BIGGER DOES NOT NECESSARILY ALWAYS MEAN BETTER

PRESENTOR:

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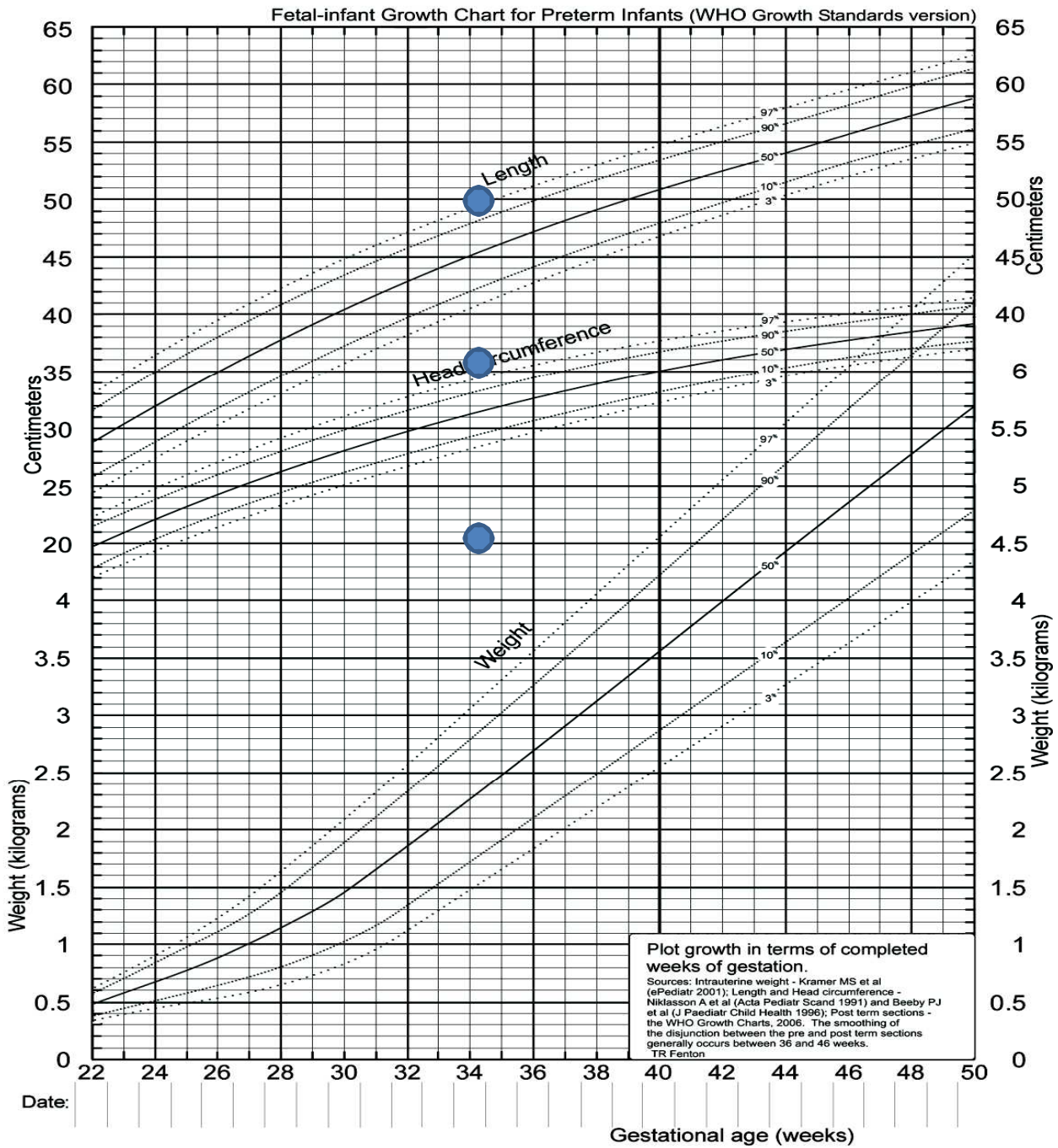
A BRIEF HISTORY

- Term / LGA / BOY / BREECH PRESENTATION
- ANTENATAL HISTORY
- G2 P1 L1 mother - 37 wks + 6 days
- Spontaneous conception
- AN scans - normal
- Rh Positive mother
- NATAL HISTORY
- Emergency LSCS – fetal distress
- APGAR – 8/10, 9/10

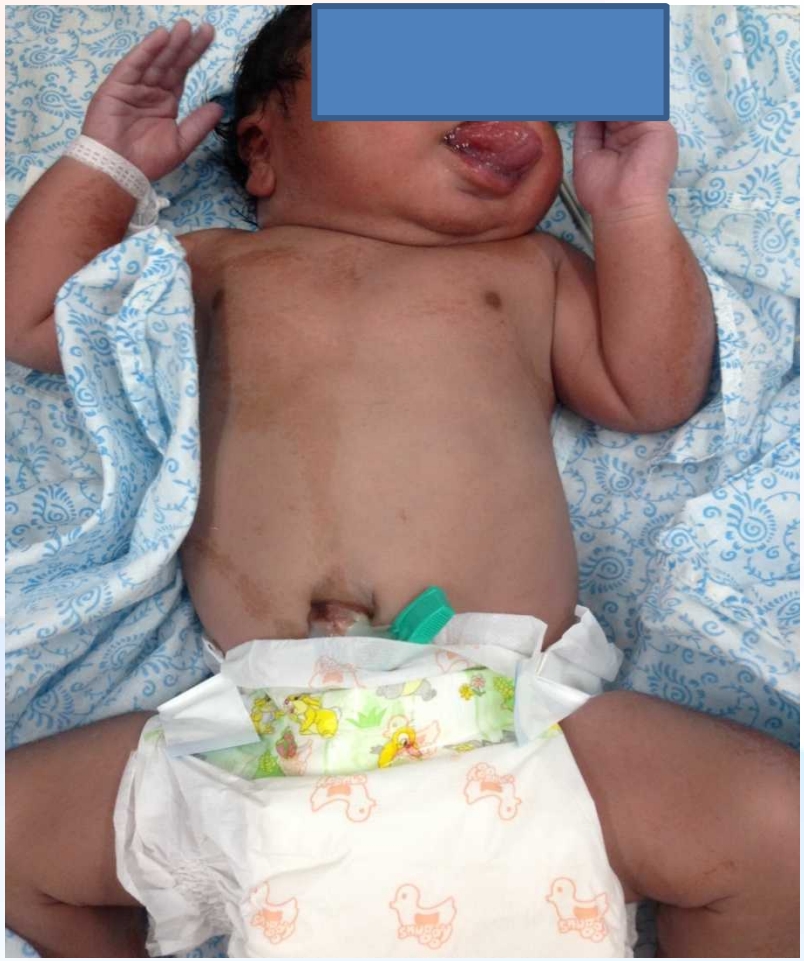
A DETAILED CLINICAL EXAMINATION

FENTONS GROWTH CHART



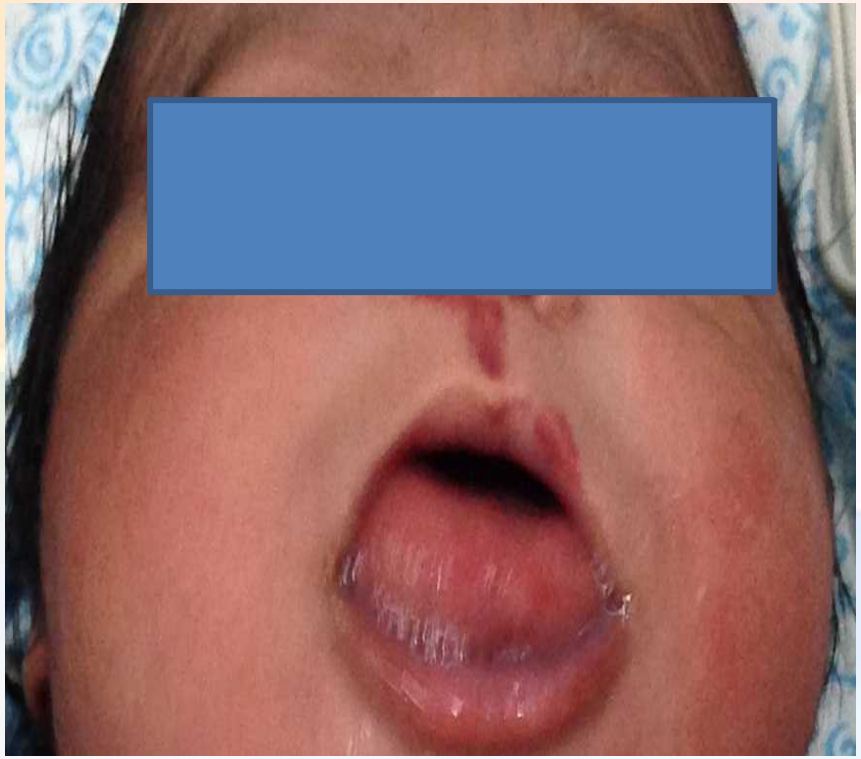
GENERAL EXAMINATION

- Cry, colour, activity – good
- All four limbs kept flexed
- HR - 150/min
- RR - 48/min
- SpO2 - 94% in room air
- CFT < 3 secs
- BP – 70/44 mm Hg

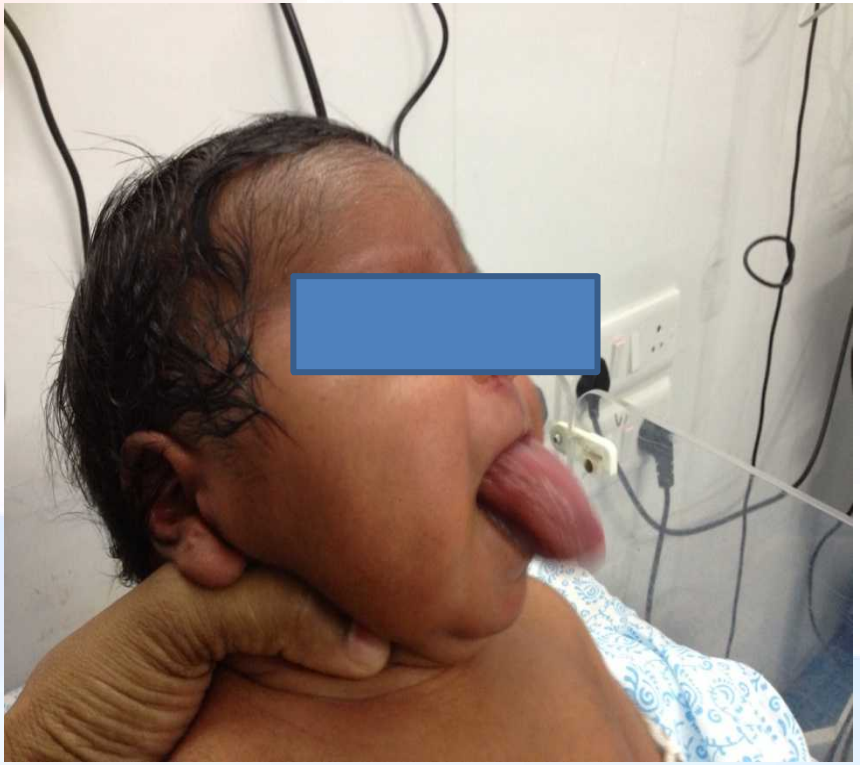


HEAD TO FOOT EXAMINATION

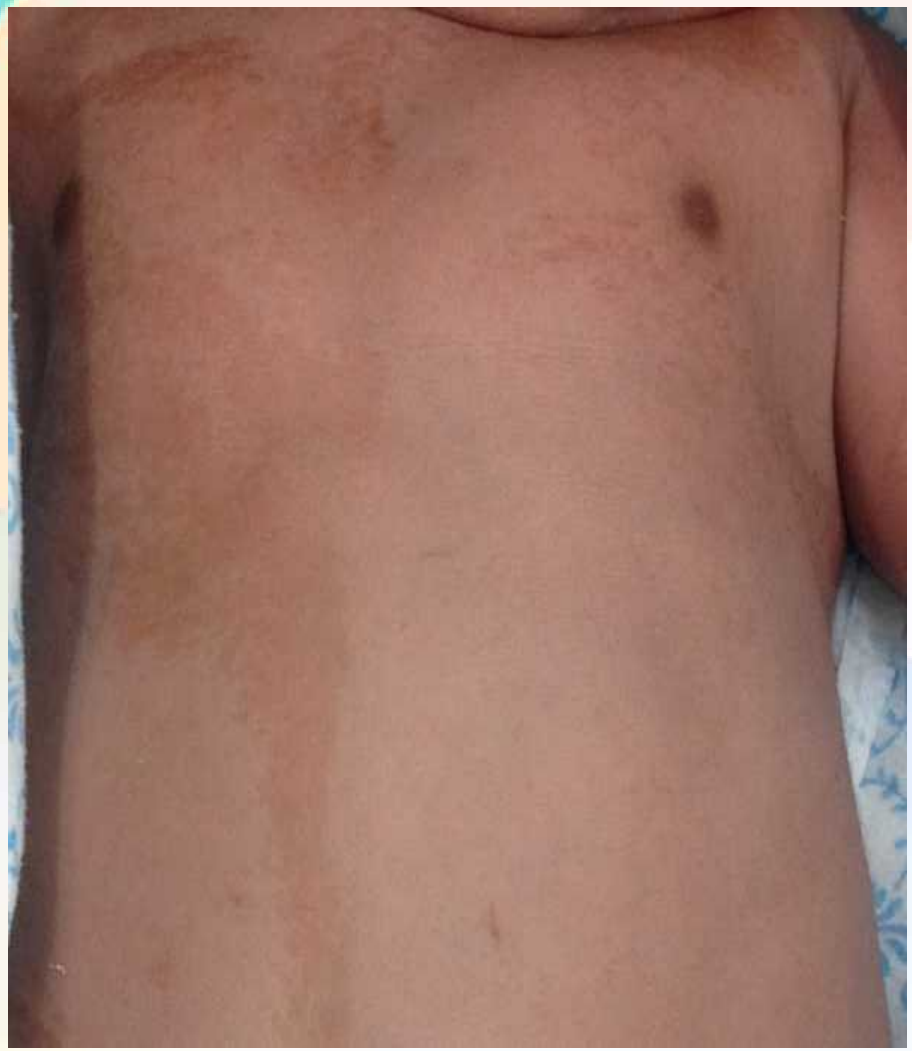
Facial hemangioma



Macroglossia – Tongue not compressible or transilluminant



Truncal Naevus



Umbilical defect

Hemihypertrophy

In cms	Arm	forearm	Thigh	Leg	MAC	Mid thigh
Right	8	9	12	9.5	13	18
Left	8	9	12	9	12	17

SYSTEMIC EXAMINATION

- CVS - S1+, S2+, Short systolic murmur+
- RS – B/L air entry equal
- ABDOMEN – soft

  no palpable mass

  umbilical area defect+
- CNS – moves all four limbs
- GENITALIA - normal

COURSE AT NICU

- On day 0 of life – asymptomatic hypoglycemia

Treated with 10% dextrose

- DBF- not able to suck well – Hence put on demand paladai feeds.

DIFFERENTIAL DIAGNOSIS

- Struge weber syndrome
- Beckwith wiedeman syndrome

ULTRASONOGRAM

- ABDOMEN: B/L mild renal enlargement
- CRANIUM : No calcifications

ECHO

- Congenital acyanotic heart disease
- Small PDA with bidirectional shunt
- Stucturally normal heart
- Neonatal pulmonary hypertension

MRI

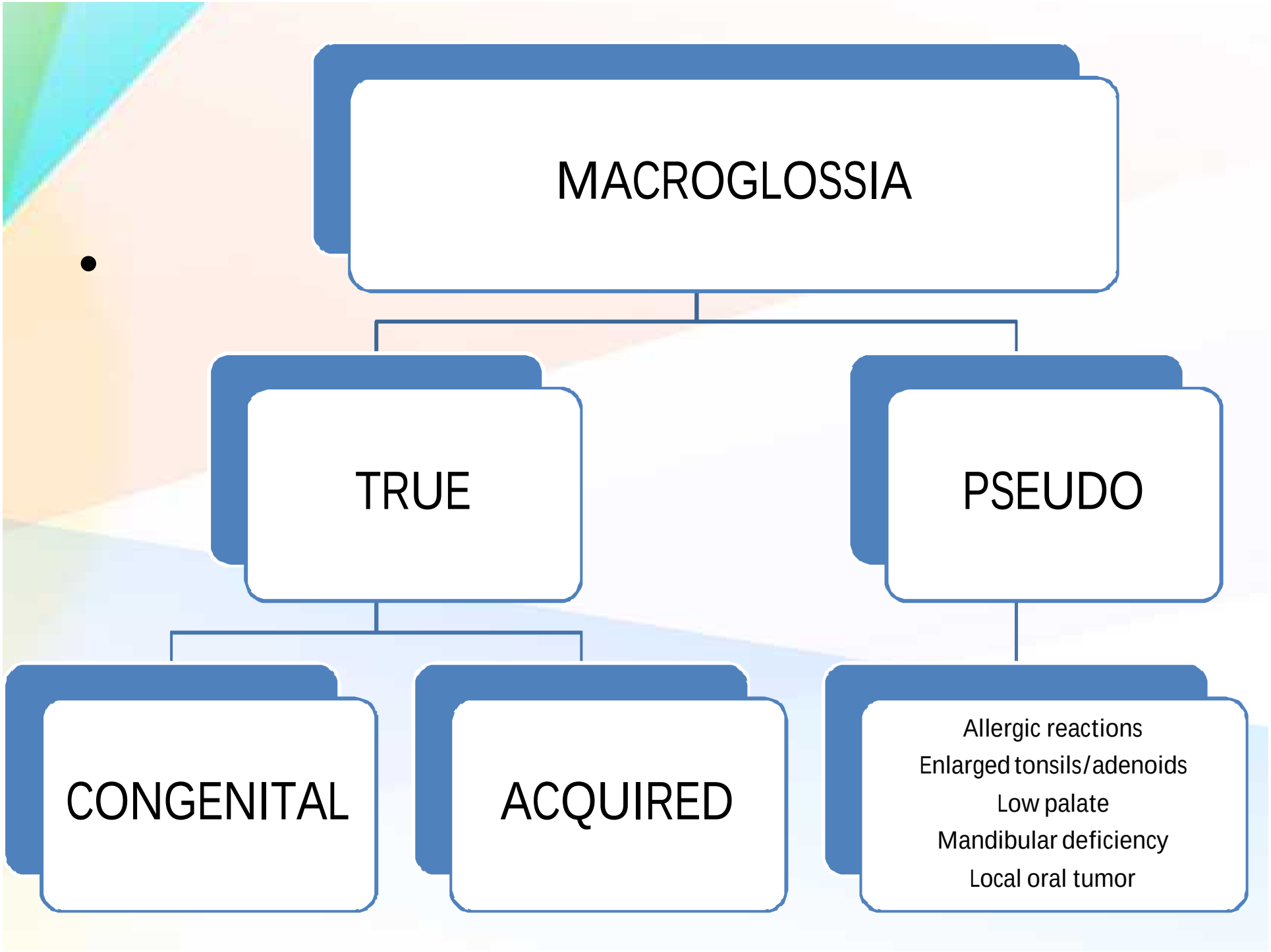
- BRAIN – normal study
- FACE – Subtle prominence of fat and soft tissue component in the right hemiface.
- Diffuse macroglossia. The upper airway appear is mildly narrowed at retroglossal level.
- EYE EXAMINATION: No bupthalmos. Clear media

Beckwith wiedemann syndrome

TREATMENT AND FOLLOW UP:

- Propranolol therapy for tongue hemangioma
- USG abdomen triannually till 5 yrs of life
- Serum AFP levels
- Genetic studies (reports awaited)

DISCUSSION


MACROGLOSSIA
TRUE
PSEUDO
CONGENITAL
ACQUIRED
Allergic reactions
Enlarged tonsils/adenoids
Low palate
Mandibular deficiency
Local oral tumor

CONGENITAL

- Idiopathic tongue muscle hypertrophy
- Salivary gland tumor
- Hemangioma
- Lymphangioma
- Syndromes (beckwith-weidemann syndrome, Behmel, Laband)
- Lingual thyroid
- Mucopolysacchaidoses
- Hamartoma

ACQUIRED

- TRAUMA: hematoma
- INFLAMMATORY:
  Ludwig angina, Pemphigous vulgaris, diptheria, TB, sarcoidosis, actinomycosis
- METABOLIC/ ENDOCRINE:
  Hypothyroidism, cretenism, amyloidosis, acromegaly, myxoedema
- NEOPLASM: Lymphoma, plasmocytoma, carcinoma
- SYSTEMIC: NF

Genetic Causes of Macroglossia: Diagnostic Approach

AUTHORS: Carlos E. Prada, MD,[a,b] Yuri A. Zarate, MD,[c] and Robert J. Hopkin, MD[a,b]

[a]*Division of Human Genetics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio;* [b]*Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio; and* [c]*Greenwood Genetic Center, Greenwood, South Carolina*

WHAT'S KNOWN ON THIS SUBJECT: Macroglossia is a clinical feature of several disorders and a common reason for additional diagnostic investigations during infancy. Limited research has been done on the evaluation of macroglossia when other features are not suggestive of Beckwith-Wiedemann syndrome.

135 macroglossia children identified. Classified on initial examination as isolated macroglossia (n = 24), provisional BWS (n = 36), and syndromic (n = 24).

10 patients the reason -undetermined. Among the elucidated cases, BWS was the most common cause of macroglossia (39/84).

6/24-isolated macroglossia group had an abnormal molecular test for BWS .

BWS was the most common cause of macroglossia even in the absence of additional clinical findings.

OVERGROWTH SYNDROMES

- Heterogeneous group of diseases- mostly genetic
- Dysfunction in the tyrosine kinase (RTK)/PI3K/AKT receptor pathway and increased expression of the insulin receptor.
- Localized or diffuse tissue enlargement
- Often manifest at birth or in the postnatal period
- Many increase the risk of cancer.

Overgrowth Syndromes . By Michael Cohen, Jr.; Giovanni Neri; and Rosanna Weksberg. New York: Oxford University Press, 2002.

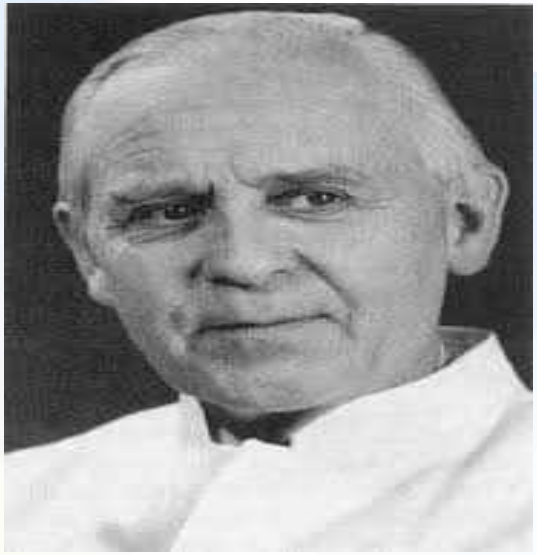
EXAMPLES

- Beckwith-Wiedemann syndrome
- Simpson-Golabi-Behmel syndrome
- Perlman syndrome
- Sotos syndrome
- Weaver syndrome
- Bannayan-Riley-Ruvalcaba syndrome
- Proteus syndrome
- Klippel-Trenaunay, Parkes Weber
- Sturge-Weber syndromes
- Maffucci syndrome
- Neurofibromatosis
- Fragile X syndrome

BECKWITH-WIEDEMANN SYNDROME

HISTORY

- Dr. Hans-Rudolf Wiedemann coined the term exomphalos - macroglossia - gigantism(EMG)



- Renamed Beckwith–Wiedemann syndrome
- Prof. John Bruce Beckwith
- Increase in adrenal gland size.

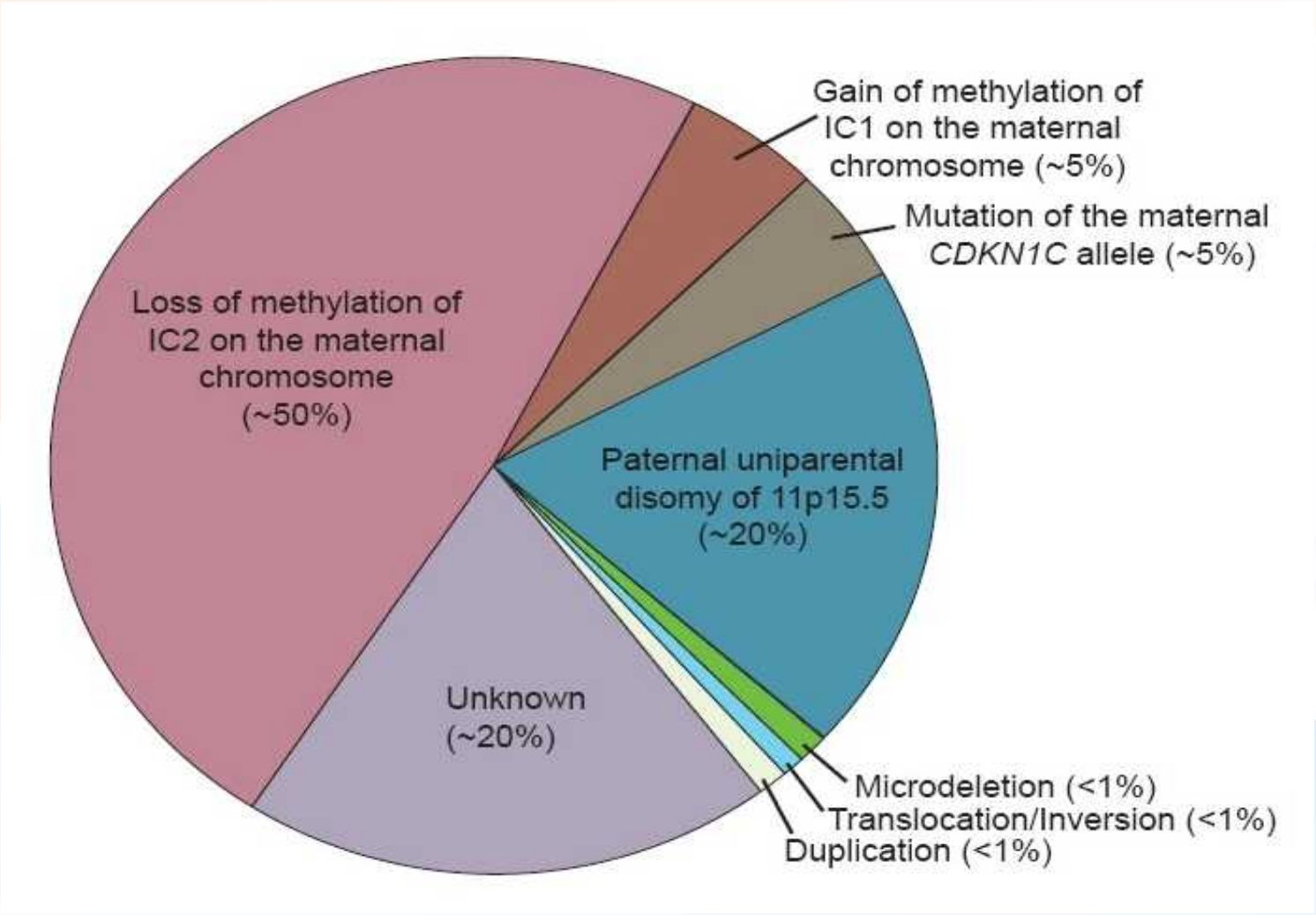
- Most common over growth syndrome
- Incidence: 1 in 13,700 live birth
- Males = Females
- Sporadically – 85 % , Familial-15 %

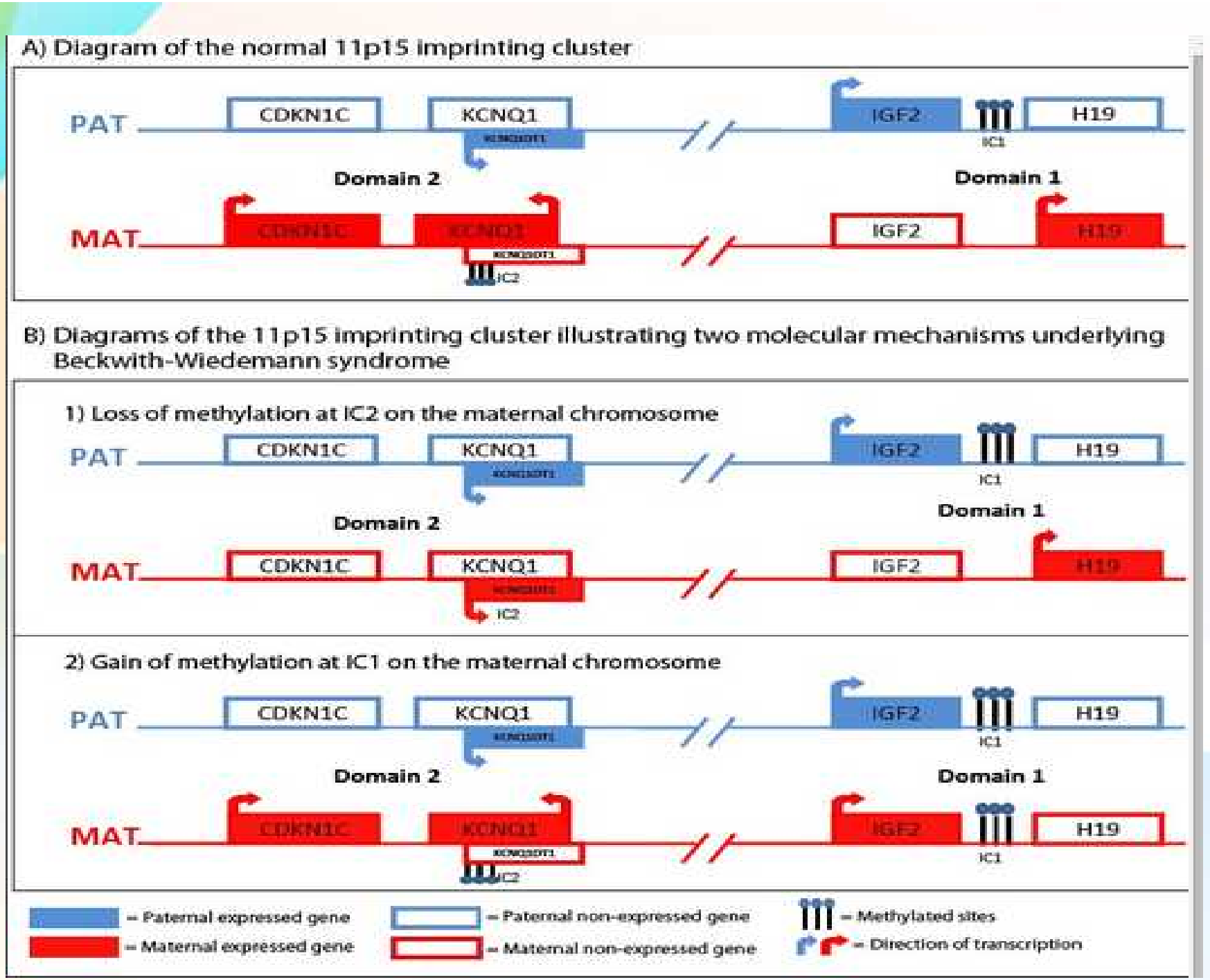
GENETICS

- Deregulation of imprinted gene expression in the chromosome 11p15.5 region - AD
- The critical BWS genes –
- insulin-like growth factor 2 (IGF2)
- H19
- cyclin-dependent kinase inhibitor 1C (CDKN1C)
- Voltage-gated potassium channel KQT-like subfamily member 1 (KCNQ1), and KCNQ1-overlapping transcript 1.

Beckwith-Wiedemann Syndrome- GENE REVIEWS
Cheryl Shuman, MS, CGC, J Bruce Beckwith, MD, Adam C Smith, PhD, and Rosanna Weksberg, March 3, 2000; Last Update: December 14, 2010.

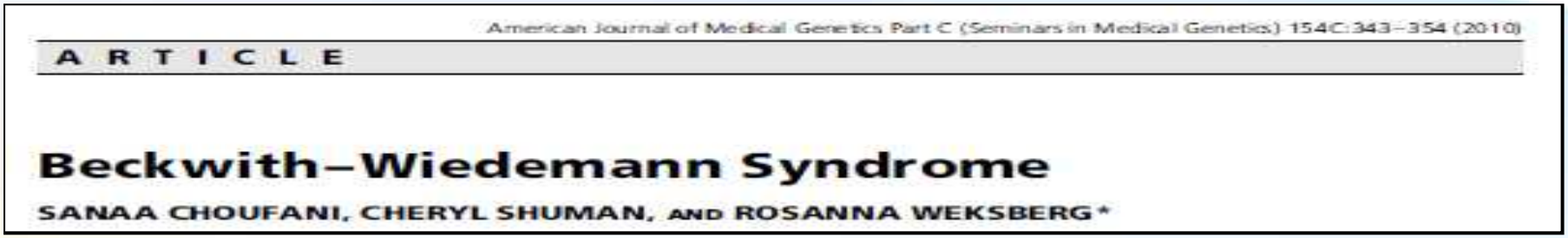
MOLECULAR ALTERATIONS




A) Diagram of the normal 11p15 imprinting cluster
PAT
CDKN1C
KCNQ1
IGF2
H19
IC1
Domain 2
Domain 1
MAT
IC2
B) Diagrams of the 11p15 imprinting cluster illustrating two molecular mechanisms underlying Beckwith-Wiedemann syndrome
1) Loss of methylation at IC2 on the maternal chromosome
2) Gain of methylation at IC1 on the maternal chromosome
= Paternal expressed gene
= Maternal expressed gene
= Paternal non-expressed gene
= Maternal non-expressed gene
= Methylated sites
= Direction of transcription

BWS and ART

- Children conceived in vitro have a greater risk of rare disorders involving imprinted genes.
- Idiopathic male infertility -shown to be strongly associated with aberrant methylation
- Ovarian stimulation- also been associated with perturbed genomic imprinting.


American Journal of Medical Genetics Part C (Seminars in Medical Genetics) 154C:343–354 (2010)

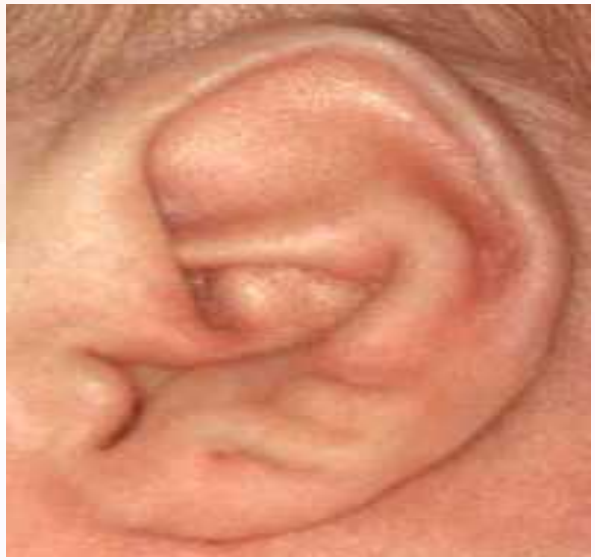
ARTICLE

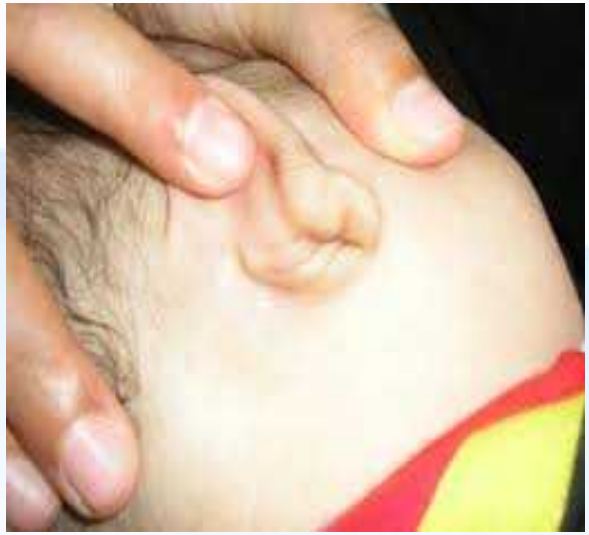
Beckwith–Wiedemann Syndrome

SANAA CHOUFANI, CHERYL SHUMAN, AND ROSANNA WEKSBERG*

CLINICAL PRESENTATION

- Macrosomia / macroglossia
- Hemihyperplasia/ Visceromegaly
- Omphalocele, hernia,diastasis recti
- Anterior linear ear lobe creases
- Embryonal tumors
- Cytomegaly- fetal adrenal cortex
- Neonatal hypoglycemia
- Facial nevus flammeus
- Characteristic facies- midface hypoplasia and infraorbital creases
- Renal abnormalities - structural anomalies, nephromegaly, calcinosis, medullary sponge kidney
- Cardiomegaly/structural cardiac anomalies; cardiomyopathy (rare)





NEOPLASM

- >80% with BWS do not develop cancer
- 600 times more prone than other children to develop certain childhood cancers

❖ Wilms' tumor

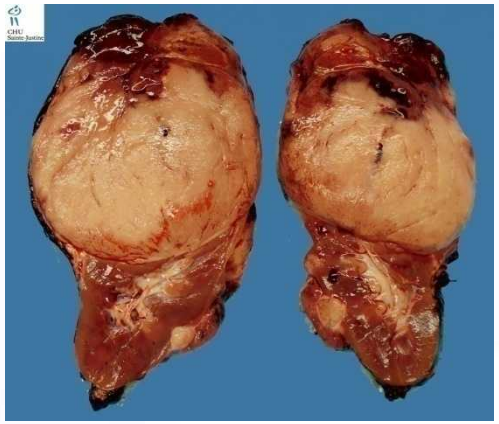
❖ Pancreatoblastoma

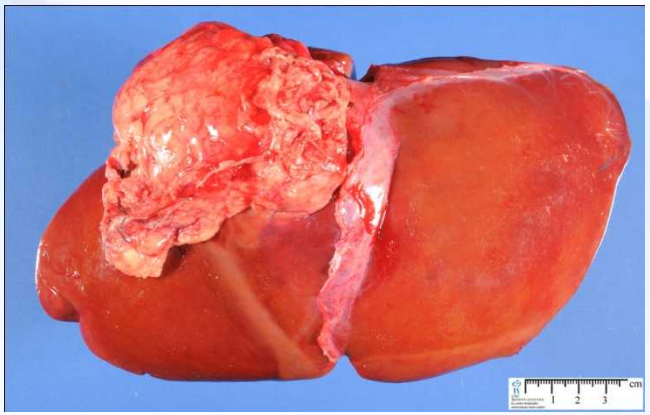
❖ Hepatoblastoma

❖ Adrenal cortical carcinoma

❖ Neuroblastoma

❖ Rhabdomyosarcoma





DIAGNOSIS

- No consensus diagnostic criteria exist
- Methylation-sensitive multiplex ligation probe analysis (MS-MLPA) is the most robust method clinically available for detecting genetic etiologies.
- Karyotype analysis detects maternally transmitted translocations/inversions and will also detect paternally derived duplications of chromosome 11p15.5.
- DNA sequencing is required to detect genomic alterations in the cyclin-dependent kinase inhibitor

PRENATAL diagnosis

- Prenatal testing may be undertaken by chorionic villus sampling or amniocentesis, if the cytogenetic or genomic abnormality in the affected family member is known

MANAGEMENT

Treatment of manifestations:

HYPOGLYCEMIA	• Dextrose fluids
MACROGLOSSIA	• ET intubation • Specialized nipples or NG tube feedings • Tongue reduction surgery • Speech therapy
HEMIHYPERPLASIA ABD WALL DEFECTS	• Limb and cranio facial surgeries • Abdominal wall repairs
NEOPLASIA	•standard pediatric oncology protocols

Prevention of secondary complications

- Annual renal USG – 8 yrs and mid-adolescence to identify nephrocalcinosis or medullary sponge kidney disease.

Surveillance

- Hypoglycemia, especially in the neonatal period
- Embryonal tumors- abdominal USG every 3 mths until 8 yrs
- Serum AFP concentration every 2-3 mths in the first four years of life- early detection of hepatoblastoma.

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- Baby's parents
- Dr. P. Ramachandran, General Pediatrics
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THANK YOU