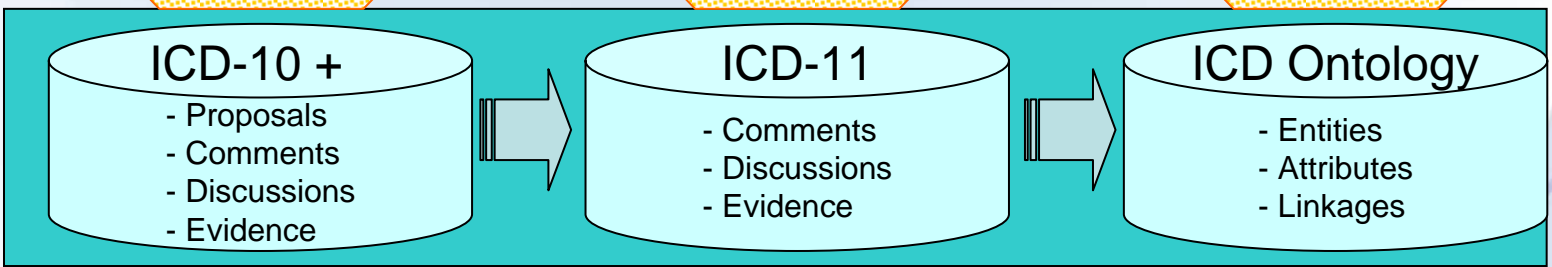
Access

- ANY USER can **POST** proposals or comments.
- ANY USER can **REVIEW** other proposals and discuss.

- **ALL USERS** can see drafts and comment.

- **ALL USERS** can see drafts and comment

Technical Layer



Hierarchy of Hiki Authority by ICD Domain

- 0 Revision Steering Committee
- 1 Revision Domain/Topic Working Groups
- 2 Accredited Experts
 - Designated by Working Group Members
- 3 Accredited Persons
 - Designated by Experts
- 4 Registered Interested Persons (Public)

Tentative timeline

- 2010 : **Alpha version** (ICD 10+ → ICD 11draft)
 - +1 YR : **Commentaries and consultations**
- 2011 : **Beta version & Field Trials Version**
 - 20+2 YR : **Field trials**
- 2013 : **Final version** for public viewing
 - 2014 : **WHA Approval**
- 2015+ **implementation**

RDTF WG Coding and Classification

– RDTF Workshops:

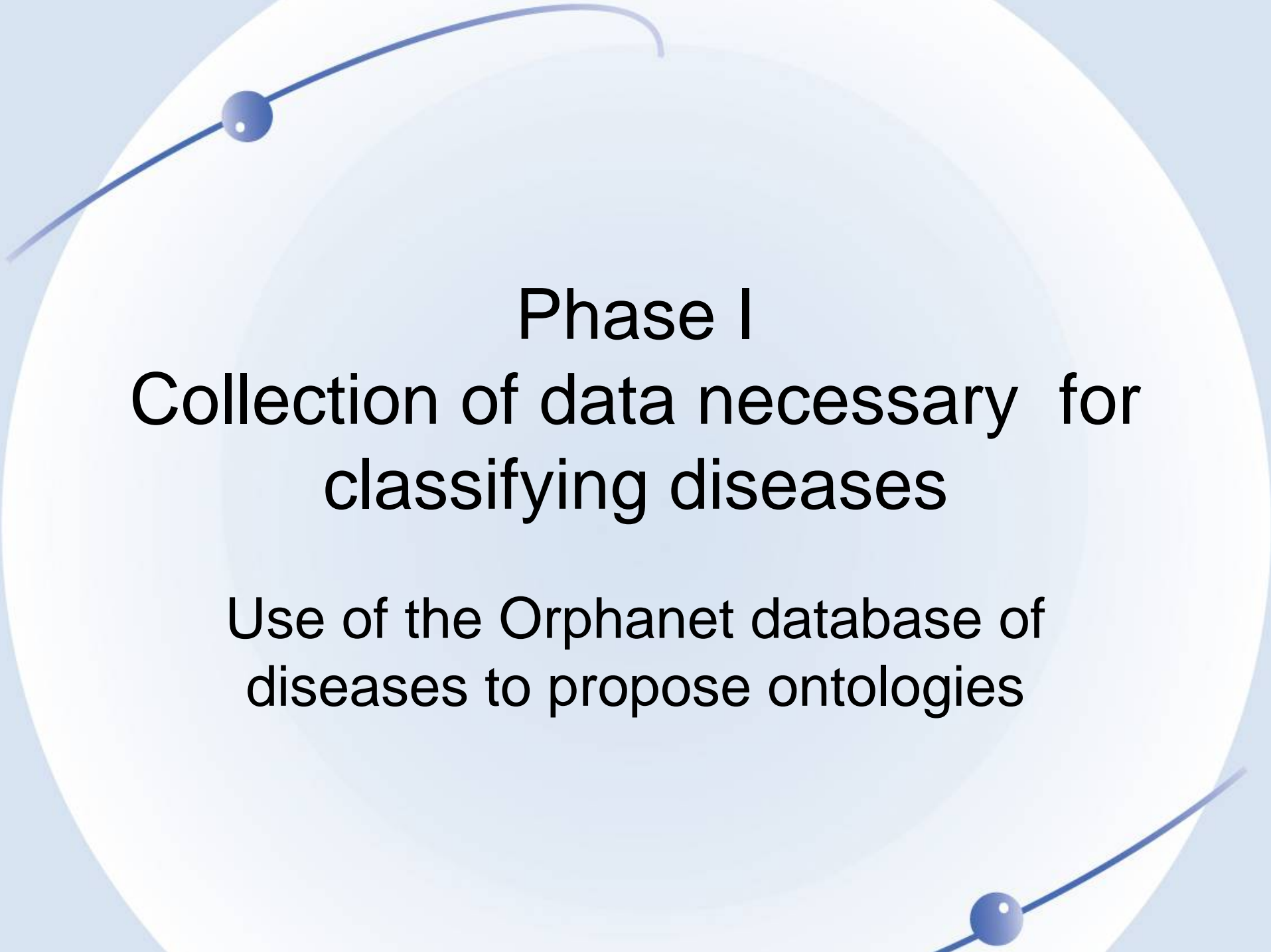
- 11 October 2006**
- 2 May 2007**
- 13 November 2007**
- 6 February 2008**

– Participation to WHO revision committee:

- 15-18 April 2007 in Tokyo**
- 29-31 October 2007 in Trieste**
- 9-11 April 2008 in Geneva**

Principles guiding action

- Rare Diseases should be traceable in mortality and morbidity information systems
- There are two categories of RD
 - The recurrent RD (about 1,500)
 - should have a specific code in ICD11
 - The ultra-rare (over 4,000)
 - should be coded as “other specific RD”
 - within relevant subcategory



Phase I

Collection of data necessary for classifying diseases

Use of the Orphanet database of
diseases to propose ontologies

Orphanet platform as a tool

- Relational database of 5,800 rare diseases
 - Encyclopaedia
 - Genes + proteins + ICD10 + MIM + MeSH
 - Epidemiology, mode of inheritance, age at onset + textual information
 - ontologies
- Shared tools between partners
 - Access to files
 - Protected website with all data

Simple search: by disease name

orphanet The portal for rare diseases and orphan drugs

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Homepage » Rare diseases » Search

SIMPLE SEARCH OTHER SEARCH OPTION(S)

Rett Disease name > Alphabetical list

Epidemiologic data

Orpha number: ORPHA778
Prevalence: 1-9/100 000
Mode of inheritance: X-linked dominant
Age of onset: Neonatal/infancy
ICD 10 code: F84.2
MIM number: 312750

Summary

Rett syndrome (RTT) is a severe neurodevelopmental disorder affecting the central nervous system. Prevalence is estimated at 1/30,000. RTT primarily affects females, making it one of the most common genetic causes of severe intellectual deficiency in females. RTT is characterised by apparently normal development for the first 6-18 months of life followed by the loss of acquired fine and gross motor skills and the ability to engage in social interaction, and the development of stereotypic hand movements. Scoliosis is seen in about 87% of patients by the age of 25 years. There is a wide variability in the rate of progression and severity of the disease, and several atypical variants are recognised. In addition, a number of males with a phenotype comparable to females with classical or atypical RTT have been described, as well as rare males with a severe neonatal-onset encephalopathy and prominent breathing abnormalities. Despite the identification of mutations in the X-linked gene *methyl CpG-binding protein 2 (MECP2)* in the majority of RTT patients, the aetiology remains unclear. More recently mutations in two other genes, *cyclin-dependent kinase like 5 (CDKLS)* and *Netrin G18*, have been identified in patients with a clinical phenotype that strongly overlaps with RTT. The diagnosis of RTT is clinical, based on established criteria (such as Trevathan diagnostic criteria, revised in 2001). As pathogenic *MECP2* mutations in RTT patients are mostly *de novo*, the recurrence risk for future pregnancies is low, although gonadal mosaicism cannot be excluded. Prenatal screening should be discussed for families with a proband having a pathogenic mutation. Management is mainly symptomatic and individualised, focussing on optimising each patient's abilities. A dynamic multidisciplinary approach is most effective, with specialist input from dietitians, physiotherapists, occupational therapists, speech therapists and music therapists. Attention needs to be paid to scoliosis and the development of spasticity as well as to the development of effective communication strategies. Psychosocial support for families is essential. Pharmacological approaches aim at improving sleep disturbances (melatonin), breathing disturbances, seizures, stereotypic movements and general well-being (L-carnitine). RTT patients have an increased risk of life threatening arrhythmias associated with a prolonged QT interval, and so avoidance of a number of drugs is recommended (prokinetic agents, antipsychotics, tricyclic antidepressants, antiarrhythmics, anaesthetic agents and antibiotics). The clinical picture evolves in stages over a number of years, culminating in motor deterioration and ultimate demise. *Authors: Dr S. L. Williamson and Prof. J. Christodoulou (January 2006)*.

RELEVANT INFORMATION

additional information

> website

health care resources

> clinics (428)
> clinical laboratories (76)
> patients organisations (42)
> orphan drugs (0)

research activities

> research projects (35)
> clinical trials (0)
> registries/databases (3)

related services

> glossary
> prevalence

getting involved

> register for the newsletter
> contact other patients/families
> participate in clinical research

Services for professionals

> Professional encyclopaedia
> Search by sign
> Emergency guidelines
> Orphanet Journal Of Rare Diseases
> Newsletters
> Powerpoint

Services for patients

> Patient encyclopaedia
> Information about a disease
> Patient organisations
> Clinics
> Participate in clinical research
> Contact other patients / families
> Training sessions

NEWS

Orphanet's 10th birthday Conference presentation highlights
EC Rare Disease webpages
French National Plan for Rare

Scientific news

New scientific facts (+)
Clinical signs (2/7/7)

DETAILED INFORMATION

Practical genetics English(2006,pdf)
Review article English(2004)

Get Adobe Reader

'Review articles/Practical genetics'

Simple search: by gene name

Languages Français | **English** | Español | Deutsch | Italiano | Portugueso

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SIMPLE SEARCH

MECP2

Disease name
 Gene name or symbol
 MIM number
 ICD 10 code
 Orpha number

OTHER SEARCH OPTION(S)
> Alphabetical list

→ OK

::: 5 Result(s)

[Angelman syndrome](#)

[Autism](#)

[Mental retardation - progressive spastic](#)

[Mental retardation X-linked - psychosis](#)

[Rett syndrome](#)

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SIMPLE SEARCH

Rett

Disease name
 Gene name or symbol
 MIM number
 ICD 10 code
 Orpha number

OTHER SEARCH OPTION(S)
> Alphabetical list

→ OK

::: Rett syndrome

Synonym(s):

Orpha number: ORPHA778
Prevalence: 1-9/100 000
Mode of inheritance: X-linked dominant
Age of onset: Neonatal/infancy
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SUMMARY

Rett syndrome (RTT) is a severe neurodevelopmental disorder affecting the central nervous system. Prevalence is estimated at 1/10,000. RTT primarily affects females, making it one of the most common genetic causes of severe intellectual deficiency in females. RTT is characterised by apparently normal development for the first 6-18 months of life followed by the loss of acquired fine and gross motor skills and the ability to engage in social interaction, and the development of stereotypic hand movements. Scoliosis is seen in about 87% of patients by the age of 25 years. There is a wide variability in the rate of progression and severity of the disease, and several atypical variants are recognised. In addition, a number of males with a phenotype comparable to females with classical or atypical RTT have been described, as well as rare males with a severe neonatal-onset encephalopathy and prominent breathing abnormalities. Despite the identification of mutations in the X-linked gene *methy/CpG-binding protein 2 (MECP2)* in the majority of RTT patients, the aetiology remains unclear. More recently mutations in two other genes, *cyclin-dependent kinase like 5 (CDKL5)* and *MeCP1 G18*, have been identified in patients with a clinical phenotype that strongly overlaps with RTT. The diagnosis of RTT is clinical, based on established criteria (such as Trevathan diagnostic criteria, revised in 2001). As pathogenic *MECP2* mutations in RTT patients are mostly de novo, the recurrence risk for future pregnancies is low, although gonadal mosaicism cannot be excluded. Prenatal screening should be discussed for families with a proband having a pathogenic mutation. Management is mainly symptomatic and individualised, focussing on optimising each patient's abilities. A dynamic multidisciplinary approach is most effective, with specialist input from dietitians, physiotherapists, occupational therapists, speech therapists and music therapists. Attention needs to be paid to scoliosis and the development of spasticity as well as to the development of effective communication strategies. Psychosocial support for families is essential. Pharmacological approaches aim at improving sleep disturbances (melatonin), breathing disturbances, seizures, stereotypic movements and general well-being (L-carnitine). RTT patients have an increased

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Disease name
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 ICD 10 code
 Orpha number

OTHER SEARCH OPTION(S)
> Alphabetical list

→ OK

::: 1 Result(s)

[Methyl CpG binding protein 2 \(Rett syndrome\)](#)

Inserm

Ministère de la Santé
Ministère des Solidarités
et de la Prévention

EUROPEAN UNION
LIFE-COOPERATION

HON @ CODE

Orphanet | Rare diseases | Orphan drugs | Clinics | Clinical laboratories | Research projects | Research and trials | Patient organisations

Phase II: analysis of data to define classification approach

- Comparison of ICD10 codes
 - Between databases of rare diseases
 - To identify true mismatches
 - To have a typology of possible approaches
- Collection of classifications
 - already published
 - By medical specialty: established by Orphanet

Phase III: Document true mistakes in ICD10

- Due to
 - the evolution of knowledge
 - the structure of the current classification
- Propose an evolution to WHO
 - ICD10+
 - Wikipedia-like tool

Ex: possible different interpretations

- CADASIL (OMIM 125310)
 - UKGTN I77.8
 - Other specified disorders of arteries and arterioles
 - Orphanet F01.1
 - Multi-infarct dementia (In: vascular dementia)

Ex: incorrect specific code

- Marfan syndrome

- Q87.4

- In: Q87 Other specified **congenital malformation** syndromes affecting multiple systems

Could have been included in

- M30-M36 Systemic connective tissue disorders

Ex: inappropriate categories

- VATER association
 - Q87.2 Congenital malformation syndromes predominantly involving limbs
 - Holt-Oram
 - Klippel-Trenauney-Weber
 - ...
 - VATER

VATER = **V**ertebral defects, **A**nal atresia, **T**racheo**E**sophageal fistula with esophageal atresia and **R**adial dysplasia

Problematic groups of diseases

- Systemic diseases (Internal medicine)
 - Marfan disease in Q87.4 (malformations)
 - Amyloidosis in E85 (metabolic disorders)
 - Mastocytosis in:
 - Q82 (Other congenital malformations of skin)
 - C96.2 (Malignant mast cell tumour)
 - Mediterranean fever
 - E85.0 (Non-neuropathic heredofamilial amyloidosis) in Metabolic disorders

Ex: Problematic groups of diseases

- Skin diseases
 - Some skin diseases are coded as malformations
 - Q80 Congenital ichthyosis
 - Q81 Epidermolysis bullosa
 - Q82.1 Xeroderma pigmentosum
 - *etc.*

Problematic groups of diseases

- Mental retardation
 - ICD-10 codes for MR are based on QI
 - Coding can only be done on an individual basis
 - Coding for syndromes with MR it is, therefore, not possible

Phase IV: Propose a new classification

- Proposal from the Topic Advisory Group
 - Criteria: Scientific evidence + clinical utility + health system utility + public health usefulness
 - Draft by Orphanet team: core concepts and structures
 - First review by TAG members
 - Second Review open to all for comments



Thank you for your attention

Register with us if you wish to be
involved