Genetics and the mouth

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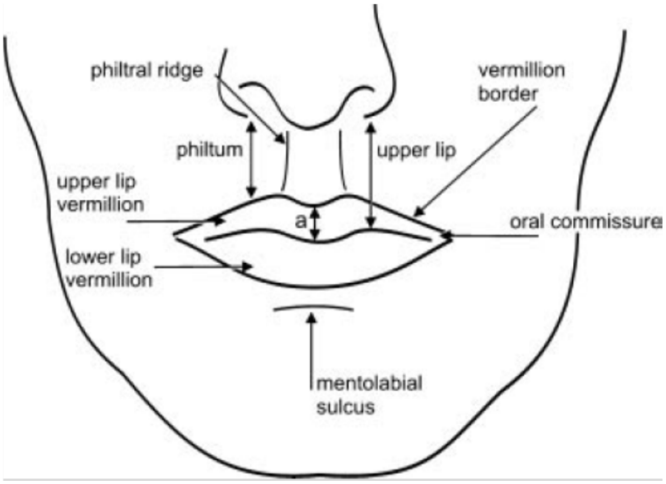
Overview

- Overview of terminology
- Lips
- Tongue
- Clefts – palate and lip

Terminology



Lips

- Size = eg full, thin
- Shape = eg everted, cupid's bow
- Colouration = eg freckling
- Additional structure = eg lip pits

Full lips

- Williams syndrome – microdeletion syndrome involving 7q11.23. Distinctive facial features, hoarse voice, cardiovascular abnormality.
- Coffin-Lowry syndrome – X-linked intellectual disability syndrome. Down-slanted palpebral fissures, bulbous nose, tapering fingers
- Coffin-Siris syndrome – hypoplastic 5th finger, coarse facies and hirsutism with ID. Mostly dominant inheritance
- X-linked a-thalassemia – X-linked intellectual disability with characteristic facies and genital abnormalities. HbH detected
- Costello syndrome - RAS-opathies spectrum with macrocephaly, coarse facies, loose skin over hands and feet
- FG syndrome – X-linked intellectual disability syndrome with imperforate anus, hypotonia and prominent forehead
- MPS…..

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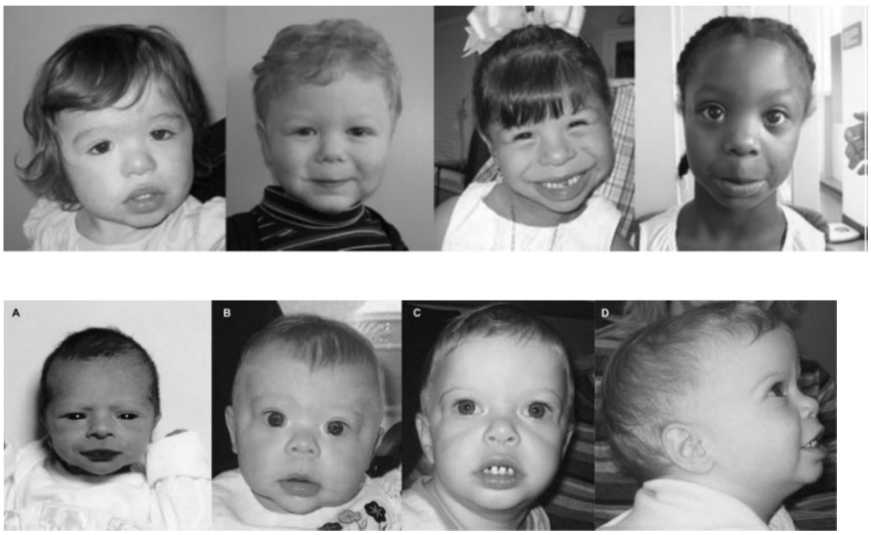
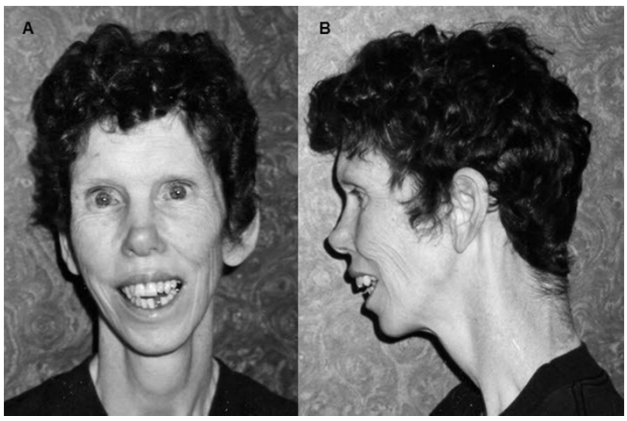

A
B
C
D


A
B

Additional features:
- Development
- Personality
- Cardiovascular lesions
- Urinary malformations
- Calcium disturbances

Diagnosis:
- FISH
- MLPA

Treatment:
- Guidelines - https://kr.ihc.com/ext/Dcmnt?ncid=521096048&tfrm=default

Recurrence:
- Autosomal dominant

http://www.ncbi.nlm.nih.gov/books/NBK1249/

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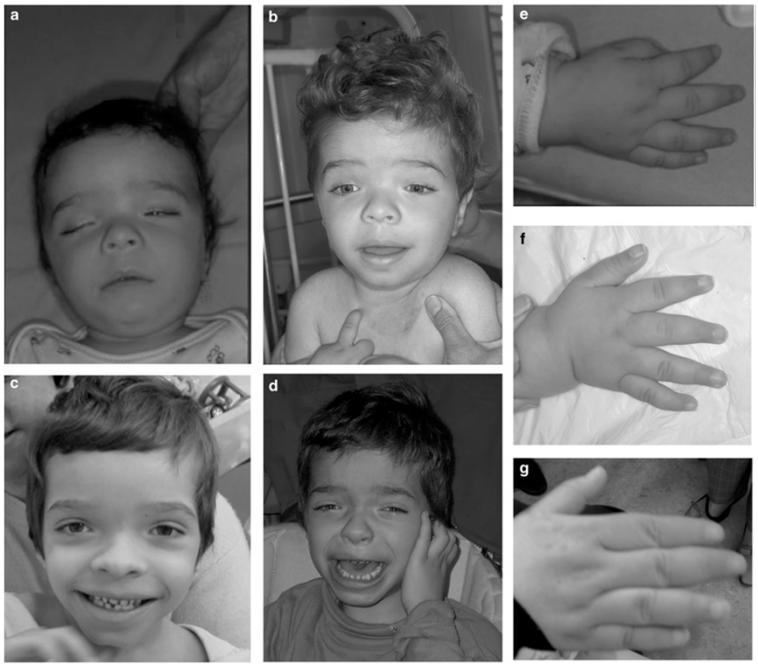

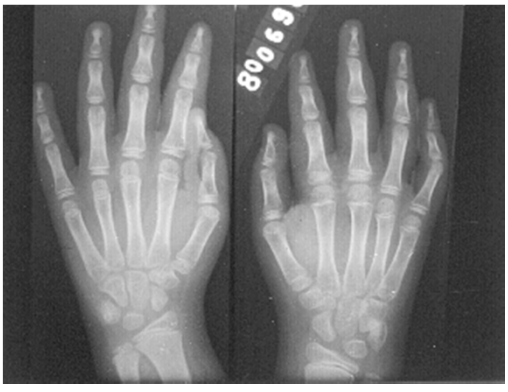

Additional features:
- Development
- Dental manifestations
- Skeletal abnormalities
- Radiological features
- Cardiac

Diagnosis:
- *RPS6KA3* in 50%
- Clinical and X-rays

Management:
- Recent article http://www.nature.com/ejhg/journal/v18/n6/full/ejhg2009189a.html

Inheritance
- X-linked dominant

Coffin-Lowry syndrome. European Journal of Human Genetics 2010
http://www.ncbi.nlm.nih.gov/books/NBK1346/

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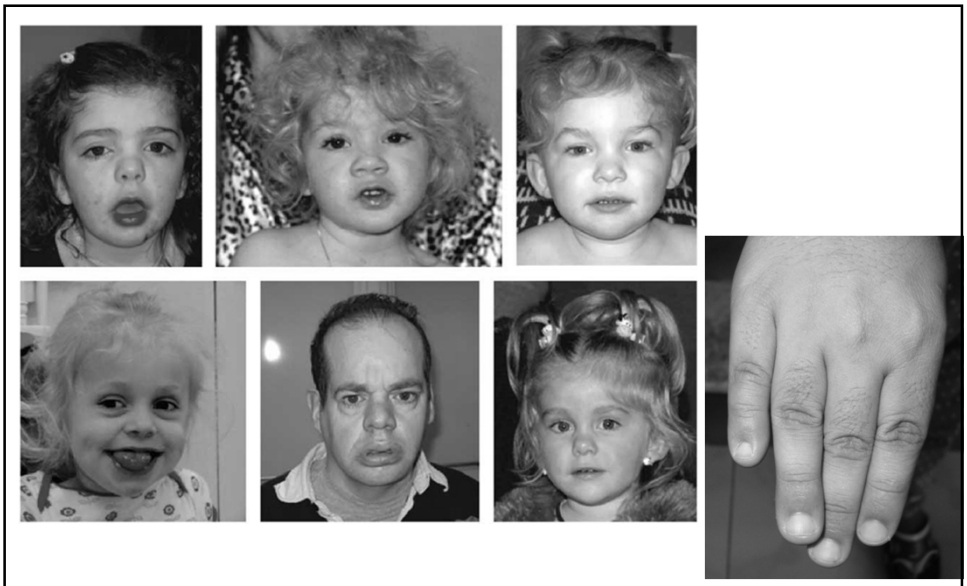

- http://www.ncbi.nlm.nih.gov/books/NBK131811/http://www.ncbi.nlm.nih.gov/books/NBK131811/

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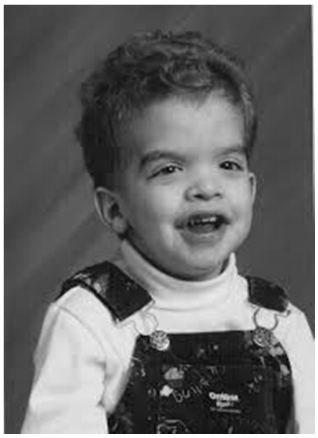

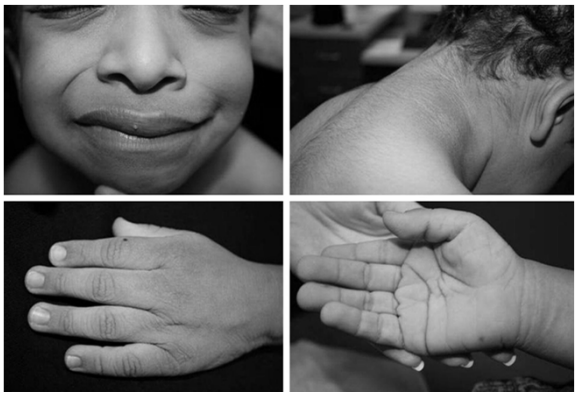

1. https://waltersfamily.wordpress.com/micahs-journey/costello-syndrome/
2. Google images

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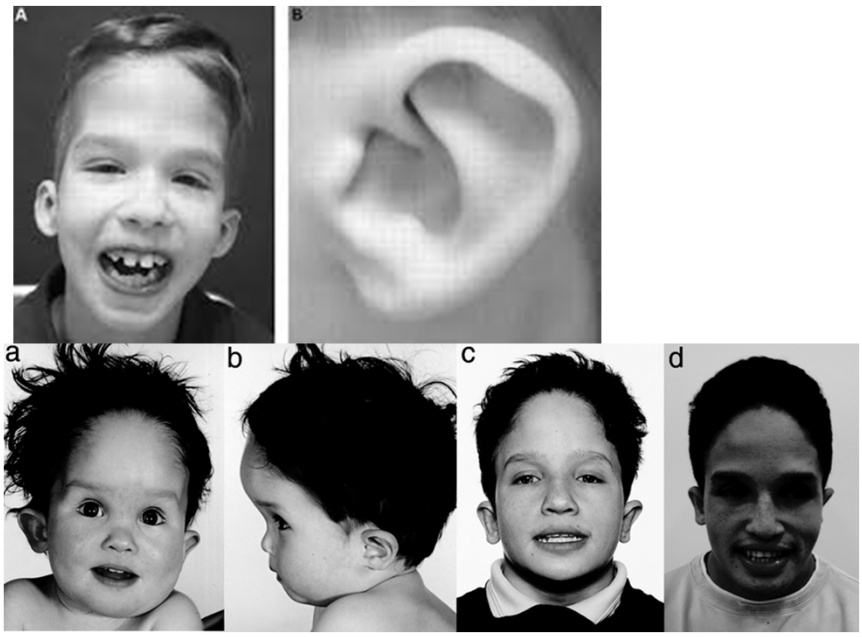


http://trialx.com/curebyte/2011/08/19/fg-syndrome-photos-and-related-clinical-trials/

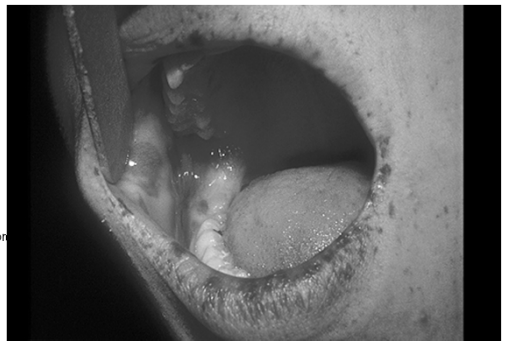
FG syndrome, an X-linked multiple congenital anomaly syndrome: The clinical phenotype and an algorithm for diagnostic testing(genetics in medicine, 2009)

Colouration

- Freckling

Peutz-Jegher syndrome

http://www.medicinenet.com/image-collection



Lip pits

- Van der Woude syndrome – lower lip pits, cleft lip and missing second premolars
- Popliteal pterygium syndrome – popliteal webs, cleft palate and lip pits
- Branchio-oculo-facial syndrome – branchial defects, lacrimal duct obstruction, pseudocleft upper lip
- Kabuki syndrome – large palpebral fissures, eversion lower eye lid, persistent fetal fingerpads

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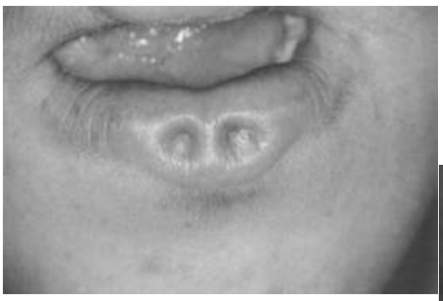

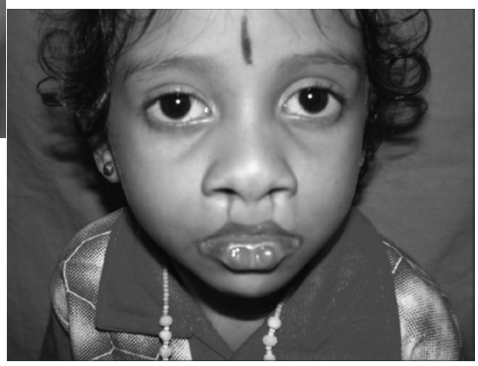

https://embryology.med.unsw.edu.au/embryology/index.php?title=File:Van_der_Woude_syndrome_with_lower_lip_pits.jpg

- Additional features

Cleft palate

- Diagnosis

IRF6

Clinical

- Inheritance:

Autosomal dominant (variable expression)

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- Oral-facial-digital syndrome – see later

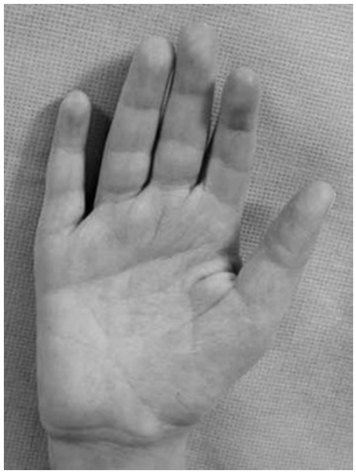
- Additional features:

Intellectual disability
Cardiac abnormalities
Skeletal abnormalities
Cleft palate

- Diagnosis:

MLL2 (KMT2D) gene (KDM6A)

www.Kabukisyndrome.com



Tongue

- Size – microglossia or macroglossia
- Shape – lobulated

Macroglossia

- Beckwith-Wiedeman syndrome – macrosomia, large tongue, anterior abdominal defect, ear creases
- MPS
- Simpson-Golabi-Behmel syndrome - X-linked, multiple congenital abnormality, intellectual disability syndrome
- X-linked thalassemia

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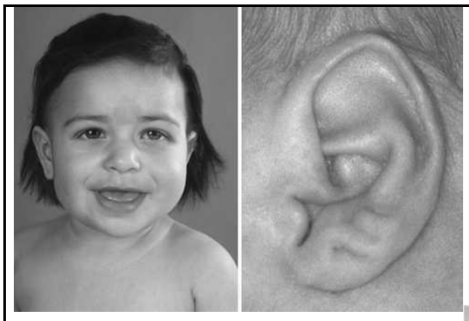

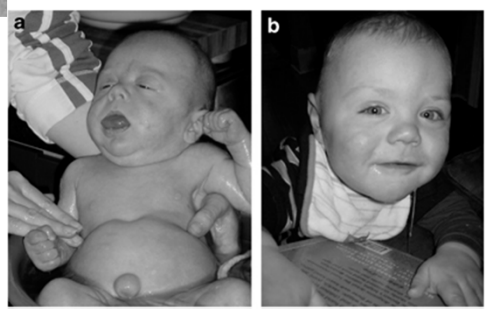

Beckwith-Wiedeman syndrome (European Journal Human Genetics 2009)
http://atlasgeneticsoncology.org/Kprones/BeckwithWiedemannID10037.html

- Additional features:

Major findings-fam hx, macrosomia, macroglossia, ear creases/pits, omphalocele, visceromegaly, embryonal tumour, hemihyperplasia, cytomegaly fetal adrenal cortex, renal abn, cleft palate, placental mesenchymal dysplasia, cardiomegaly, cardiomyopathy

Minor findings- antenatal, hypoglycaemia, naevus flammeus, cardiac abn, facial features, diastasis recti, advanced bone age

- Diagnosis

Molecular not available in SA.

Multiple different mechanisms.

- Management:

Large newborn

Tumour surveillance

- Inheritance:

Mostly sporadic but few familial

Cleft lip and palate

- 1 in 700
- M:F 2:1 for cleft lip and 1:2 for cleft palate
- 70% of CL/P is non-syndromic
- 50% CP is non-syndromic

Etiology

Syndromic	Non-syndromic
Chromosomal – trisomy 13, 4p-	Environmental – smoking, infections, medication, temperature, alcohol
Single gene disorders – van der woude syndrome, Stickler syndrome, 22q deletion syndrome, Treacher-Collins syndrome, Kabuki syndrome, Opitz syndrome	Single genes – IRF6, MSX1
	Multifactorial – family history and combination of susceptibility genes

Recurrence risk

- Dependent on the cause
- Multifactorial:

Relationship to index case	Recurrence risk
Sibling with unilateral CL	2-3%
Sibling with unilateral CL/P	4%
Sibling with bilateral CL/P	5-6%
Two affected siblings	10%
Affected sibling and parent	10% (excluding dominant)
Affected parent	4%

- Folic acid!!

- Very brief overview of some oral manifestations genetic syndromes
- Recognition and literature reviews

- Thank you