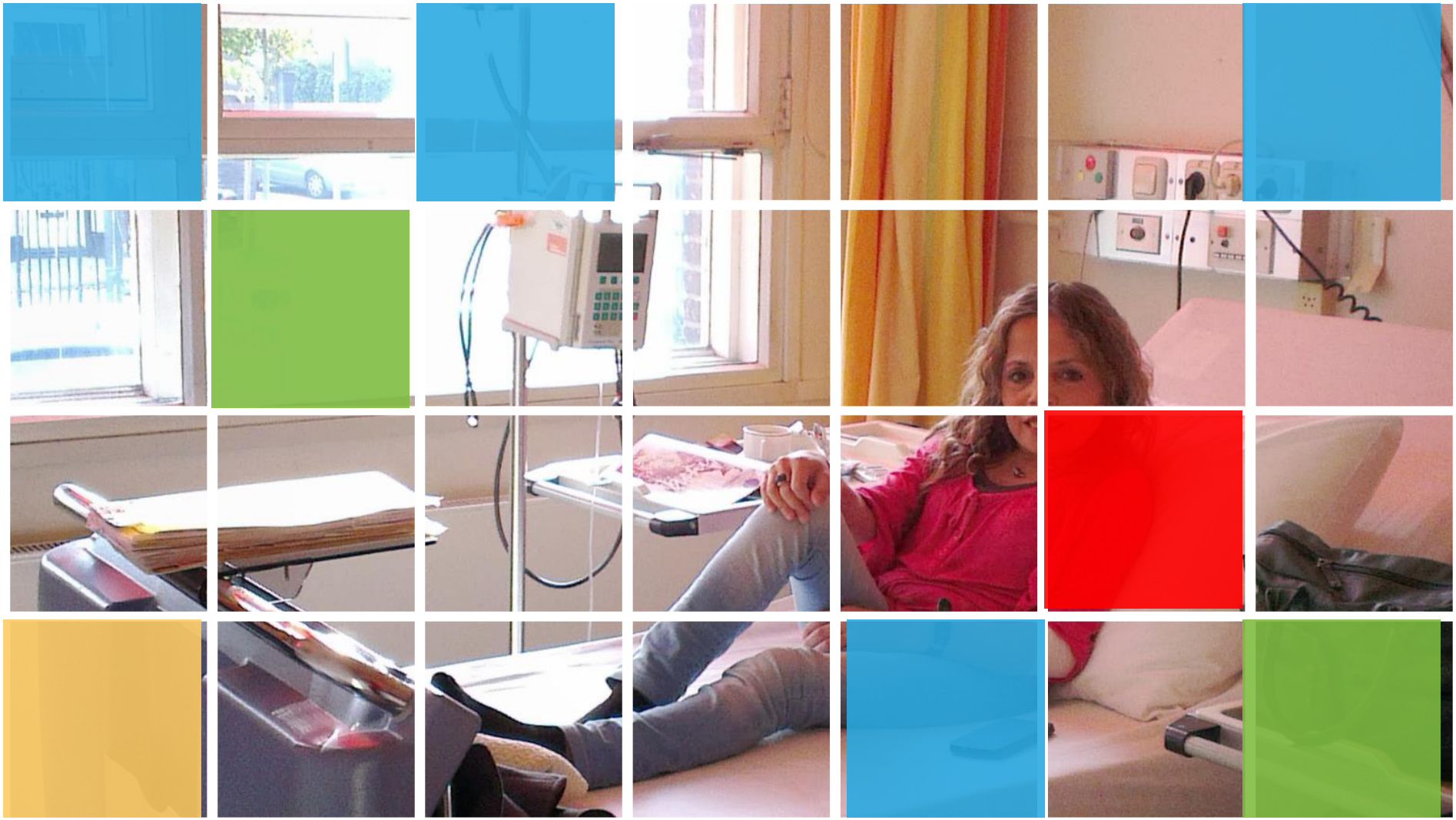


A Semantic Information Standard for Global Child Health

Liesbeth Siderius, pediatrician

Introduction

- **(Dis)abled child**

Rare is common

- **The Diagnosis**

Early recognition

- **Universal Health Coverage**

Leave no child behind

- **Digital Health for all**

Global child health

Disabled child

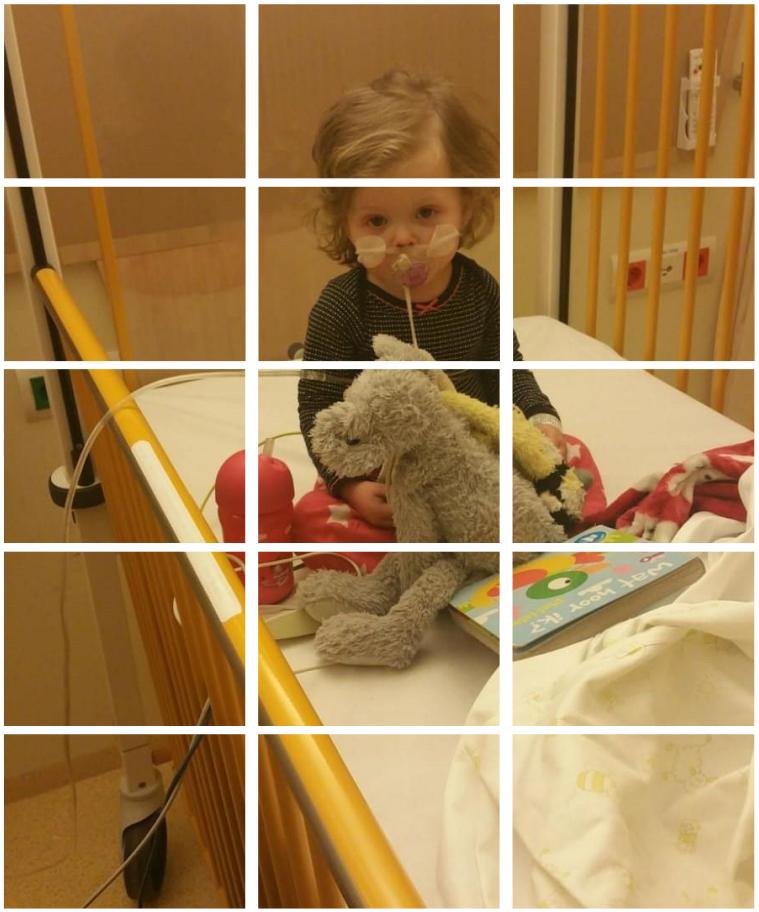
Children living with the diagnosis

- autism,
- developmental delay,
- cerebral palsy,
- hearing deficits and
- visual impairment

may very well have a

rare condition with

➢ specific health risks and treatment.



Disabling and Rare Conditions

70 % manifests in childhood

Health and well being for all

< 5 year 2-3 % have a rare disease

Early recognition

chronic and life-threatening

Reduce inequalities

72% of genetic origin

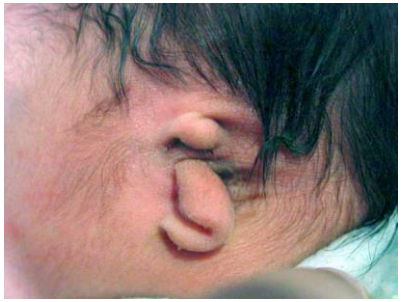
Shwachman Diamond Syndrome


#ADay4All
Most rare and disabling conditions
manifest in early childhood
EAP

What can we do?

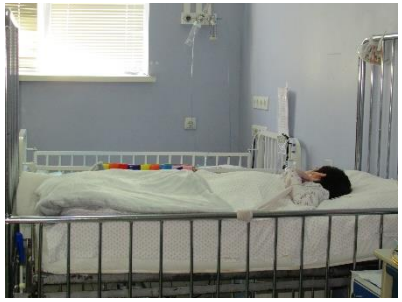
The Netherlands

Day Centre
Coffin Lowrey Syndrome



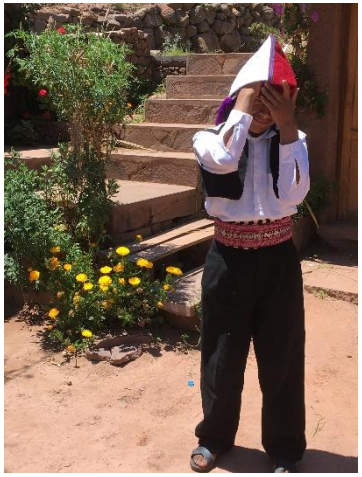
Sri Lanka

Pediatric Clinic
To be diagnosed



Georgia

Abandoned
Undiagnosed



South America

Living with family
In rural village
‘ Birth trauma’

Leave no one behind

When new techniques available and affordable for all

Importance of a diagnosis

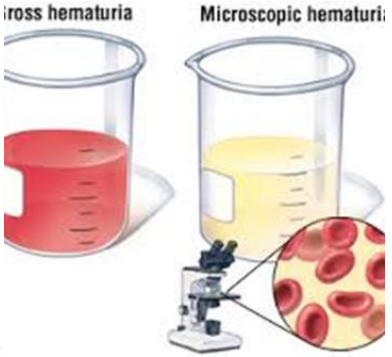
Physical and mental disabilities reported due to **birth trauma**; may be caused by **GATAD2b gene** mutation.

.

Most parts of the world these diagnostics are not available, and pricing of foreign laboratories unaffordable.

The Netherlands, South America , 2019

Nephrotic Syndrome



☐ **Renal cysts in adulthood / autosomal dominant tubulointerstitual kidney disaese (ADTKD)** (NEF26v18.1; 20 genes)

ALG8, COL4A1, DNAJB11, GANAB, HNF1B, MUC1, OFD1, PKD1, PKD2, PKHD1, PRKCSH, REN, SEC61A1, SEC61B, SEC63, TMEM104, TSC1, TSC2, UMOD, VHL

☐ **Nephrotic syndrome (NPHS) / Focal segmental glomerulosclerosis (FSGS)** (NEF11v18.1; 74 genes)

ACTN4, ADCK3, ADCK4, ALG1, ANLN, APOL1, ARHGAP24, ARHGDIA, CD151, CD2AP, CFH, CLCN5, COL4A3, COL4A4, COL4A5, COQ2, COQ4, COQ6, COQ7, COQ8, CRB2, CUBN, DGKE, EMP2, FAT1, FN1, FOXC2, GLA, GPC5, GSN, INF2, ITGA3, ITGB4, KANK1, KANK2, KANK4, LAGE3, LAMB2, LCAT, LMNA, LMX1B, LYZ, MAFB, MAGI2, MYH9, MYO1E, NPHS1, NPHS2, NUP107, NUP205, NUP93, NXF5, OSGEP, PAX2, PDSS1, PDSS2, PLCE1, PMM2, PODXL, PTPRO, SCARB2, SEC61A1, SLC7A7, SMARCAL1, SMARCAL1, TP53RK, TPRKB, TRPC6, TTC21B, WDR73, WT1, XPO5, YRDC, ZMPSTE24

☐ **Chronic kidney disease of the young (CKD-Y) (includes PKD1 and PKD2)** (NEF24v18.1; 141 genes)

ACE, ACTN4, ADCK4, AGT, AGTR1, AGXT, ALG1, AMN, ANKS6, APOA1, APOL1, ARHGDIA, ATXN10, B2M, BBIP1, BCS1L, C3, CD151, CD2AP, CD46, CEP164, CEP290, CFB, CFH, CFHR5, CFI, CHD7, CLCN5, COL4A3, COL4A4, COL4A5, COQ2, COQ6, CRB2, CTNS, CUBN, CYP11B1, CYP11B2, DACT1, DCDC2, DGKE, DSTYK, EMP2, EYA1, FAN1, FAT1, FGA, FN1, FOXC2, FRAS1, FREM1, FREM2, GATA3, GLA, GLIS2, GRHPR, GRIP1, GSN, HNF1B, HOGA1, HPSE2, IFT27, IFT81, INF2, INVS, IQCB1, ITGA3, ITGA8, JAG1, KANK1, KANK2, KANK4, KIAA0556, KIAA0586, LAMB2, LMNA, LMX1B, LRIG2, LYZ, MAFB, MAGI2, MAPTD3, MAPKBP1, MUC1, MYH11, MYH9, MYO1E, NEK8, NOTCH2, NPHP1, NPHP3, NPHP4,

☐ **Diabetes insipidus, nephrogenic and neurogenic** (NEF25v16.1; 3 genes)

AQP2, AVP, AVPR2

Copy number analysis *: ☐ AVPR2

☐ **Electrolyte disorder (including Bartter syndrome, Gitelm syndrome and hypomagnesemia)*** (NEF09v18.1; 29 gene

BSND, CACNA1S, CASR, CLCNS, CLCNKA, CLCNKB, CLDN16, C CNNM2, DGAT1, EGF, EPCAM, FXYD2, GUCY2C, HNF1B, KCNJ1, K MAGED2, MYO5B, NEUROG3, PCBD1, SCN4A, SLC12A1, SL SLC26A3, SLC41A1, SLC9A3, SPINT2, TRPM6

Copy number analysis*: ☐ CLCNKB ☐ SLC12A3

☐ **Hyperuricemia / Uricosuria** (NEF09v16.2; 14 genes)

ALDOB, ALMS1, ATP7B, CTNS, G6PC, GALT, HPRT1, PYGM, REN, SLC22A12, SLC2A9, SLC37A4, UMOD

☐ **Nephrocalcinosis / Nephrolithiasis*** (NEF10v18.1; 53 ger

AGXT, ALDOB, APS1, APRT, ATP6V0A4, ATP6V1B1, ATP7B, BSN CASR, CLCN5, CLCNKB, CLDN16, CLDN19, CTNS, CYP24A1, ENPP1, FAM20A, FGF23, G6PC, GALT, GNA11, GRHPR, HNF4A, HPRT1, KCNJ1, KL, MAGED2, OCRL, PHEX, PTH1R, SCNN1B, SC SLC12A1, SLC22A12, SLC2A9, SLC34A1, SLC34A3, SLC36A2, SL SLC3A1, SLC4A1, SLC5A19, SLC5A20, SLC7A9, SLC9A3R1, TRPM VPAS39, VPS33B, XDH

Copy number analysis*: ☐ SLC3A1 ☐ SLC7A9

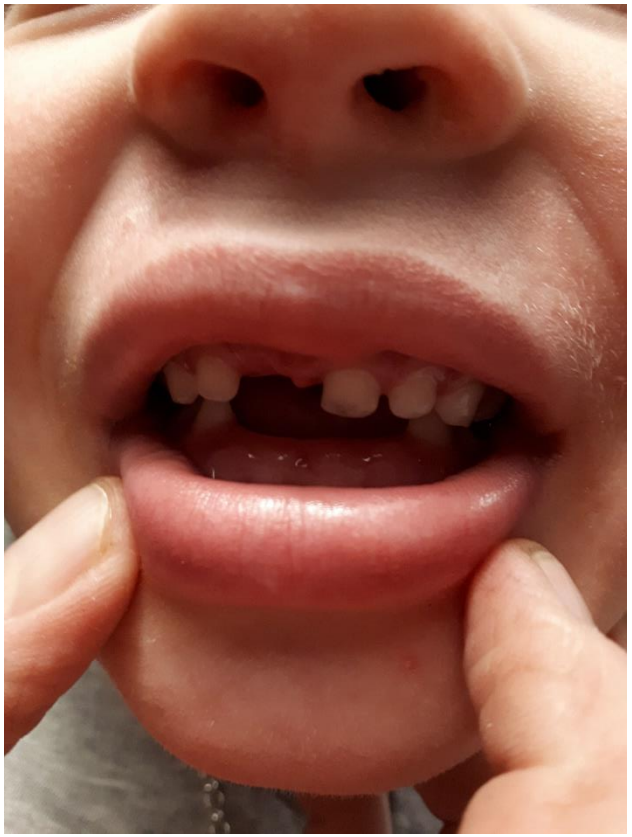
The Netherlands

Coordinated Care

-developmental delay

-**early loss of teeth**

Exoom screening, genes related to developmental delay: Gene RPSKA3: mutation c.1198C>T



Coffin Lowry Syndrome

-progressive kyphosis/scoliosis

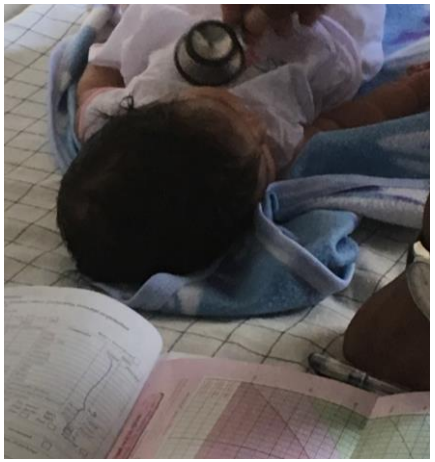
-sensorineural hearing defect .

-cardiac evaluation

-sudden loss of muscle tone induced by unexpected tactile or auditory stimuli and epilepsy.

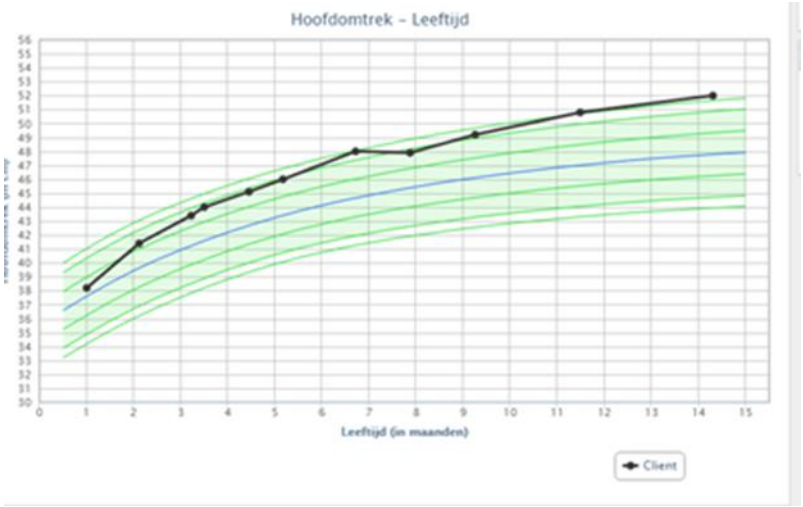
The Netherlands

World wide children are measured, examined, developmental screened, and vaccinated in Preventive child health



Global Child Health

Measure
Head circumference



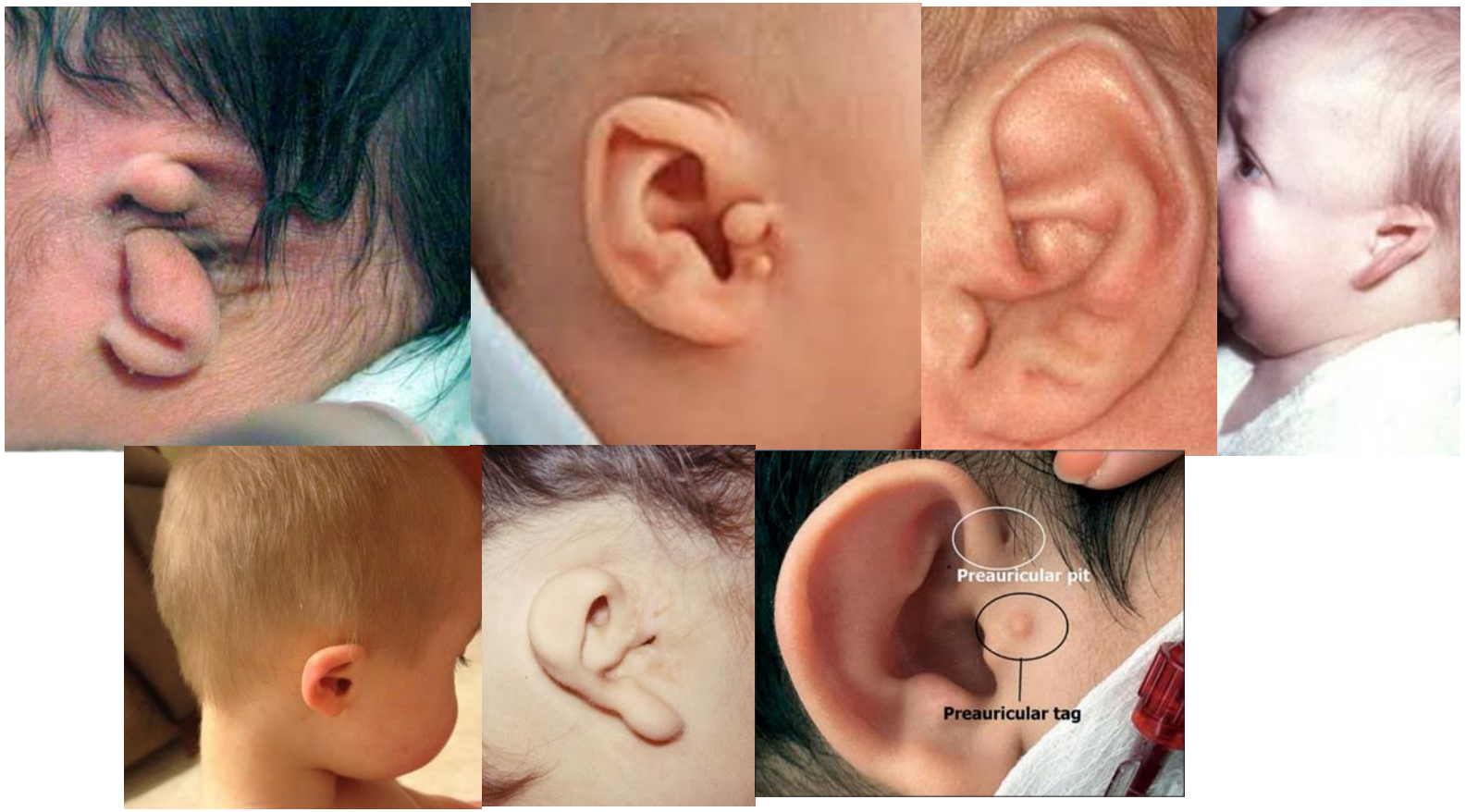
DCC gene mutation p.(Val1117Met) p.(Thr1339Ile)

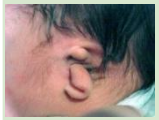
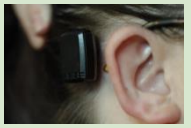
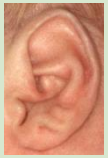
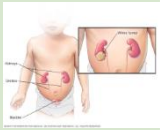
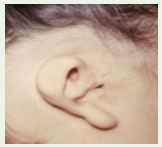
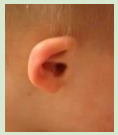
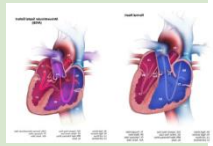
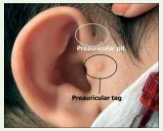
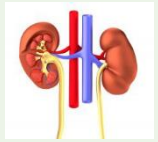
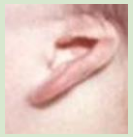
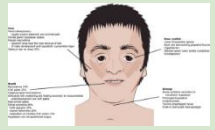
The Netherlands

Pathogenic mutation ?

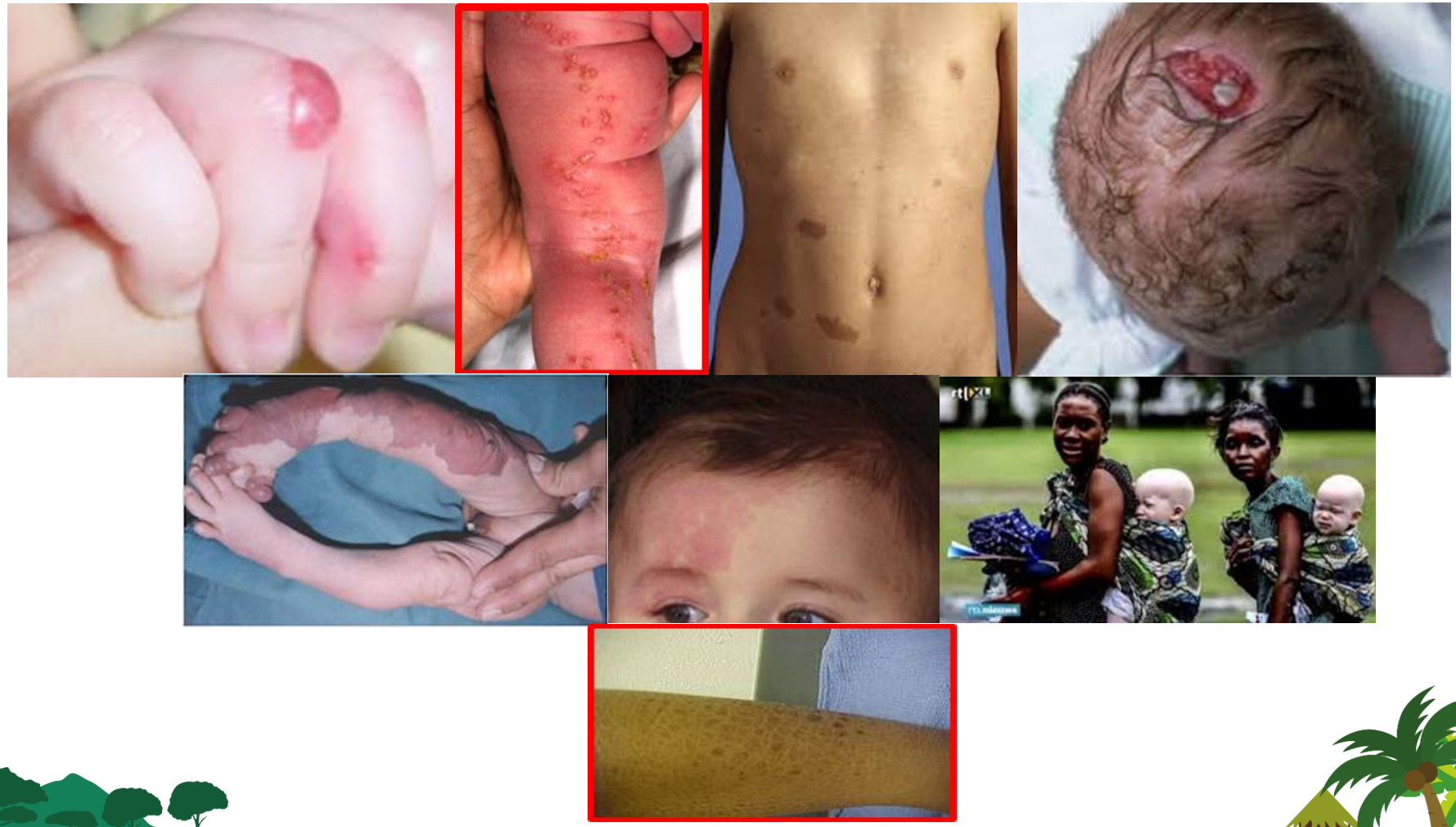
DCC gene mutations are associated with congenital mirror movement disorder

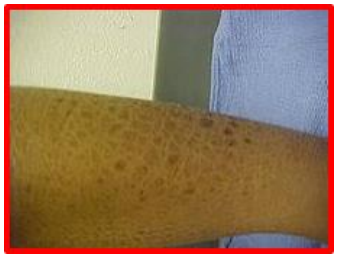
Global Child Health



	Disease	Associated RISK
	Microtia	Conductive Hearing loss 
	Ear Tags	The A.A.P. endorses universal hearing screening regardless of the presence or absence of preauricular skin. No recommendations or guidelines about the role of renal ultrasonography. 
	Beckwith Wiedemann Syndrome	Most of the tumors associated with BWS occur in the first 8–10 years of life with very few being reported beyond this age; most common are Wilms tumor and hepatoblastoma. 
	Goldenhar Syndrome	Hemivertebrae 
	Down syndrome	Congenital cardiac anomalies 
	Brachio Oto Renal Syndrome	Renal disease 
	Treacher Collins syndrome	Early operations focus on maintaining the airway, protecting the eyes, and auditory neurological development. 

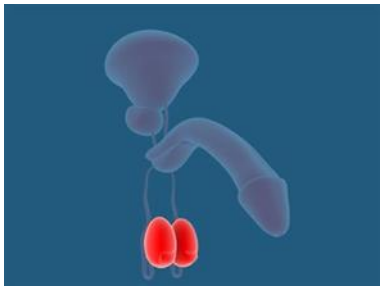
Global Child Health





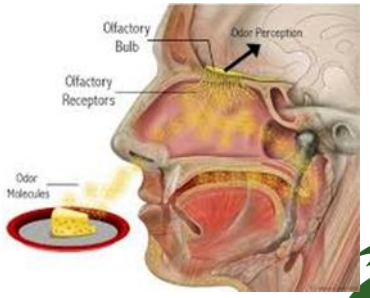
Skin> dermatologist:
ichthyosis

Small penis> endocrinologist:
hypogonadism



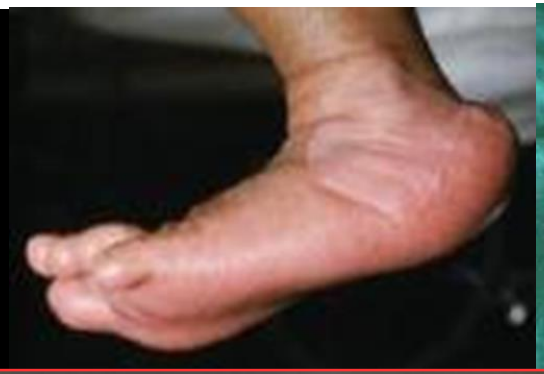
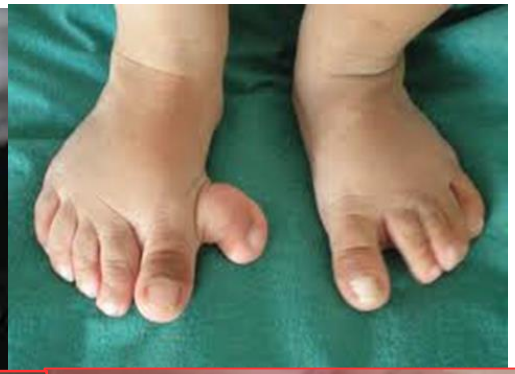
Feeding problems>
primary care

Kallmann Syndrome & Ichthyosis

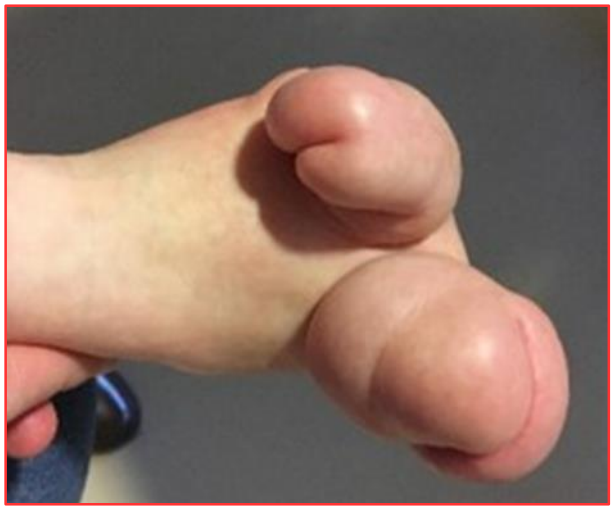


Both KAL1 and steroid sulfatase gene are located in the Xp22.3 region
Kallmann syndrome and ichthyosis: a case of **contiguous gene deletion syndrome.**
Berges-Raso I, Giménez-Palop O, Gabau E, Capel I, Caixàs A, Rigla M. Spain
Endocrinol Diabetes Metab Case Rep. 2017 Sep 28;2017

Global Child Health


Global Child Health



PIK3CA-related over- growth spectrum

The Netherlands

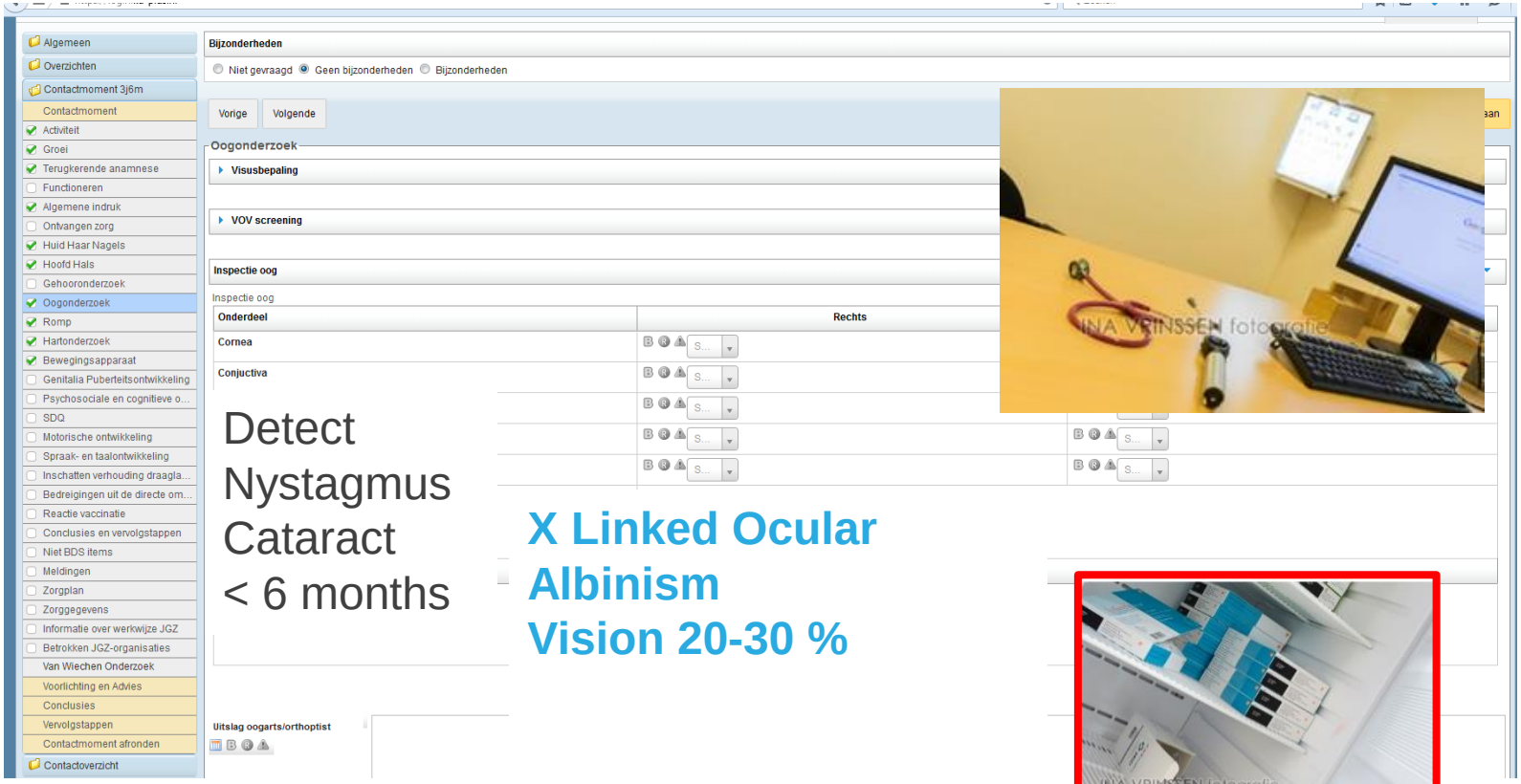
Google

- **Health Conditions Related to Genetic Changes**
  - Klippel-Trenaunay syndrome
  - Megalencephaly-capillary malformation syndrome
  - Epidermal nevus
  - Head and neck squamous cell carcinoma
  - Lung cancer
  - Ovarian cancer
  - Cancers
  - Other disorders

Global Child Health

Eye screening test

Preventive Child Health Scheme

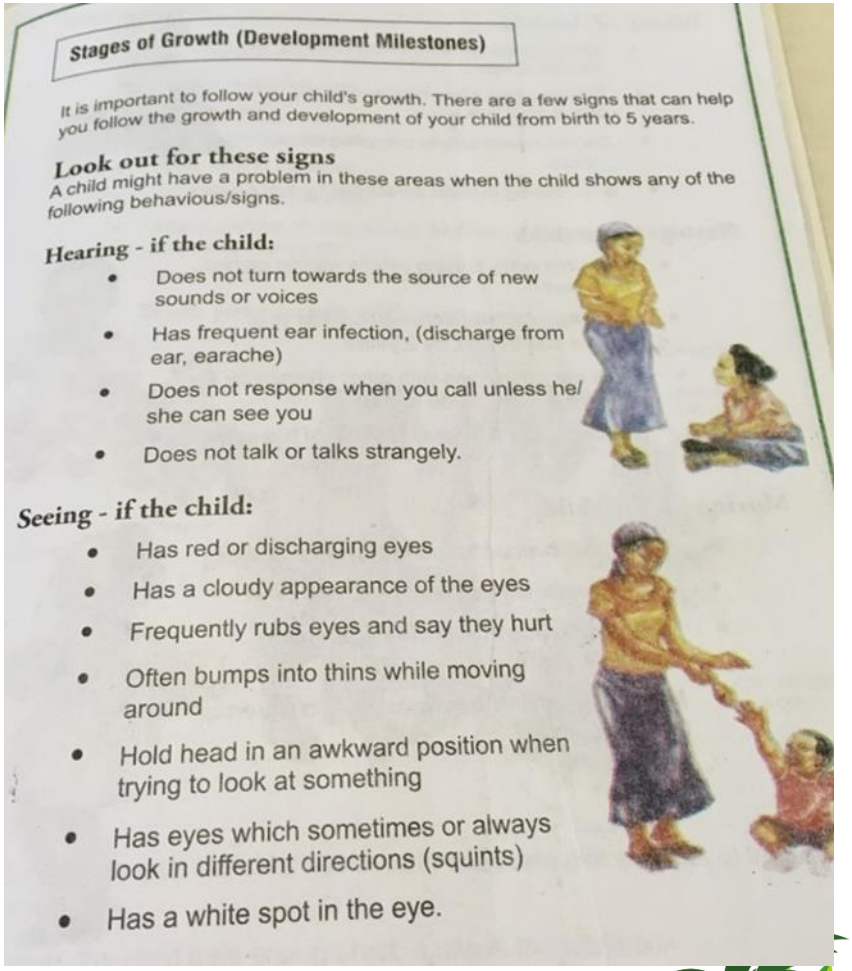


Detect
Nystagmus
Cataract
< 6 months

X Linked Ocular Albinism
Vision 20-30 %

Global Child Health

World Health Organization



Stages of Growth (Development Milestones)

It is important to follow your child's growth. There are a few signs that can help you follow the growth and development of your child from birth to 5 years.

Look out for these signs

A child might have a problem in these areas when the child shows any of the following behavious/signs.

Hearing - if the child:

- Does not turn towards the source of new sounds or voices
- Has frequent ear infection, (discharge from ear, earache)
- Does not response when you call unless he/she can see you
- Does not talk or talks strangely.

Seeing - if the child:

- Has red or discharging eyes
- Has a cloudy appearance of the eyes
- Frequently rubs eyes and say they hurt
- Often bumps into thins while moving around
- Hold head in an awkward position when trying to look at something
- Has eyes which sometimes or always look in different directions (squints)
- Has a white spot in the eye.

Ghana

90% agree — To access their own health data (requiring interoperable and quality health data)

80% agree — To share their health data (if privacy and security are ensured)

80% agree — To provide feedback on quality of treatments

Kolkata, India

Co - Management

Patient Information	Primary Care	Diagnosis Collaborative care	Social Services
www.shwachman.nl https://rarecare.world	Growth retardation Recurrent infections (LOINC)	Guideline SDS (Orphanetcode; SNOMED, ATC e.a.)	Recurrent illness Fatigue, Short (ICF-CY; ISO 9999)

Stichting Shwachman syndroom Support Holland

New Diagnostics

HPO
LOINC
ICPC

Diagnosis
Hurler syndrome
PKU, Duchenne MD, FOP
Shwachman Diamond Syndrome

ICD - 10
Orphacode
OMIM
SNOMED -CT
DCOM

Sign primary care
Heelstick screening
Hearing screening
Growth; Development

Guideline
Collaborative Health Care

Interoperable data model

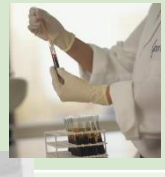
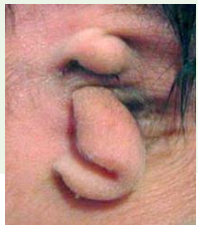
ISO 3166-1

HL7/ FHIR

ATC
New Therapeutics
ICF
ISO9999

Registry
Data collection with systematically organised computer processable collection medial terms

Guideline
Social services and rehabilitation

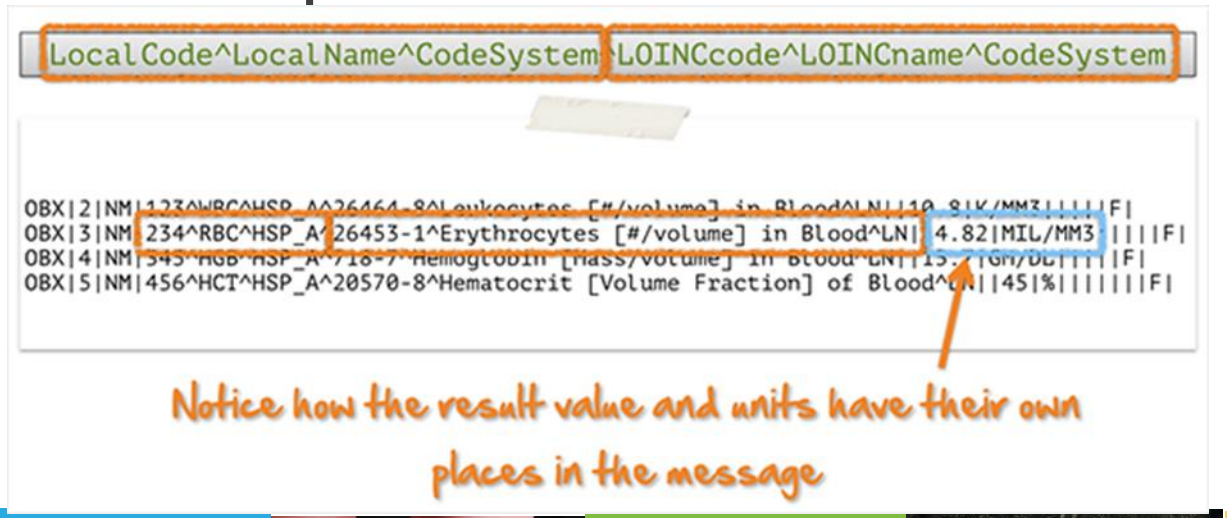
Codification	Meaning
ICD & Orpha code	International Code of Diseases / Orphanet code
ICF (-CY) 	The *International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY)* is a derived vers the *International Classification of Functioning, Disability a Health* (ICF, WHO, 2001) designed to record characteris the developing child and the influence of environments surrounding the child .
LOINC 	A universal code system for tests, measurements, and observations.
ATC 	The purpose of the ATC/DDD system is to serve as a tool for drug utilization research in order to improve quality of drug use.
ISO 9999 	ISO 9999:2011 establishes a classification of assistive products, especially produced or generally available, for persons with disability.
HPO 	The Human Phenotype Ontology (HPO) provides a standardized vocabulary of phenotypic abnormalities encountered in human disease.

World Health Organization

LOINC

The international standard for identifying health measurements, observations, and documents.

Interoperable codes in care



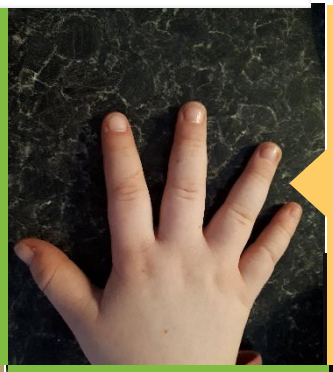
Goldenhar s
Abnormal ear

.

HP:0008551

FOP
Abnormal toe

HP:0010109



Coffin Lofry s
Tapered fingers

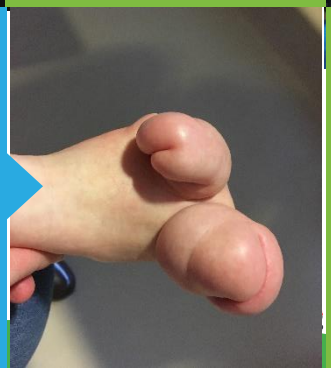
HP:0001182

Measuring Head Circumference

LOINC
8287-5

Lower limb asymmetry

HP:0100559



Shwachman DS

ATC

. A09AA02
Pancreatine

Global Child Health

Recommendations for Preventive Pediatric Health Care

Bright Futures/American Academy of Pediatrics

	Feature	Diagnosis + #OMIM	Code
History	Family XLinked Inheritance	Coffin Lowry Syndrome # 303600 Ocular Albinism # 300500	HP:0001423 HP:0001419
Measurenents	Failure to thrive	ShwachmanDiamond S #260400	HP:0001531 LOINC:LP36298-5C ICPC: T10
	Head Circumference	DCC gene mutation	LOINC 8287-5
Sensory screening	Nystagmus	Ocular Albinism # 300500	HP:0000639
Developmantal Health	Developmental Delay, general	Coffin Lowry Syndrome # 303600 Autosomal dominant mental retardation-18 # 615074	HP:0001249 Intellectual disability
Physical examination	Malformed ears	Goldenhar syndrome #164210	HP:0008551 ICPC:H80
	Skin abnormalities	Ichthyosis	HP:0008064
	Foot abnormalities	Fibrodysplasia Ossificans progressiva # 135100	HP:0010109
Laboratory Test	Hematuria	Alport Syndrome # 301050 Nephrotic Syndrome	LOINC 13945-1 Erythrocytes in Urine sediment by high power field
Vaccination	National scheme	DKTP	ATC J07CA02

HL7 Netherlands

Building the Rare Disease

knowledge and information ecosystem

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Thalassemia

SEARCH

Find and share knowledge about

Rare diseases all over the world

Sri Lanka

ATC

- L01XX05 Hydroxycarbamide (Hydroxyurea) (1)
- V03AC01 Deferoxamine (1)
- V03AC02 Deferipron (1)
- V03AC03 Deferasirox (1)

ICD

- D57 Sickle-cell disorders (1)

ICPC Reference

- B78.01 Thalassemia (1)
- B87 Splenomegaly (1)

LOINC

- 718-7 Hemoglobin in blood (1)
- 20567-4 Ferritin in Serum or Plasma (1)
- 46740-7 Hemoglobin disorders newborn screen interpretation (1)
- 53857-9 Hemoglobin F (1)

... causes bone marrow expansion and cortical thinning. **Thalassemia** major, when not properly t... fractures or vertebral deformities. **Thalassemia** major or Beta **Thalassemia** ...
Rare Condition
Thalassemia major or Beta Thalassemia

Large spleen

Feature

... costal margin. A large spleen is a feature of for example **Thalassemia** Infections Nieman Pick ... Splenomegaly Splenomegaly in **thalassemia Thalassemia** major or Beta **Thalassemia** ...
Rare Condition
Thalassemia major or Beta Thalassemia
Symptom
Splenomegaly in thalassemia
Abnormality
Splenomegaly

Carrier screening thalassemia

Symptom

... Carrier screening **thalassemia** Related family members with elevated HbA2 In carrier screening for the classical beta-**thalassemia** trait, the hallmark is the presence of an ... 2 (α 2 δ 2). Another way of identifying people with **thalassemia** major is neonatal screening. Neonatal screening ...
Rare Condition
Thalassemia major or Beta Thalassemia
Disease

(Dis) Abled People in Society

22qdeletion

The Family

Skeletal Dysplasia

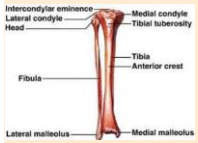
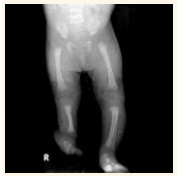
At work

Fibrodysplasia Ossificans Propressiva

Studies
Animal Science

Fibula Hypoplasia

ICF International Classification, Functioning, Disability and Health

	First Feature
	Diagnosis Fibula Hypoplasia
	Medical Guideline
	ICF : Body Functions & Structures
	ICF: Activity Participation

World Health Organization

ICS › 11 › 11.180 › 11.180.01

ISO 9999:2016

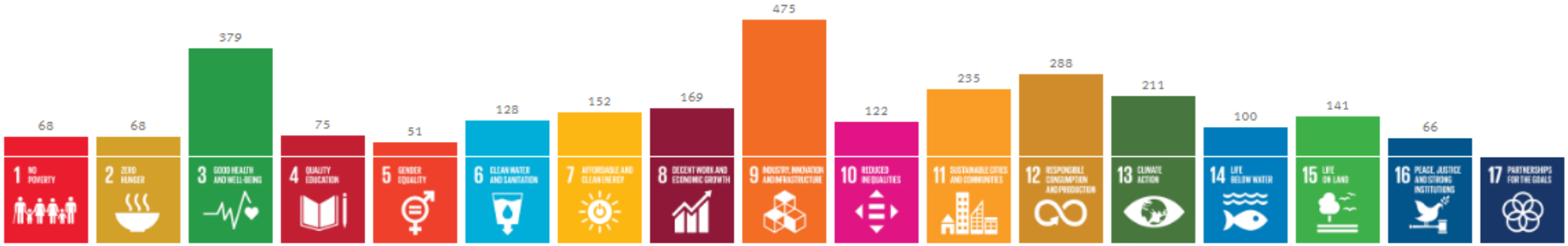
Assistive products for persons with disability — Classification and terminology

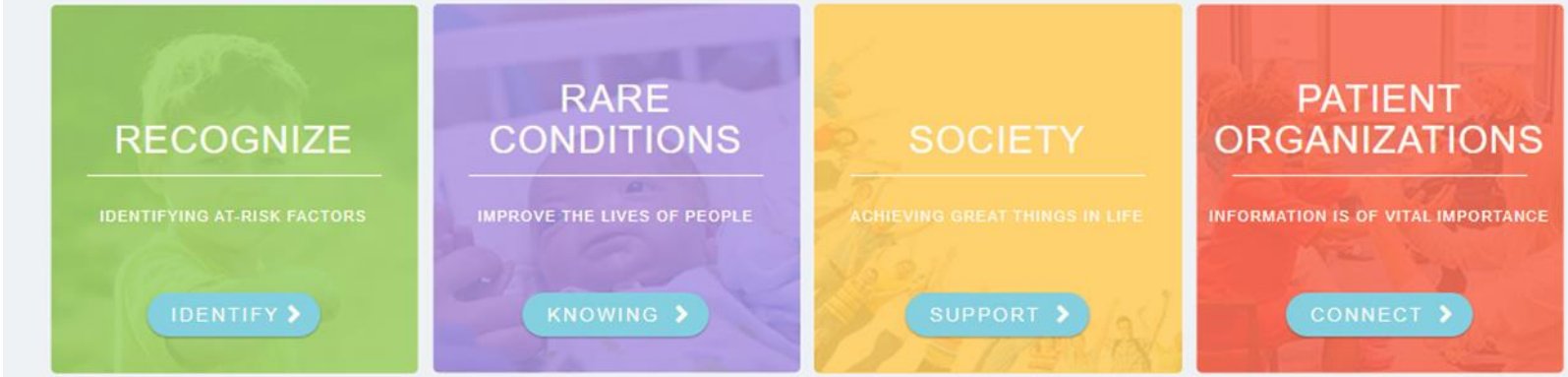
ISO= International Standards globally recognized guidelines and frameworks

ISO | Standards | All about ISO | Taking part | Store | EN

IMPACT AT A GLANCE

ISO contributes to all of the SDGs. Here you can see the number of ISO standards that are directly applicable to each Goal.





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থ্যালাসেমিয়া প্রধান বা বিটা থ্যালাসেমিয়া

থ্যালাসেমিয়া জেনেটিকালি (উত্তরাধিকারসূত্রে) রক্তের রোগের একটি গ্রুপ যা সাধারণ এক বৈশিষ্ট্যতে ভাগ করে; হিমোগ্লোবিনের ত্রুটিপূর্ণ উত্পাদন যা প্রোটিন যা লাল রক্ত কোষগুলিকে বহন ও অক্সিজেন সরবরাহ করতে সক্ষম করে। ত্রুটিপূর্ণ হিমোগ্লোবিন সংশ্লেষণের বিভিন্ন পদ্ধতি রয়েছে এবং অতএব, বহু ধরনের থ্যালাসেমিয়া রয়েছে।

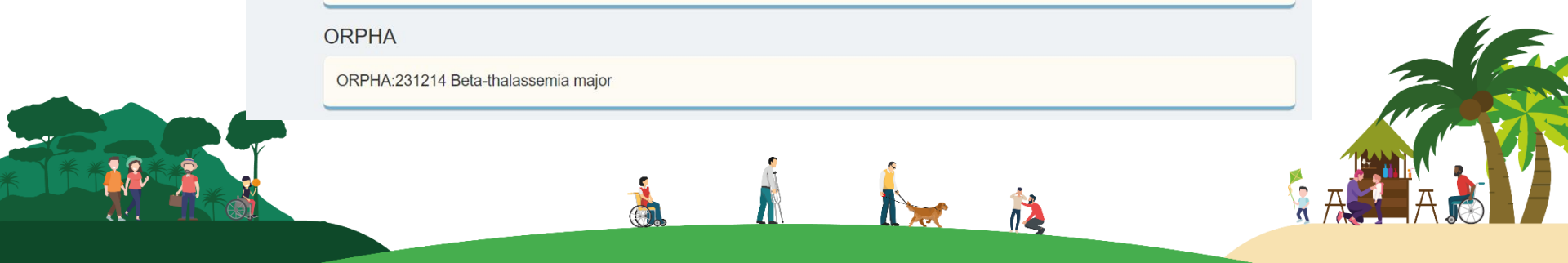
বিটা থ্যালাসেমিয়া হিমোগ্লোবিনের বিটা গ্লবিন শৃঙ্খলার অনুপস্থিতি বা হ্রাস সংশ্লেষণের কারণে ঘটে। বিটা থ্যালাসেমিয়া বৈশিষ্ট্য বা বিটা থ্যালাসেমিয়া নাবিক ব্যক্তিরা বিটা থ্যালাসেমিয়া বা বিটা-থ্যালাসেমিয়ার একজন ক্যারিয়ারের হেটারজাইজাস। বিটা থ্যালাসেমিয়া মেজারের ব্যাক্তি হ'ল বিটা থ্যালাসেমিয়ার জন্য হোমজাইজাস এবং এভাবে ত্রুটিপূর্ণ জিনের দুটি কপি রয়েছে এবং এই রোগটি বিকাশ করে: থ্যালাসেমিয়া প্রধান। জিনের সম্পূর্ণ অনুপস্থিতিটি β0 থ্যালাসেমিয়া হিসাবে বর্ণনা করা হয় এবং β + হিসাবে সংশ্লেষকে হ্রাস করা হয়। বিটা-গ্লোবিনের হ্রাস α গ্লবিন চেইনগুলিতে আপেক্ষিক অতিরিক্ত বাড়ায়।

OMIM

613985 BETA-THALASSEMIA

ORPHA

ORPHA:231214 Beta-thalassemia major



Thank

- European Pediatric Rare Disease Network

John Dodge, U.K.
Lali Margvelashvili, Georgia
Velibor Tasic, N- Macedonia
David Neubauer, Slovenia
Arunas Valiulis, Lithuania
Jola Wierzba, Poland

- Consensus in Pediatrics and Child Health

Manual Katz, Israel

- Forum Rare Diseases, Sri Lankan Pediatric Society

Anjan Bhattacharya, India

- People with a rare condition and their families

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Stichting Shwachman syndroom Support Holland

Just normal people

Advocaters

Goldenhar syndrome

Thalassemia

Chromosome abnormality

Shwachman Diamond Syndrome

Thank You
For Your Attention