Main aspects of neural tube defects (NTD) and the new Orphanet classification

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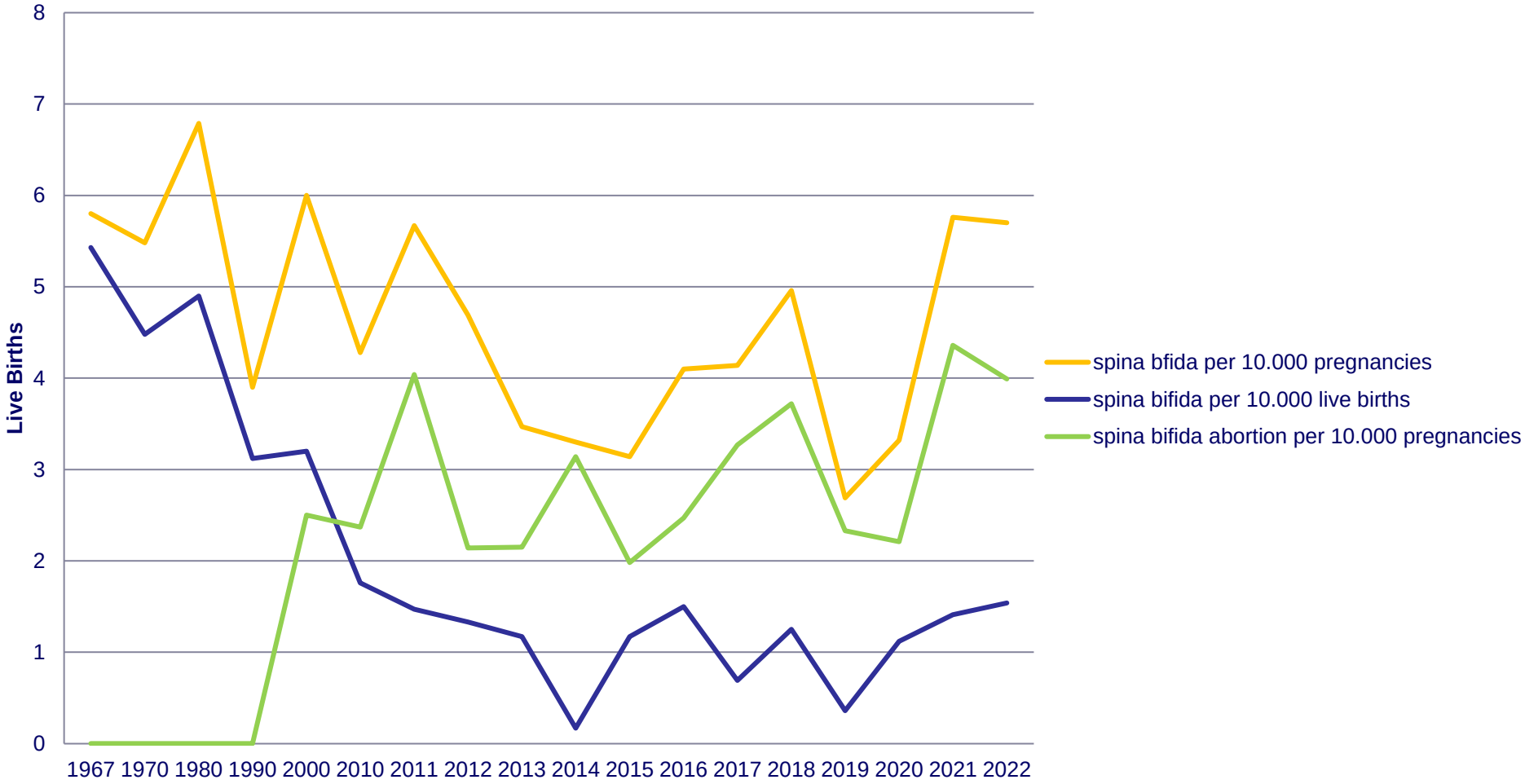
Oslo University Hospital

- Part 1 Main aspects of NTDs
  - Epidemiology
  - Embryology
  - Genetics and environment
  - Timeline open dysraphism
  - Fetal surgery

- Part 2 Orphanet
  - Nomenclature
  - «Old» classification
  - ICD-10
  - Main groups «old» and «new»
  - Orphanet use for the clinician
  - Orphanet use in Norway

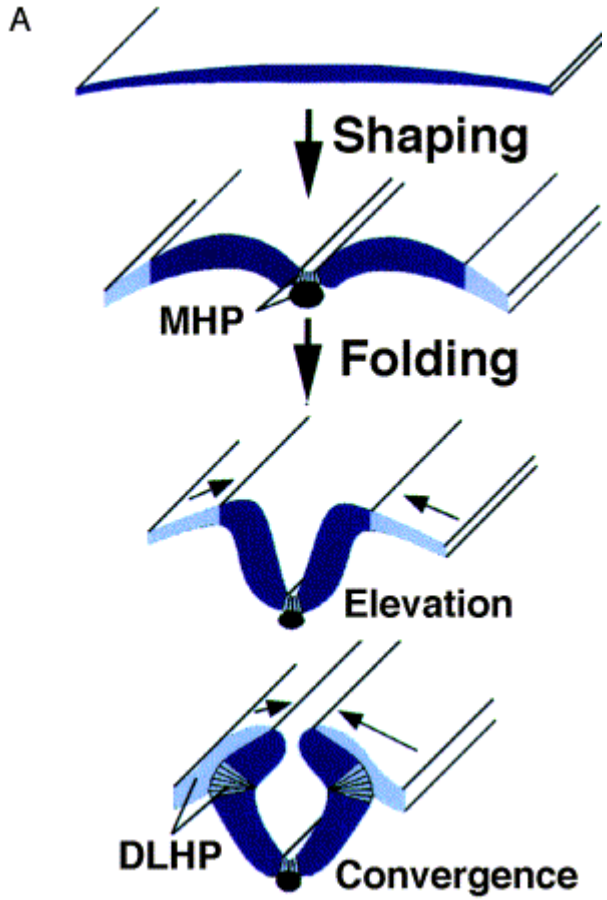
Part 1 – main aspects of NTDs

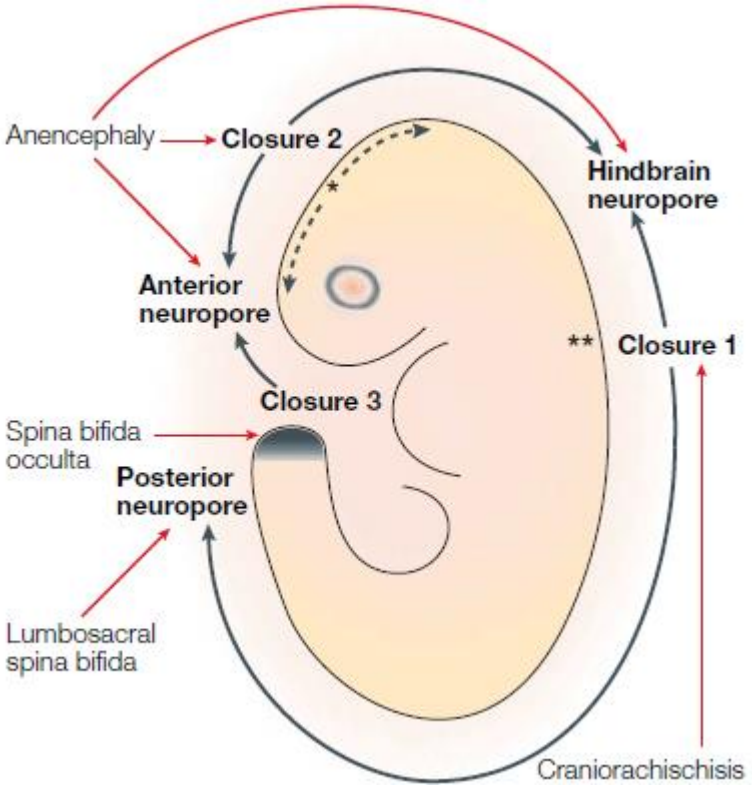
Epidemiology



Embryology

Neurolation

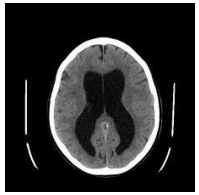


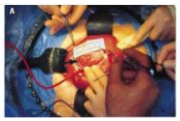


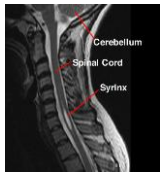
Genetics and environment

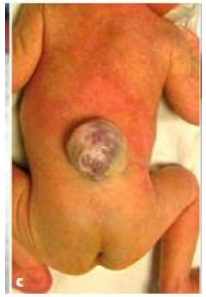
- 200 responsible genes for neural tube closure
- 40 mutant mouse strains with rare missense mutations
  - Cell polarity
  - Folate metabolism
- Maternal factors
  - Valproic acid
  - Maternal diabetes
  - Maternal overweight

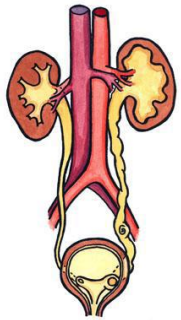
Timeline of clinical aspects of open spinal dysraphism

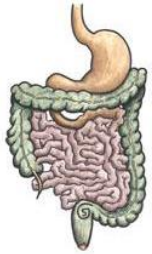


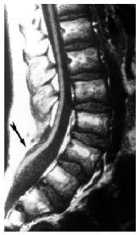


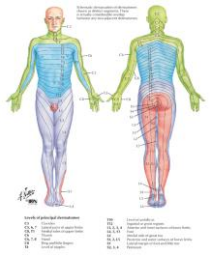


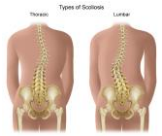


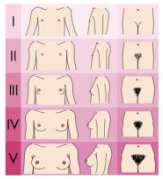












Birth
1 y
2 y
3 y
4 y
5 y
6 y
7 y
8 y

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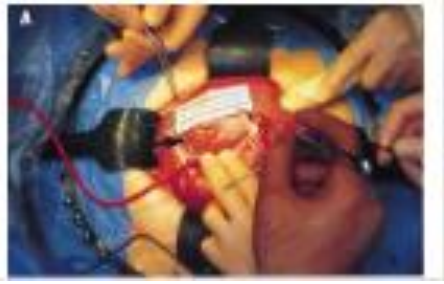
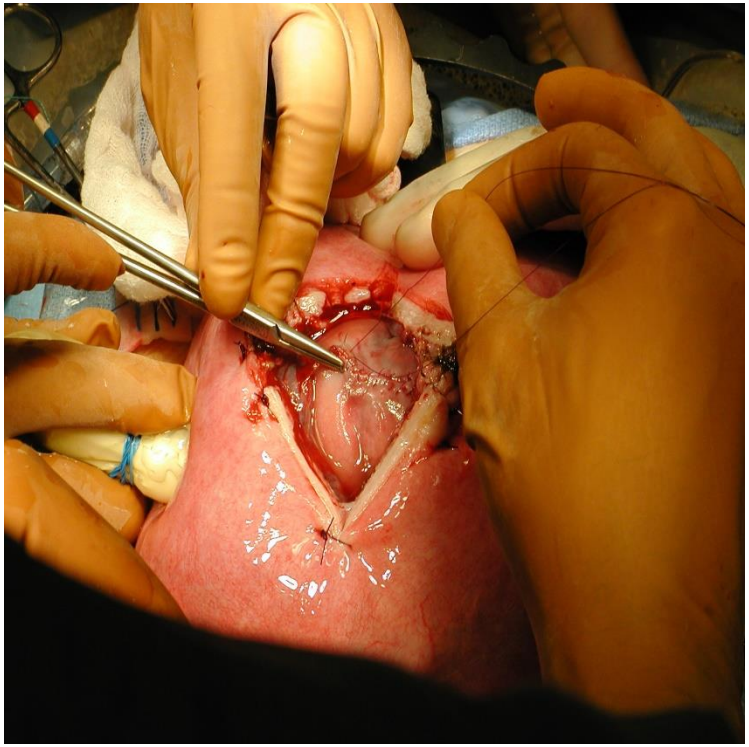


Fetal surgery

- Lamb model 1995
- First operation performed in1998
- MOMS trial 2011 Adzick et al. NEJM



Inclusion criteria
Maternal age greater or equal to 18 years
Gestational age at randomization between 19 weeks, 0 days and 25 weeks, 6 days
Normal karyotype
S1-level lesion or higher
Confirmed Arnold-Chiari II malformation on prenatal US and MRI
Exclusion criteria
Multiple-gestation pregnancy
Insulin-dependent pregestational diabetes
Additional fetal anomalies unrelated to MMC
Fetal kyphosis greater than or equal to 30 degrees
History of incompetent cervix and/or short cervix less than 20 mm by ultrasound scan
Placenta previa
Other serious maternal medical condition
Obesity, defined as body mass index of 35 or greater
Previous spontaneous singleton delivery at less than 37 weeks' gestation
Maternal-fetal Rh isoimmunization
Positive maternal human immunodeficiency virus or hepatitis B or known hepatitis C positivity
No support person to stay with the pregnant woman at the center
Uterine anomaly
Psychosocial limitations
Inability to comply with travel and follow-up

Part 2 – Orphanet classification

Orphanet nomenclature

- Group of disorders

Group of disorders
A collection of clinical entities sharing a set of common features.

Neural tube closure defect (group)

Spinal bifida and other dysraphisms (SBoD)
Synonym: Isolated spinal dysraphism (group of disorders, category)

Open spinal dysraphism (group)

- Disorder

Disorder
A clinical entity characterised by a set of homogeneous phenotypic abnormalities and evolution allowing a definitive clinical diagnosis.

Open spinal dysraphism with MMC (disorder) or MMC

Myeloschisis (disorder)

- Subtype

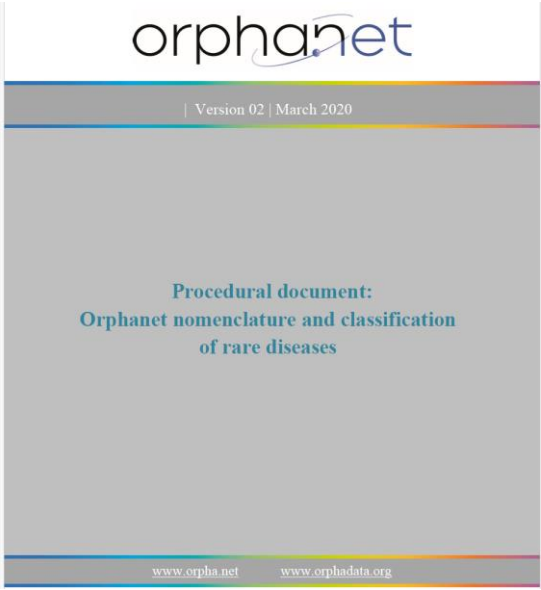
Subtype of a disorder
Subdivision of a disorder according to a positive criterion.

True Myelomeningocele (subtype)

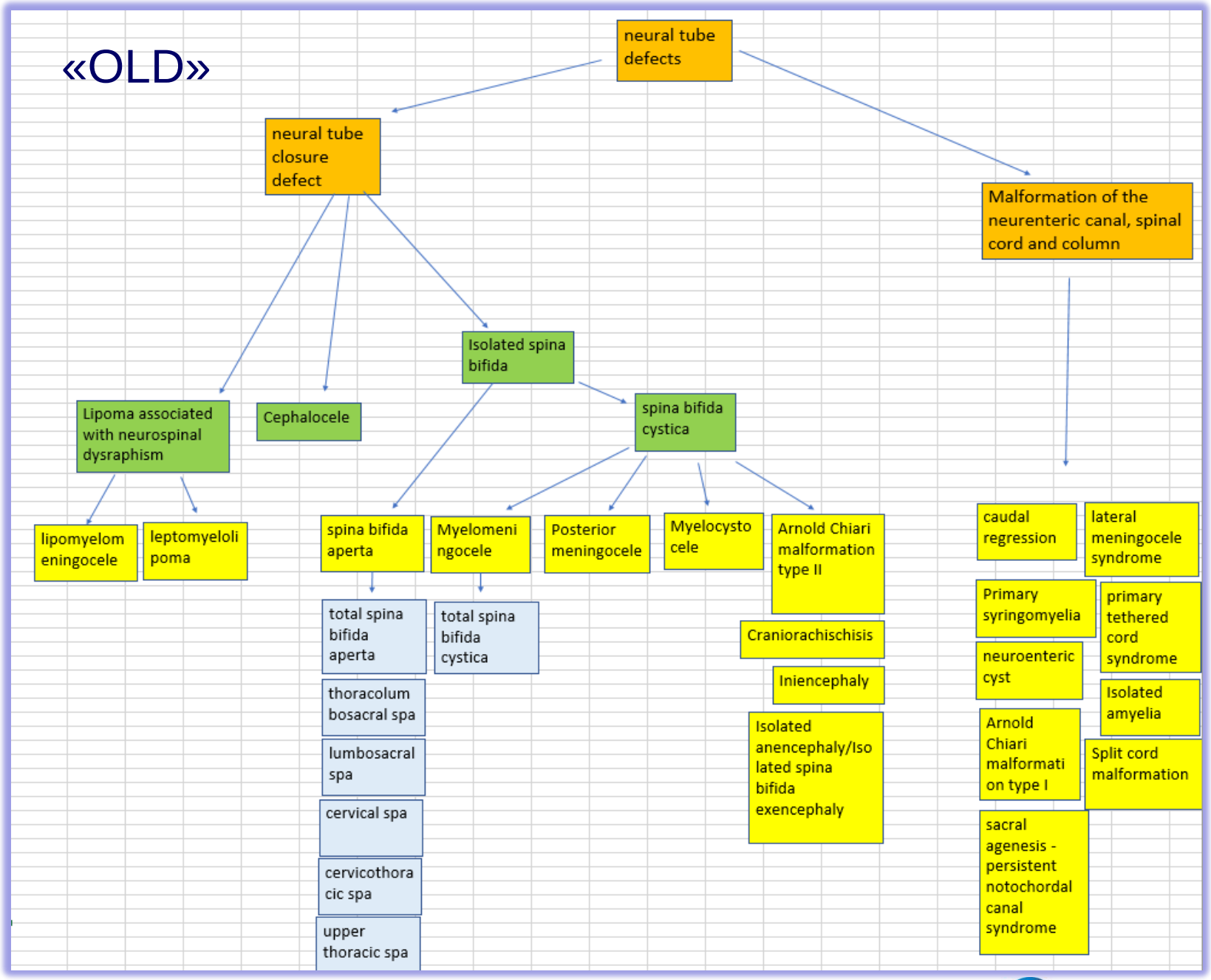
Hemi-Myelomeningocele (subtype)

True Myeloschisis (subtype)

Hemi-Myeloschisis (subtype)



«OLD»


neural tube defects
neural tube closure defect
Malformation of the neurenteric canal, spinal cord and column
Isolated spina bifida
Lipoma associated with neurospinal dysraphism
Cephalocele
spina bifida cystica
lipomyelomeningocele
leptomyeloliposma
spina bifida aperta
Myelomeningocele
Posterior meningocele
Myelocystocele
Arnold Chiari malformation type II
total spina bifida aperta
total spina bifida cystica
thoracolumbosacral spa
lumbosacral spa
cervical spa
cervicothoracic spa
upper thoracic spa
Craniorachischisis
Iniencephaly
Isolated anencephaly/Isolated spina bifida exencephaly
caudal regression
lateral meningocele syndrome
Primary syringomyelia
primary tethered cord syndrome
neuroenteric cyst
Isolated amyelia
Arnold Chiari malformation type I
Split cord malformation
sacral agenesis - persistent notochordal canal syndrome

ICD 10

Q00 Anencephaly and similar malformations

Q00.0 Anencephaly
Acephaly
Acrania
Amyelencephaly
Hemianencephaly
Hemicephaly

Q00.1 Craniorachischisis

Q00.2 Iniencephaly

Q01 Encephalocele

Incl.: encephalomyelocele
hydroencephalocele
hydromeningocele, cranial
meningocele, cerebral
meningoencephalocele

Excl.: acquired encephalocele (G93.5)
Meckel-Gruber syndrome (Q61.9)

Q01.0 Frontal encephalocele

Q01.1 Nasofrontal encephalocele

Q01.2 Occipital encephalocele

Q01.8 Encephalocele of other sites

Q01.9 Encephalocele, unspecified

Q05 Spina bifida

Incl.: hydromeningocele (spinal)
meningocele (spinal)
meningomyelocele
myelocele
myelomeningocele
rachischisis
spina bifida (aperta)(cystica)
syringomyelocele

Excl.: Arnold-Chiari syndrome (Q07.0)
spina bifida occulta (Q76.0)

Q05.0 Cervical spina bifida with hydrocephalus

Q05.1 Thoracic spina bifida with hydrocephalus

Spina bifida:
- dorsal
- thoracolumbar

with hydrocephalus

Q05.2 Lumbar spina bifida with hydrocephalus
Lumbosacral spina bifida with hydrocephalus

Q05.3 Sacral spina bifida with hydrocephalus

Q05.4 Unspecified spina bifida with hydrocephalus

Q05.5 Cervical spina bifida without hydrocephalus

Q05.6 Thoracic spina bifida without hydrocephalus

Spina bifida:
- dorsal NOS
- thoracolumbar NOS

Q05.7 Lumbar spina bifida without hydrocephalus
Lumbosacral spina bifida NOS

Q05.8 Sacral spina bifida without hydrocephalus

Q05.9 Spina bifida, unspecified

Q06 Other congenital malformations of spinal cord

Q06.0 Amyelia

Q06.1 Hypoplasia and dysplasia of spinal cord
Atelomyelia
Myelatelia
Myelodysplasia of spinal cord

Q06.2 Diastematomyelia

Q06.3 Other congenital cauda equina malformations

Q06.4 Hydromyelia
Hydrorachis

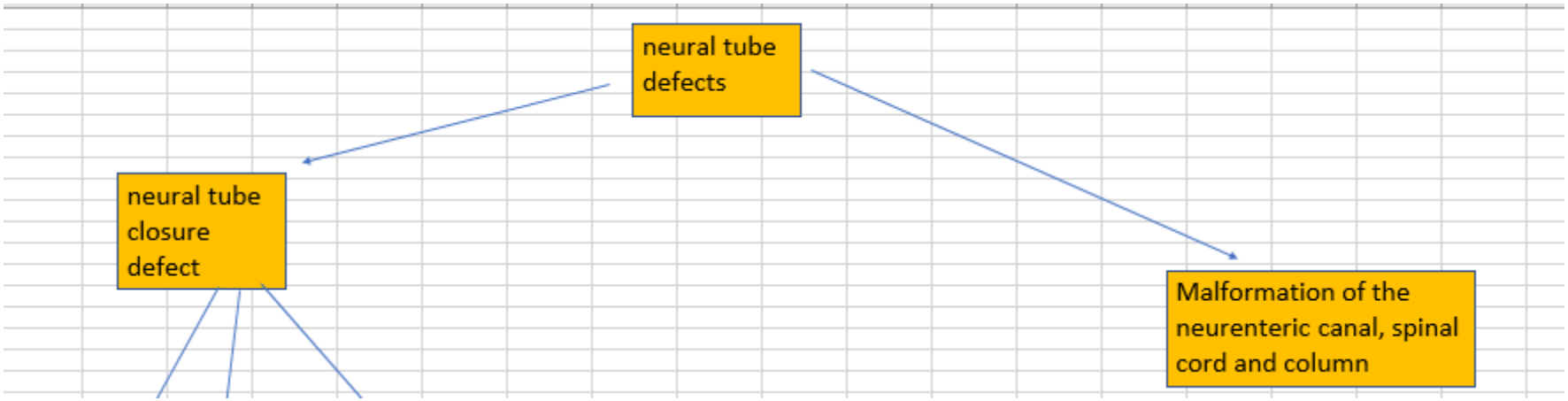
Q06.8 Other specified congenital malformations of spinal cord

Q06.9 Congenital malformation of spinal cord, unspecified

Congenital:
- anomaly
- deformity
- disease or lesion

NOS of spinal cord or meninges

Main groups, «old» and «new»



Malformation of the neurenteric canal, spinal cord and column

caudal regression

lateral meningocele syndrome

Primary syringomyelia

primary tethered cord syndrome

neuroenteric cyst

Isolated amyelia

Arnold Chiari malformation type I

Split cord malformation

sacral agenesis - persistent notochordal canal syndrome

Neural tube defects

Malformation of the neurenteric canal, spinal cord and column

SCM type 1

SCM type 2

SCM – composite type

Cephalocele

Cranial meningocele

Isolated encephalocele

Caudal regression syndrome

Primary syringomyelia

Neurenteric cyst

Arnold Chiari malformation 1

Sacral agenesis, persistent notochordal canal syndrome

Spinal segmental agenesis

Lateral meningocele syndrome

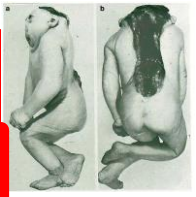
Primary tethered cord syndrome

Isolated amyelia

Craniorachischisis

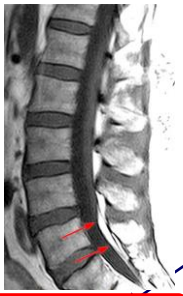
Iniencephaly

Isolated anencephaly/isolated spina bifida



Neural tube defects

Neural tube closure defect



Anomaly of the filum terminale

Spinal cord lipoma (SCL)

Spina bifida and other dysraphisms

Intramedullary non-dysraphic SCL

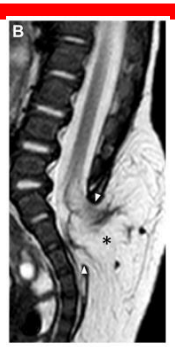
Dysraphic SCL

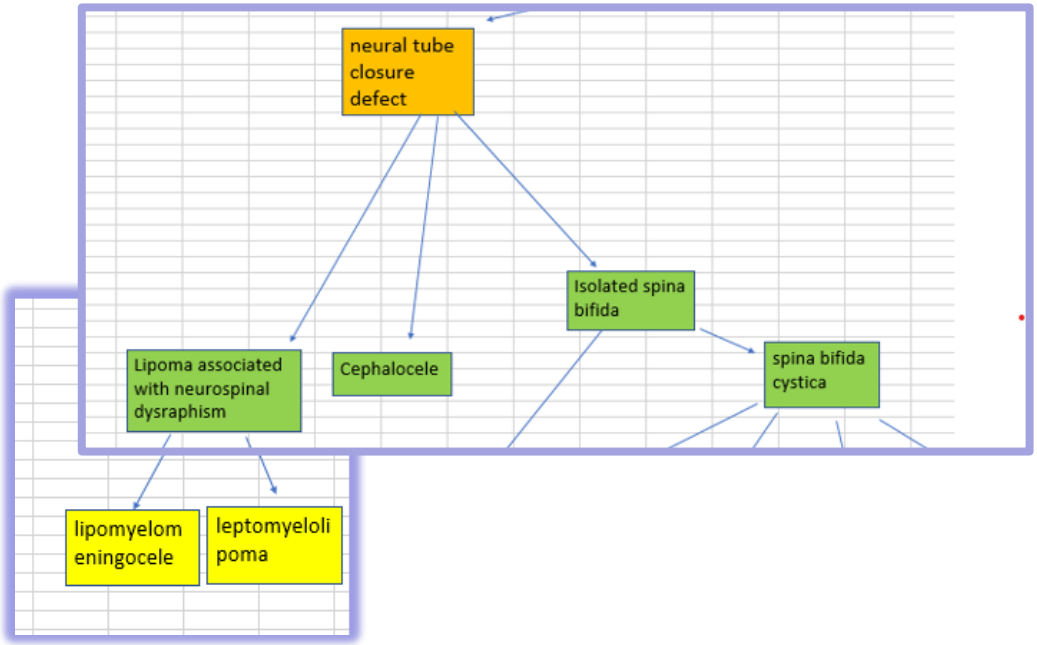
Dorsal SCL

Conus SCL

Chaotic SCL

extramedullary SCL





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Neural tube defects

Neural tube closure defect

Spina bifida and other dysraphisms

Open spinal dysraphism (OSD)

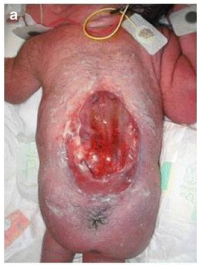
OSD with posterior meningocele

Myeloschisis (MSS)

OSD with myelomenin gocele

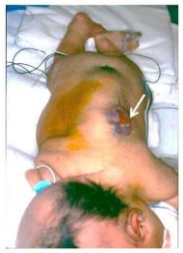
True MSS

Hemi MSS

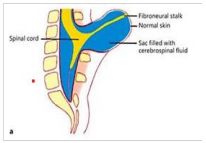


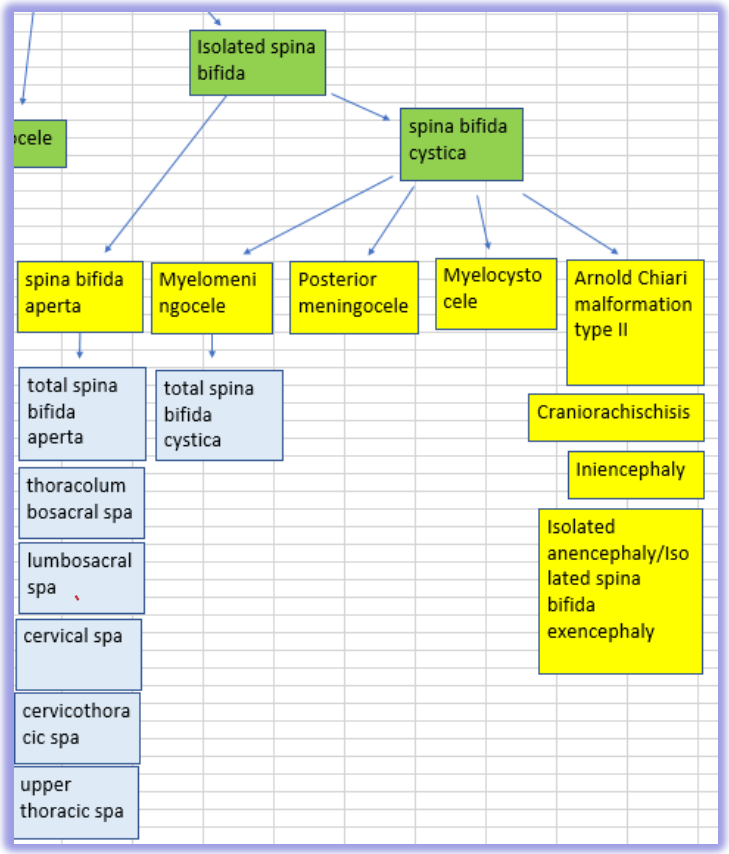
True MMC

Hemi MMC



Myelic limited dorsal malformation





Neural tube defects

Neural tube closure defect

Spina bifida and other dysraphisms

Split cord malformation (SCM)

SCM type 1

SCM type 2

SCM – composite type

Caudal regression syndrome

Dysraphic SCL

Closed spinal dysraphism

Myelocystocele (MCC)

Dysraphism with a stalk

Isolated posterior meningocele

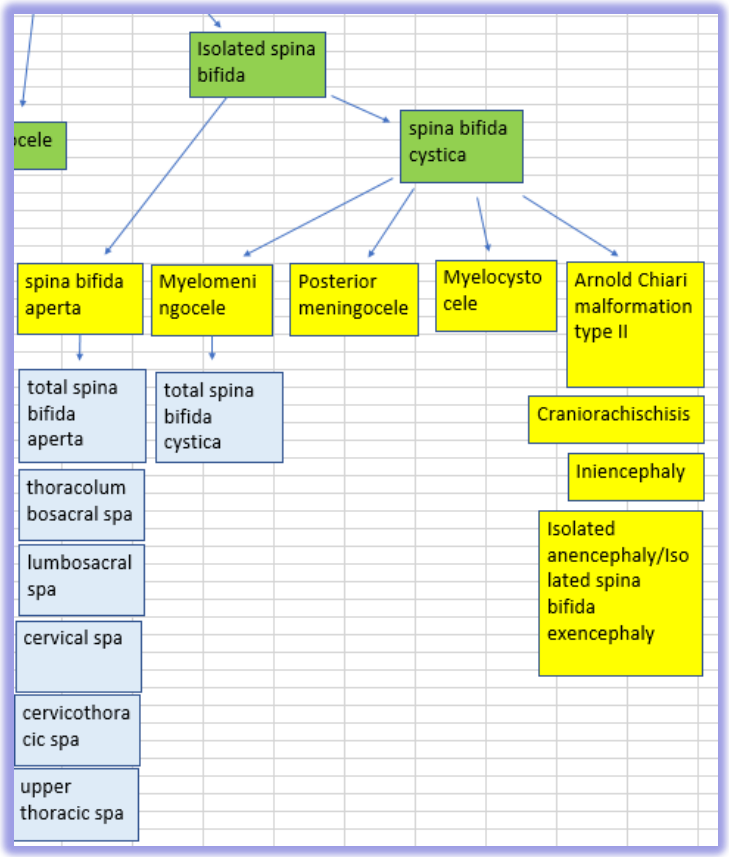
Terminal MCC

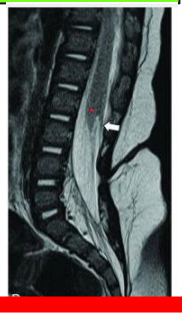
Non-terminal MCC

Limited dorsal myeloschisis

Spinal dermal sinus

Retained medullary cord



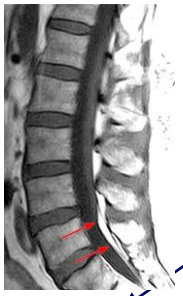


Neural tube defects

Neural tube closure defect

Malformation of the neurenteric canal, sinal cord and column

Cephalocele



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Craniorachischisis

Iniencephaly

Isolated anencephaly/isolated spina bifida

True MSS

Hemi MSS

Terminal MCC

Non-terminal MCC

Dorsal SCL

Conus SCL

Chaotic SCL

extramedullary SCL

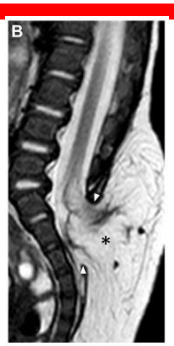
OSD with myelomenin gocele

Mye limited dorsal malformation

Limited dorsal myeloschisis

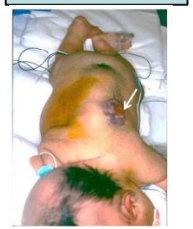
Spinal dermal sinus

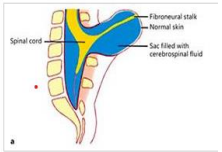
Retained medullary cord

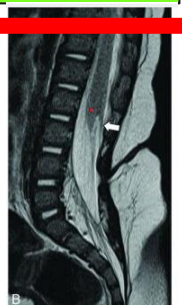


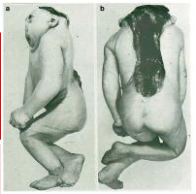
True MMC

Hemi MMC









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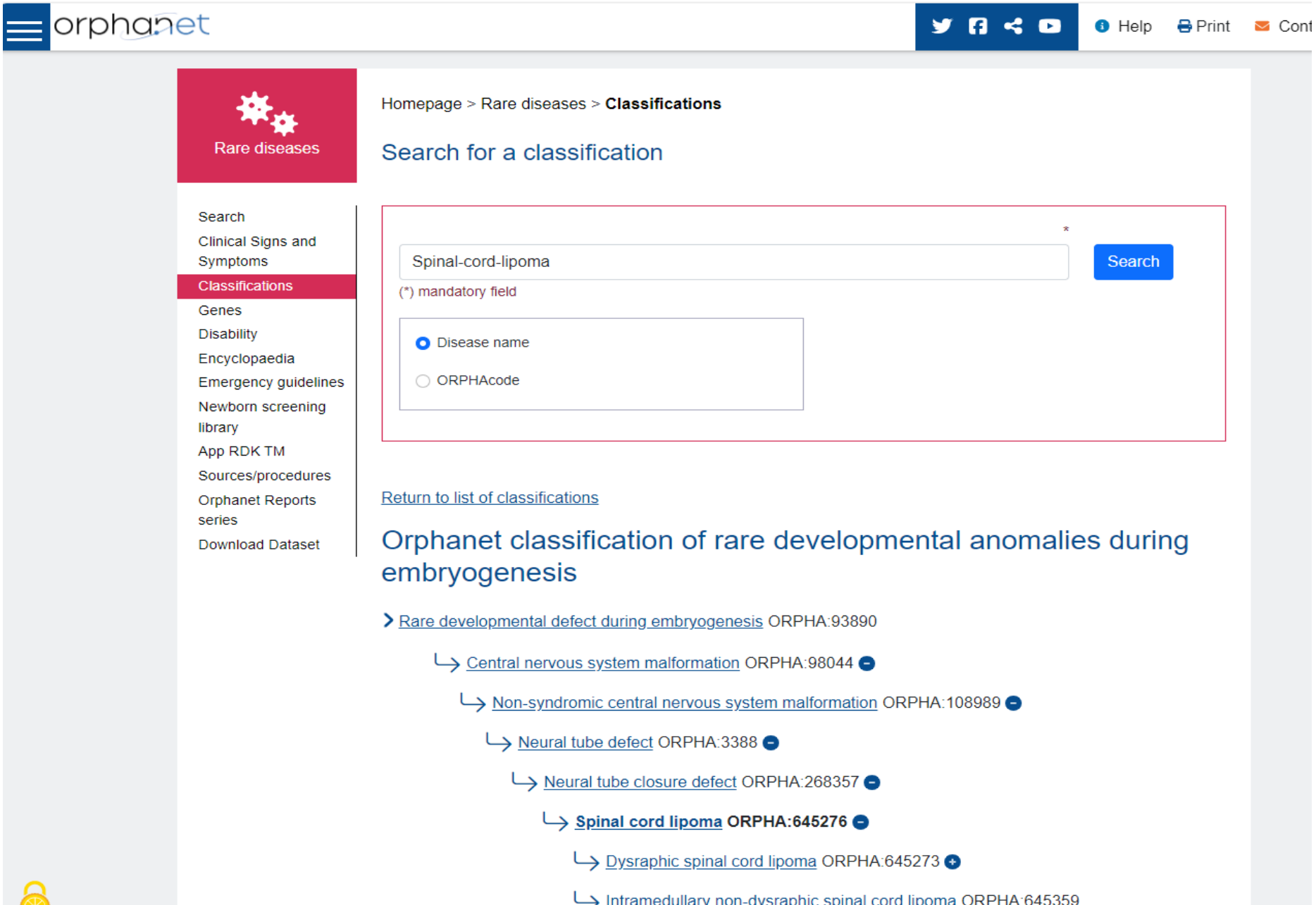
Orphanet use for the clinician



orphanet

Help

- Search
- Clinical Signs and Symptoms
- Classifications
- Genes
- Disability
- Encyclopaedia
- Emergency guidelines
- Newborn screening library
- App RDK TM
- Sources/procedures
- Orphanet Reports series
- Download Dataset

Myelomeningocele

Search

(*) mandatory field

- (•) Disease name
- ( ) OMIM disease
- ( ) Gene name or symbol
- ( ) ORPHAcode
- ( ) ICD-10
- ( ) ICD-11

Other search option(s)

6 Result(s)

ORPHA:645367 (Group of disorders) Conus spinal cord lipoma

Keywords: **Lipomyelomeningocele**

ORPHA:645388 (Subtype of disorder) Hemi-myelomeningocele

ORPHA:268835 (Disorder) Lipomyelomeningocele

ORPHA:83628 (Disorder) LUMBAR syndrome

Synonym(s): **Perineal hemangioma-external genitalia malformations-lipomyelomeningocele-vesicorenal abnormalities-imperforate anus-skin tag syndrome**

ORPHA:93969 (Disorder) Open spinal dysraphism with a myelomeningocele

Synonym(s): **Myelomeningocele**

ORPHA:645383 (Subtype of disorder) True myelomeningocele

Open spinal dysraphism with a myelomeningocele

Suggest an update

Disease definition

A rare form of spina bifida cystica (saccular, open neural tube defect (NTD)) characterized by a non-neurulated spinal cord (neural placode) on the surface of the cystic extension of dysplastic meninges (non-epidermised posterior meningocele). The spinal cord extends through a spina bifida (posterior vertebral defect) with typically everted or parallel laminae. Nerve roots are connected to the borders of the neural placode and are visible inside the sac. Myelomeningocele is characteristically associated with a Chiari II malformation. It can be either isolated or associated with split cord malformation.

ORPHA:93969

Classification level: Disorder

Synonym(s):

MMC

Myelomeningocele

Prevalence: -

Inheritance: Multigenic/multifactorial, Not applicable

Age of onset: Infancy, Neonatal

ICD-10: Q05.7 , Q05.8 , Q05.9 , Q05.0 , Q05.1 , Q05.2 , Q05.3 , Q05.4 , Q05.5 , Q05.6

ICD-11: LA02.1

UMLS: C0025312

GARD: 3475

Orphanet use in Norway

- «sjelden register» = rare disease register
- OUS Medinsight platform with submodule «spinal dysraphism»
- Integration of orphanet codes in our electronic patient journal
  - Information about the disorder
  - Finding patients with rare diseases
- Not done: presentation to radiologists
- TRS compentence center expands responsibility for disorders defined in the new classification

Final remarks

- More sophisticated classification
- Increased precision in describing disorders
- Not all interesting clinical aspects are included
- Implementation in ejournals potentially enhances
  - Flow of information to patients
  - Flow of information to specialists

Thank you for your attention!