

# Knowledge Burst | The Neonatal Dysmorphology Exam

Presenter – Jess Scott Schwoerer MD

## Learning Objectives

- Differentiate between major malformations (e.g. congenital heart defect, cleft palate) and minor anomalies (e.g., preauricular tags, clinodactyly)
- Describe how the dysmorphology exam can determine the likelihood of an underlying genetic syndrome and impact the decision to offer genomic testing.
- Identify resources for performing a dysmorphology exam including applying standardized terminology such as Human Phenotype Ontology (HPO) terms



# Major anomalies

- Structural defect that causes significant medical, functional, or cosmetic impact and typically requires medical or surgical intervention
- Not part of normal variation
- Examples:
  - Congenital heart disease
  - cleft lip and palate
  - neural tube defect

# Minor anomalies

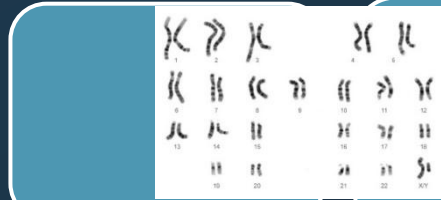
- Morphology feature that is uncommon, but does not cause significant medical, functional cosmetic consequence
- Low frequency in the general population –relatively common to have
- Example:
  - Single palmar crease
  - Preauricular ear tags/pits
  - Clinodactyly
  - Low set ears



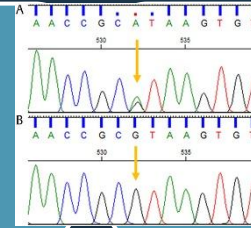
# Genetic Testing is a Key Diagnostic Tool



Phenotyping.



Karyotype



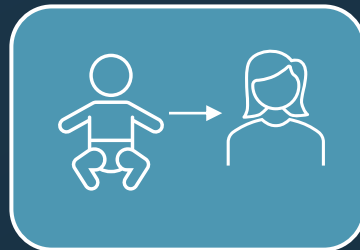
Single-Gene



Exome/Genome



Understanding of the condition



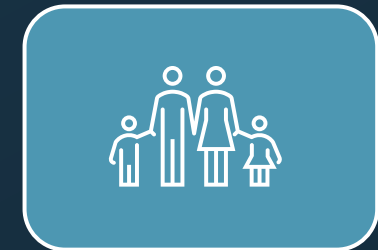
Prognosis



Management



Treatments



Implications for families



# Importance of Dysmorphology Exam with Genomic testing

- Dysmorphic features are one criterion to consider when selecting patients for genomic testing.



## Indications for ES/GS in Critically Ill Neonates

*These criteria do not exclude completion of other genetic testing or consultation in the hospitalization for indications not listed here.*

- Neonatal encephalopathy without inciting event
- Multiple congenital anomalies not suggestive of aneuploidy<sup>i</sup>
- Concern for metabolic disorder<sup>ii</sup>
- Hydrops fetalis without clear etiology
- Neonatal seizures without HIE
- Abnormal neurologic exam including significant hypotonia/hypertonia, weakness Complex congenital heart disease
- Growth abnormality including Intrauterine Growth Restriction (IUGR), Small for Gestational Age (SGA), micro/macrocephaly or overgrowth without clear etiology
- **Dysmorphic features**

<sup>i</sup> Common aneuploidies: Trisomy 21 (Down syndrome), Trisomy 13 (Patau syndrome), Trisomy 18 (Edward syndrome), Monosomy X (Turner syndrome)

<sup>ii</sup> Signs of Acute Metabolic Disorders in the Neonatal Period: Sudden, gradual or insidious onset of sepsis-like features including poor feeding, vomiting, lethargy, seizures, hypoglycemia and lactic acidosis, abnormal urine organic acids, hyperammonemia

# Importance of Dysmorphology Exam with Genomic testing

- Dysmorphic features that the provider identifies are used in the analysis of broad genomic sequencing and can be helpful in identifying an underlying etiology for a child
- Describe the features using Human Phenotype Ontology (HPO) terms
  - a database that provides a standardized vocabulary of phenotypic abnormalities found in human disease
  - Human Phenotype Ontology

## PRIMARY FINDINGS: Heterozygous for a Pathogenic Variant in *BRAF*

**INDICATION FOR TESTING:** Polyuria (resolved), Anteverted nares, Anteriorly placed anus, Polyhydramnios, Premature birth, Ventricular septal defect, Abnormal pulmonary valve morphology (domed pulmonary valve), Pulmonic stenosis, Patent foramen ovale, Thrombocytopenia, Deep philtrum, Vomiting, Abnormal stomach morphology (small), Respiratory failure requiring assisted ventilation, Abnormality of the palmar creases ("hockey stick" palmar crease bilaterally), Fetal pyelectasis (bilateral mild renal pyelectasis), Abnormal lateral ventricle morphology (mild prominence & small echogenic foci in caudothalamic subependymal regions), Periventricular white matter hyperintensities

Variants in genes known to be associated with phenotype:

Sequence Variant(s):

| Gene, Transcript          | Mode of Inheritance, Gene OMIM | DNA Variants, Predicted Effects, Zygosity | ClinVar ID | Highest Allele Frequency in a gnomAD Population | In Silico Missense Predictions | Interpretation |
|---------------------------|--------------------------------|-------------------------------------------|------------|-------------------------------------------------|--------------------------------|----------------|
| <i>BRAF</i> , NM_004333.4 | AD, 164757                     | c.1403T>C, p.Phe468Ser, Heterozygous      | 40366      | 0.00068% European (Non-Finnish)                 | Damaging                       | PATHOGENIC     |



# Importance of Dysmorphology Exam with Genomic testing

- Important in interpretation of testing particularly with variants of uncertain significance
- When dysmorphology of a patient matches some or all of the dysmorphism expected in a variant of uncertain significance, the clinical interpretation may move that variant to disease causing.

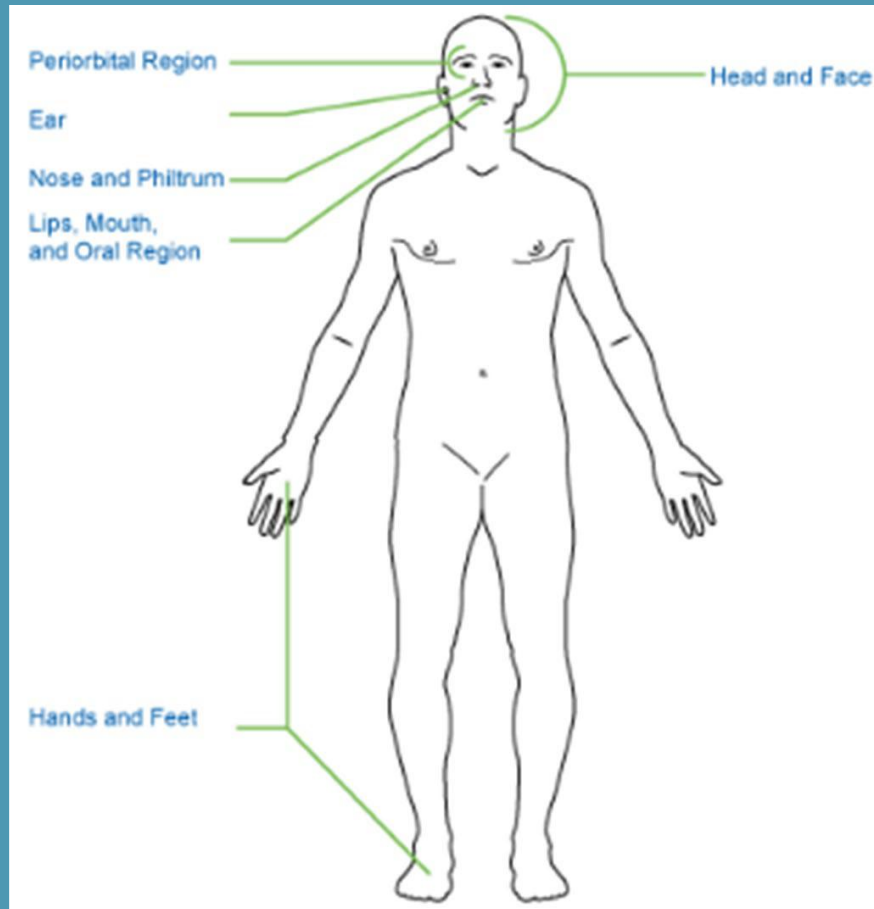


# Approach to Dysmorphology exam

- Observe
  - Gestalt – does the child look atypical?
  - Details of each component –size, shape, quality, proportion, placement, extra/missing,
- Identify a few of the most striking features
- Photos into the EMR with Haiku
- Note for interacting with patient and families:
  - Normalize differences and discuss differences may be a tool to help see if there is an underlying genetic cause for the patient's health concern.
  - Consider the language used.



# Approach to Dysmorphology exam



# Approach to Dysmorphology exam

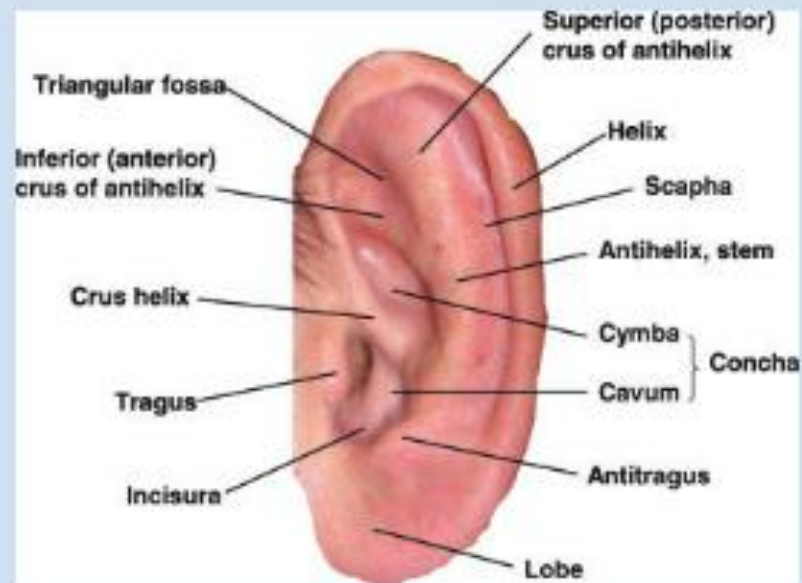


FIG. 1. Normal anatomy of the external ear.

## Anatomical Variation

Anomalies of the ear include quantitative traits and qualitative features of the entire ear, and of the individual components.

- (1) Variation in size (macrotia; microtia; anotia).
- (2) Variation in position (low-set ears; posterior angulation of the ear).
- (3) Variations of the individual anatomical parts: antihelix; anti-tragus; concha; helix; lobe; scapha; tragus; triangular fossa.
- (4) Named ear anomalies (crumpled ear; cryptotia; cupped ear; lop ear; preauricular and auricular pits; preauricular and auricular tags; preauricular ectopias; prominent ear; question mark ear; detachment of ascending helix; satyr ear; shell ear; Stahl ear).

## Ear, Cupped

**Definition:** Laterally protruding ear that lacks antihelical folding (including absence of inferior and superior crura) (Fig. 22).  
*subjective*

**Replaces:** Ear, Capuchin

Ear, cupped, severe/type III: see *Microtia, second degree*



# Approach to Dysmorphology exam

## General Descriptors and Background for the Terms

1. The use of the word “digit” versus “finger” and “toe” is problematic. “Finger” is usually specific to digits 2–5 of the hand and “toe” to digits 2–5 of the foot whereas “digit” is a more general term that can be used to describe any finger or toe. We generally use the word “finger” to be distinct from “thumb” (pollex, although this latter term is used rarely in English) and “toe” is distinct from “hallux” (which, oddly enough, is more commonly used in English than is “great toe”). It is important for the user to read the definition to understand the context in which the term “finger” or “toe” is used. We recognize that some languages do not use a term equivalent to “finger” and “toe” and instead use a modifier of digit (e.g., dita della mano). The term “ray” is a yet more general term that can refer to a finger, toe, thumb, or hallux, but it also includes metacarpals/tarsals, whereas “digit,” “thumb,” “hallux,”

## Foot, Rocker Bottom

**Definition:** The presence of both a “prominent heel” and a “convex contour of the sole” (Fig. 30). *subjective*

**Comment:** The term is a bundled definition but is in common usage. For that reason, it was included by consensus of the group.



FIG. 30. Rocker bottom foot, left.

## Hand, Preaxial Polydactyly of

**Definition:** Duplication of all or part of the first ray (Fig. 40). *objective*

**Comment:** There is a wide spectrum of this malformation. The mild end of the spectrum is a bifid (not cleft) nail or a distal phalanx of the thumb with a central lacuna or bifid tip. Broadened thumbs



FIG. 40. A: Preaxial polydactyly of the left hand, partial. B: Preaxial polydactyly of the right hand.



# Approach to Dysmorphology exam

The American Journal of Medical Genetics - Elements of Morphology series in 2009 and 2022 – Free access

- Elements of morphology: Standard terminology for the head and face.
  - doi:10.1002/ajmg.a.32612.
- Elements of morphology: standard terminology for the periorbital region.
  - doi: 10.1002/ajmg.a.32597
- Elements of morphology: standard terminology for the nose and philtrum.
  - doi: 10.1002/ajmg.a.326004.
- Elements of morphology: standard terminology for the lips, mouth, and oral region.
  - doi: 10.1002/ajmg.a.32602
- Elements of morphology: standard terminology for the ear.
  - doi: 10.1002/ajmg.a.325996
- Elements of morphology: Standard terminology for the trunk and limbs.
  - doi: 10.1002/ajmg.a.62965
- Elements of morphology: standard terminology for the hands and feet.
  - doi: 10.1002/ajmg.a.32596.



# Approach to Dysmorphology exam



# Approach to Dysmorphology exam



# Approach to Dysmorphology exam



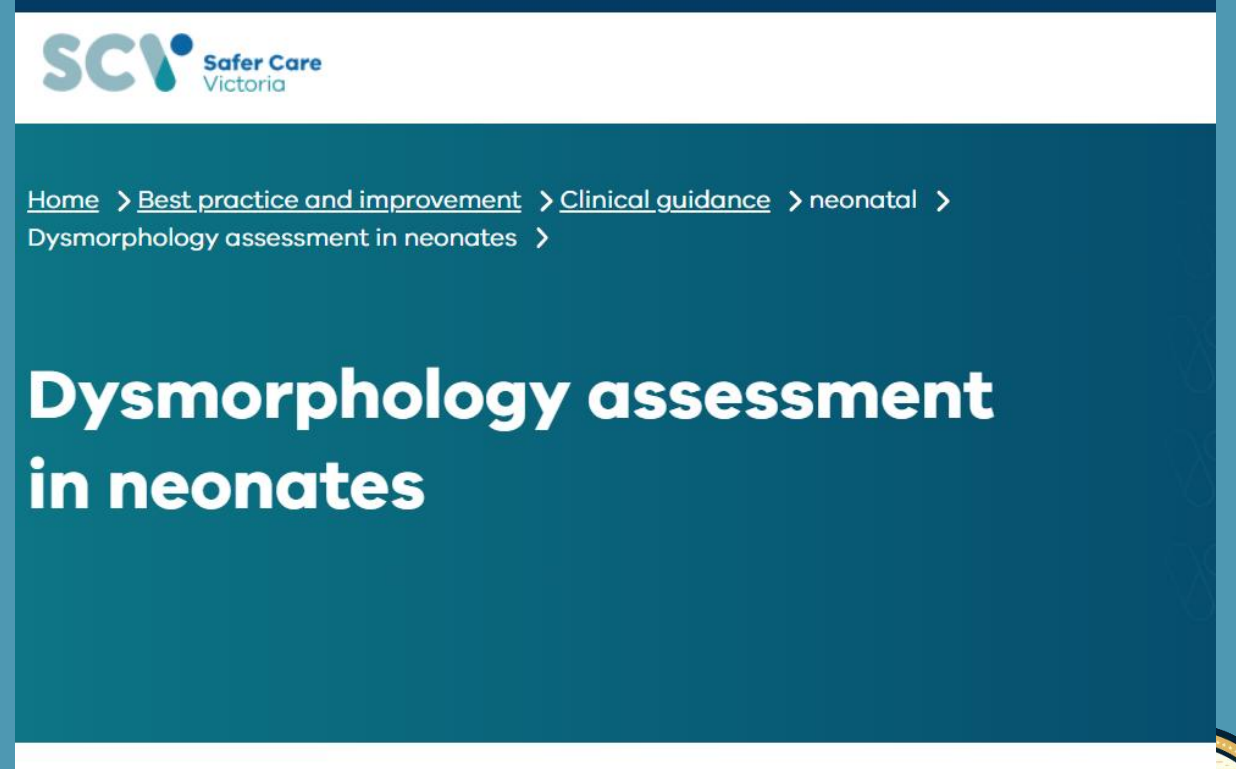
Broad forehead  
Down slanted palpebral fissures  
Epicanthal folds  
Coarse features



# Resources

Information including exam checklist

<https://www.safercare.vic.gov.au/best-practice-improvement/clinical-guidance/neonatal/dysmorphology-assessment-in-neonates>

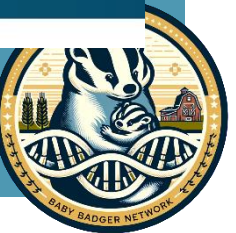


The screenshot shows the top of a web page from Safer Care Victoria. The header includes the SCV logo and the text 'Safer Care Victoria'. Below the header is a breadcrumb trail: 'Home > Best practice and improvement > Clinical guidance > neonatal > Dysmorphology assessment in neonates >'. The main content area has a dark teal background with the title 'Dysmorphology assessment in neonates' in large white text.

SCV Safer Care Victoria

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## Dysmorphology assessment in neonates



# Resources

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# Resources



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## Baby Badger Network – 2024 ECHO Training & Resources

This free, virtual series is a part of the Baby Badger Network (BBN) collaborative. The target

### Dysmorphology and Human Phenotype Ontology (HPO) in the NICU Setting

#### Didactic Presentation:

*Carolyn Scoptur, APNP and Jennifer Stengrevics, PAC*

July 26, 2024 @ 11:30 am

#### Session Resources

- [Didactic Presentation Slides](#)
- Midwest Genetics Network Region 4 webinar – [Dysmorphology 101: Using Your Observation Skills](#) – Susan A. Berry, MD

