The Genetics Evaluation: Who to Refer and What to Expect

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Greenwood Genetic Center
Where Compassion Inspires Progress

Disclosures

- *I have no relevant relationships with ineligible companies to disclose within the past 24 months.*

- Founding Member and Treasurer of the Society of PAs in Genetics and Genomics (SPAGG)
- Serve on the Planning Committee for the Clinical Genetics Advanced Practice Provider (CGAPP) Conference
- Serve on the Membership Committee for the American College of Medical Genetics and Genomics (ACMG)

Educational Objectives

- At the conclusion of this session, the participants should be able to:
  - Recognize patients who may benefit from a genetics evaluation
  - Understand the overall process of a genetics evaluation
  - Identify web-based resources for locating a genetics provider
  - Identify web-based genetics resources to enrich one's knowledge and understanding of genetic disorders

Mission

- Established in 1974, the Greenwood Genetic Center (GGC) is a nonprofit institute, organized to provide clinical genetic services and laboratory testing, to develop educational programs and materials, and to conduct research in the field of medical genetics.

The Greenwood Genetic Center

PAs at the GGC

Wesley

Laura

Purpose of Today's Talk

- In 2016, the *PA Genomic Competencies* were updated to be consistent with current medical education guidelines and the collaborative nature of PAs in interprofessional health care teams

Identify patients who would benefit from referral to genetics professionals.

- Describe the various types of inheritance patterns and mechanisms by which genetic disease may occur.
- Recognize the breadth of data involved in making a genetic diagnosis, including physical examination, personal and family medical history, and laboratory tests, which may include genetic testing.
- Understand that patients may present with a genetic condition for which there is no family history.
- Use family history information to perform genetic risk assessment and to make appropriate health management recommendations.
- Know when and how to refer patients to genetics professionals.

(Goldgar et al. 2016)

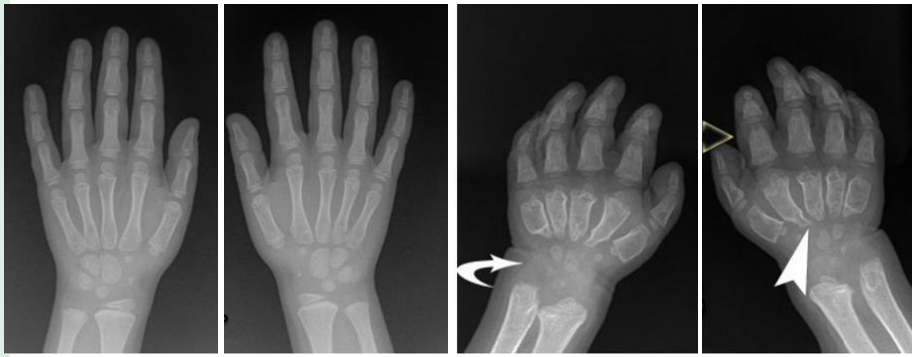
What is a Genetics Evaluation?

- A health service that provides information and support to people who have, or may be at risk for, genetic conditions
- During an evaluation, a genetics professional meets with an individual or family to discuss genetic risks or to diagnose, confirm, or rule-out a genetic condition

(https://medlineplus.gov/genetics/)

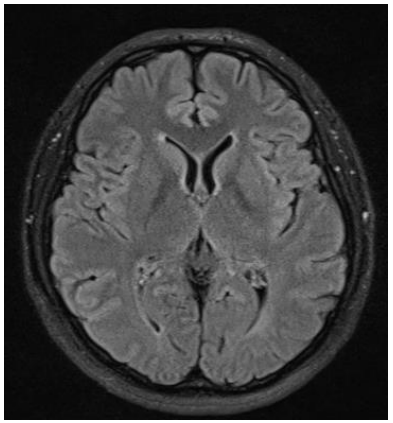
Who Gets Referred

- Individuals with a(n):
  - Concern for a genetic disorder
  - Family history of a genetic disorder
  - Known genetic disorder
  - Abnormal blood work or imaging suggestive of a genetic disorder



Normal

Abnormal



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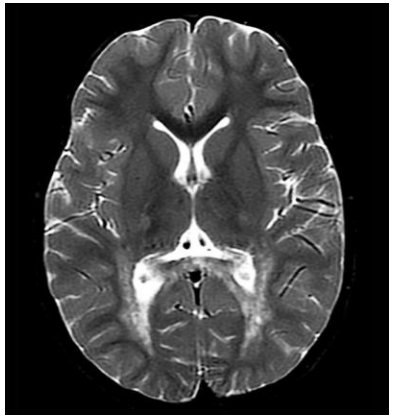


Abnormal

(Images from Google Images)

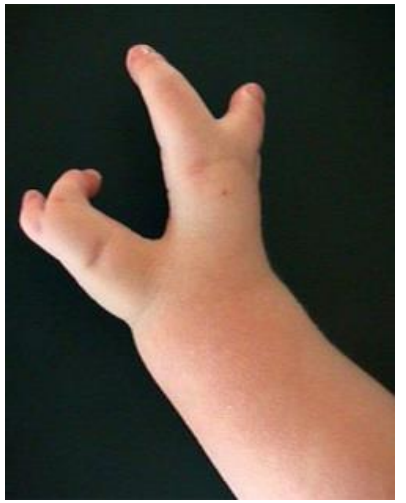
Potential Referrals

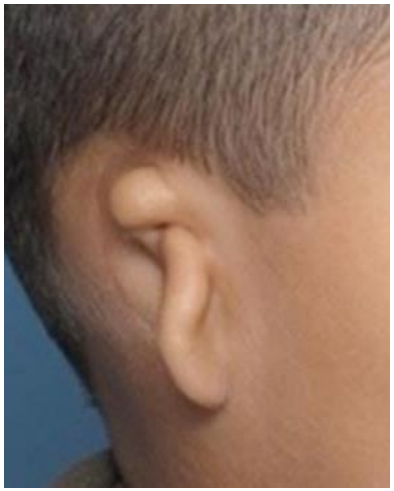
- Multiple congenital anomalies
- Distinctive features
- Dermatological findings
- Cognitive or behavioral disability
- Abnormal growth patterns
- Asymmetric growth
- Hereditary cancer
- Recurrent pregnancy loss
- Abnormal newborn screen
- Other/Unexplained issues

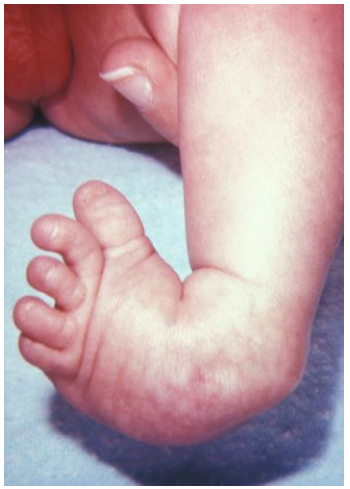
(Saul & Moeschler 2013; https://medlineplus.gov/genetics/)

Multiple Congenital Anomalies

- Congenital heart defect
- Limb anomalies
- Polydactyly (extra fingers or toes)
- Syndactyly (digits fused together)
- Cleft lip/cleft palate
- Microtia (undeveloped external ear)
- Ear tag/pits/creases
- Ambiguous genitalia
- Hypospadias



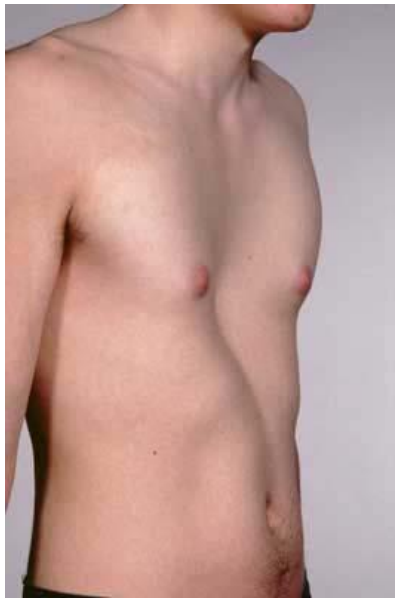


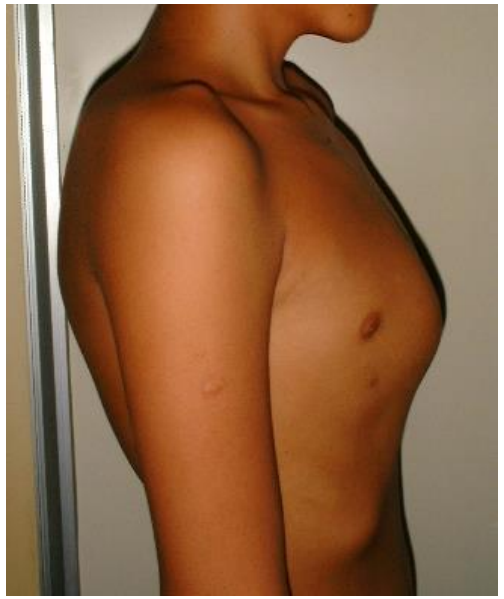


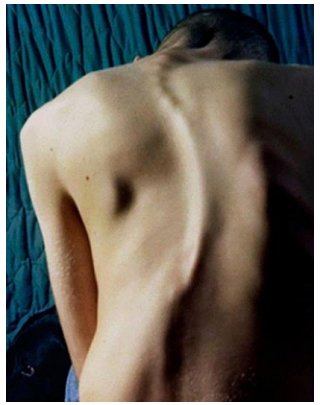
(Images from Google Images)

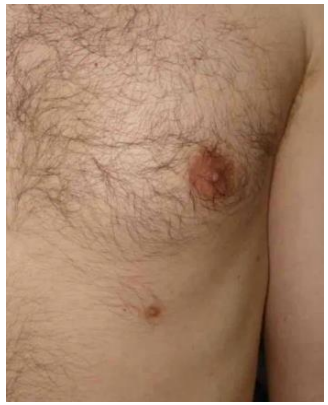
Distinctive Features

- Distinctive facies
- Physical anomalies





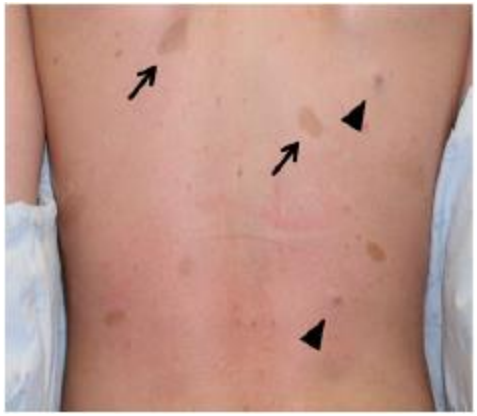


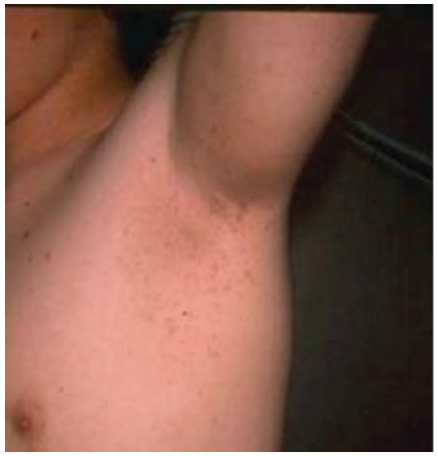


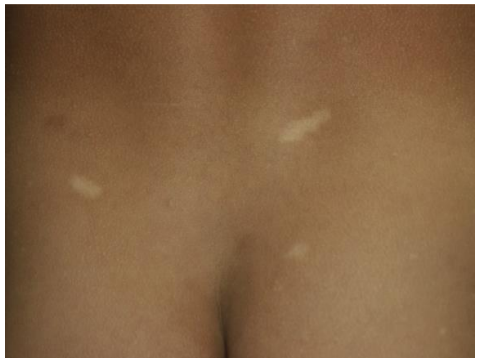
(Images from Google Images)

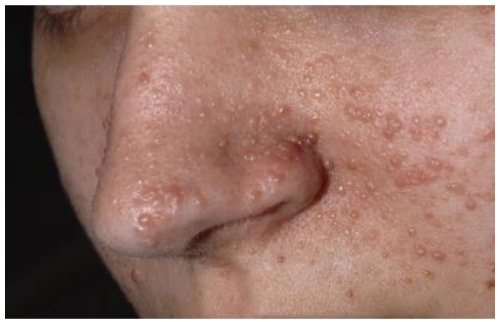
Dermatological Findings

- Atypical birth marks
- Multiple café-au-lait spots
- Axillary/inguinal freckling
- Hypopigmented macules/ash-leaf spots
- Skin tumors
- Hemangiomas
- Vascular malformations









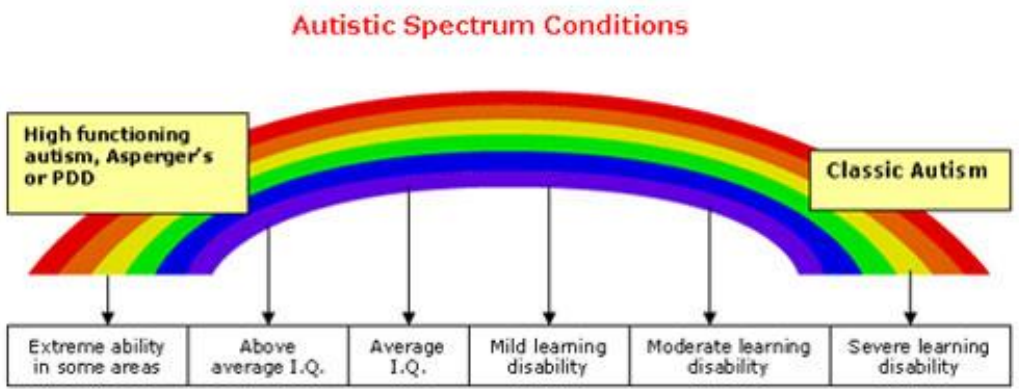
(Images from Hersh et al. 2008; Northrup et al. 2013)

Cognitive/Behavioral Disability

- Global developmental delay
  - Delayed milestones
- Developmental regression
- Intellectual disability
  - Based on IQ <70
  - Formerly MR
- Autism spectrum disorder

Age	Social Language and Self-help	Verbal Language (Expressive and Receptive)	Gross Motor	Fine Motor
4 Months	Laughs aloud	Turns to voice Vocalizes with extended cooing	Rolls over prone to supine Supports on elbows and wrists in prone	Keeps hands unfisted Plays with fingers in midline Grasps object
6 Months	Pats or smiles at reflection Begins to turn when name called	Babbles	Rolls over supine to prone Sits briefly without support	Reaches for objects and transfers Rakes small object with 4 fingers Bangs small object on surface
9 Months[b]	Uses basic gestures (holds arms out to be picked up, waves bye-bye) Looks for dropped objects Picks up food with fingers and eats it Turns when name called	Says "Dada" or "Mama" nonspecifically	Sits well without support Pulls to stand Transitions well between sitting and lying Balances on hands and knees Crawls	Picks up small object with 3 fingers and thumb Releases objects intentionally Bangs objects together

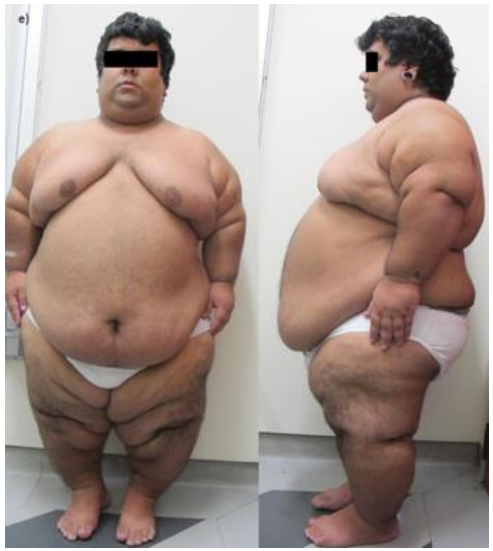
https://brightfutures.aap.org/



https://www.autism360.com/types-of-autism/

Abnormal Growth Patterns

- Failure to thrive
- Generalized overgrowth
- Macrocephaly
- Microcephaly
- Tall stature
- Short stature
- Morbid obesity



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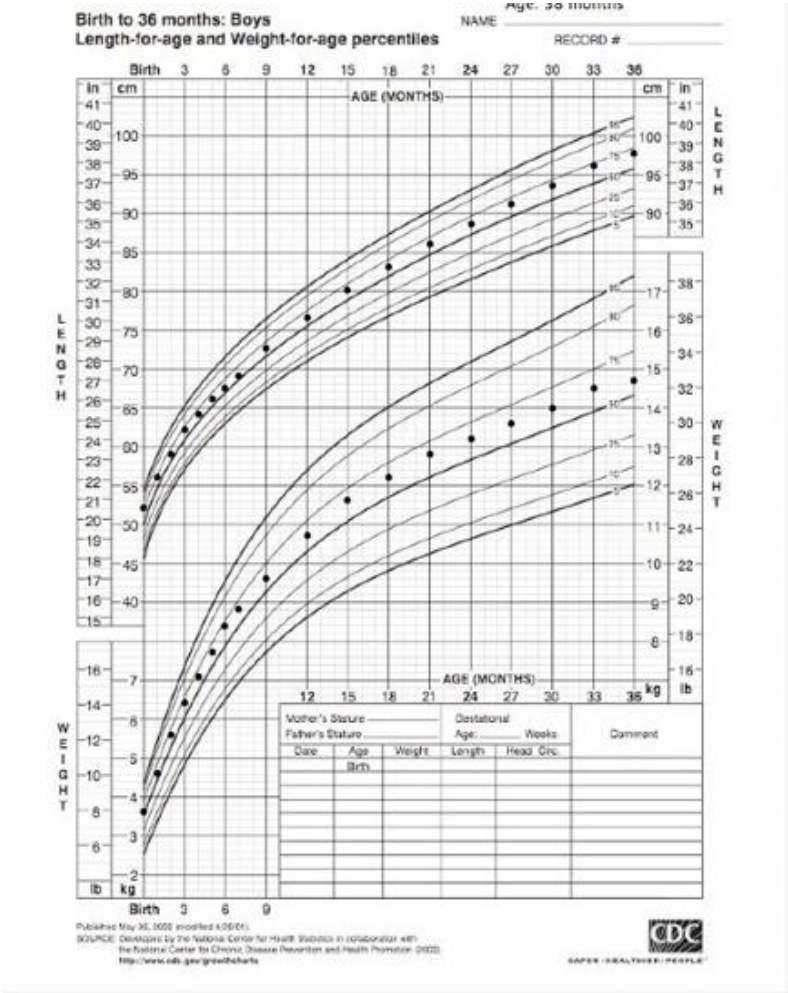
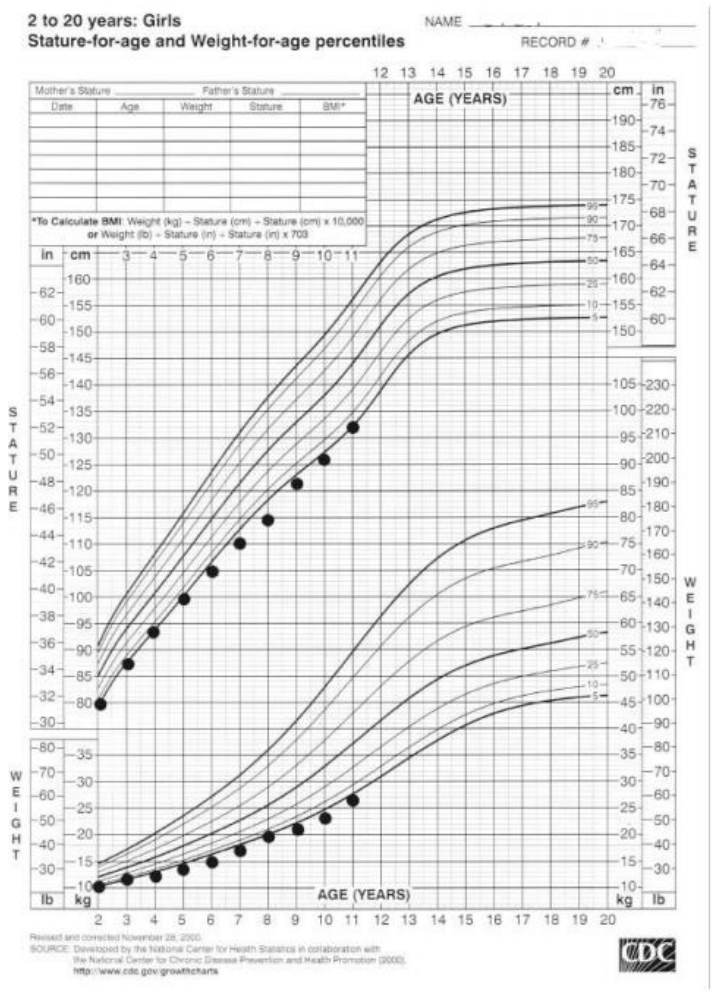
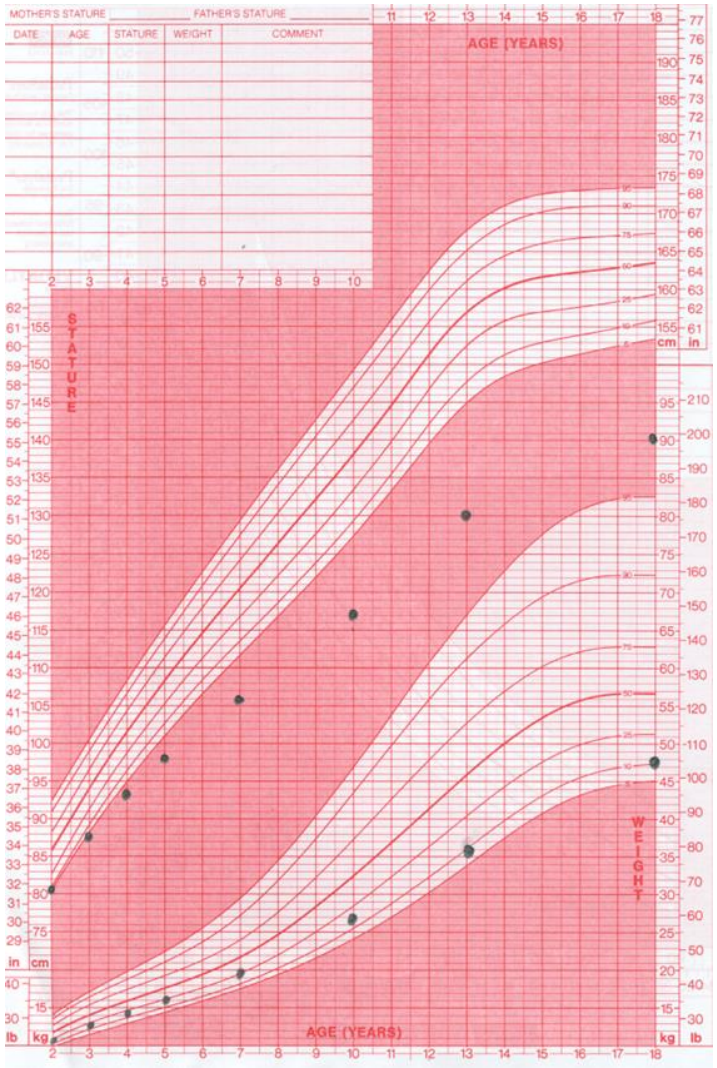
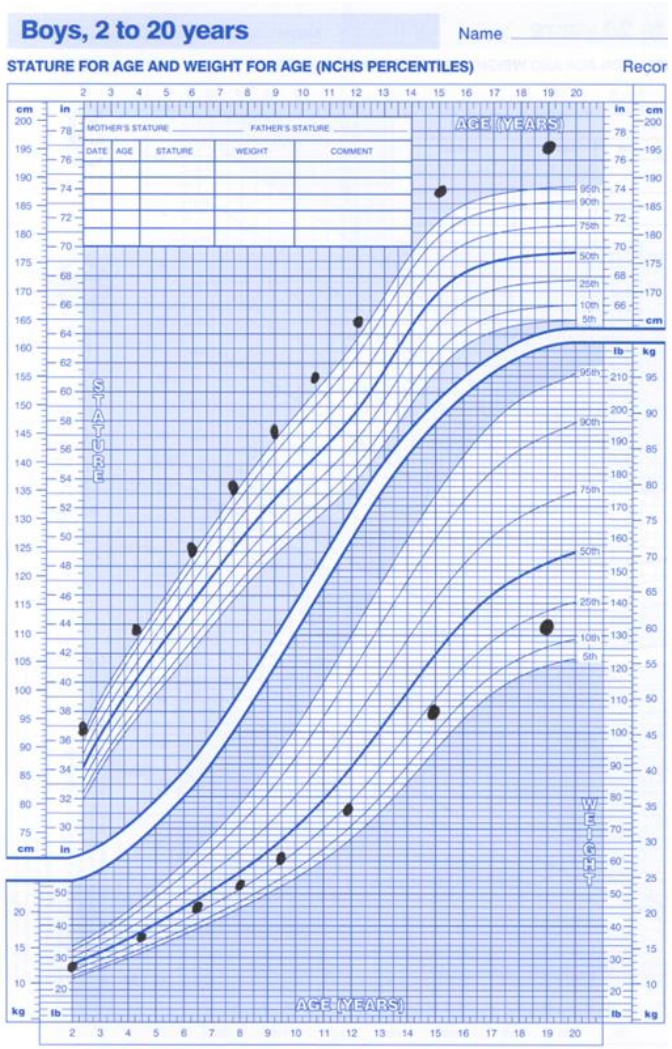
Normal Growth Patterns





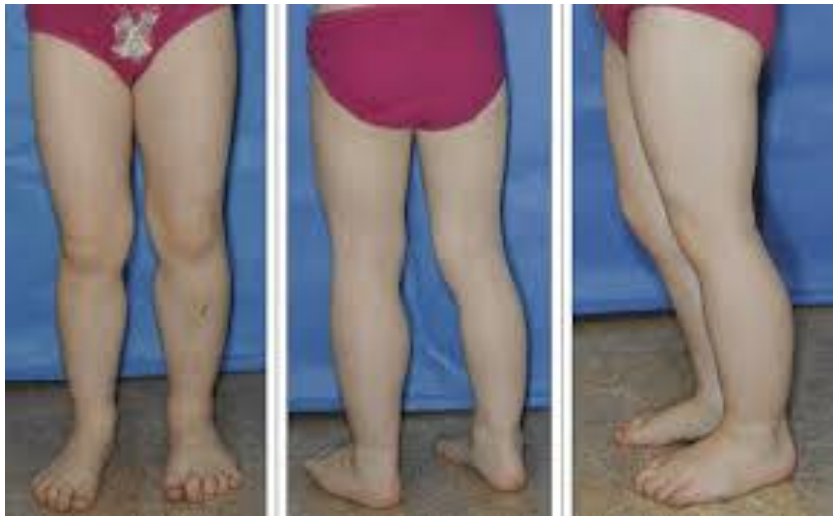
Abnormal Growth Patterns

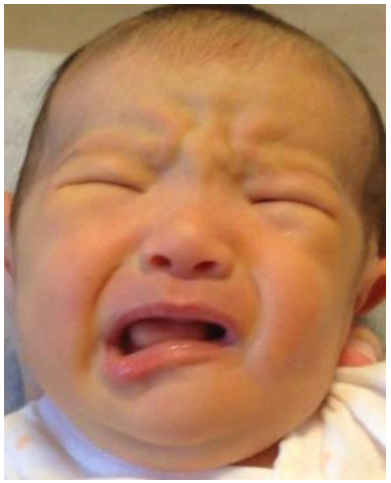


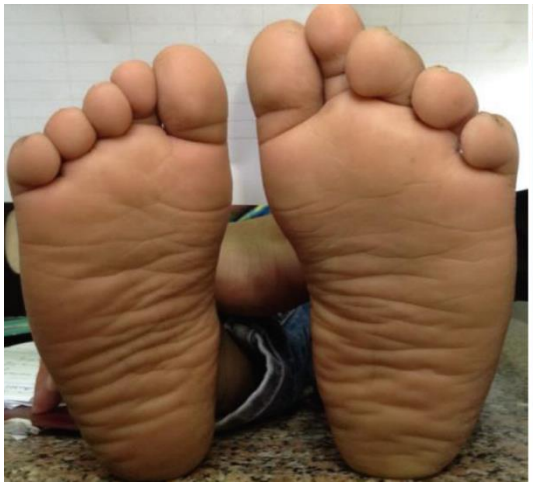


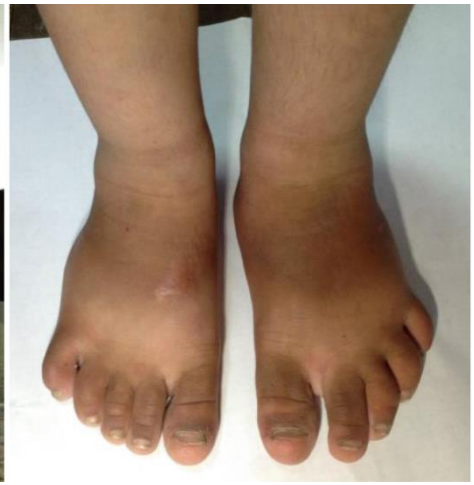
Asymmetric Growth

- Asymmetry of the body
  - Whole body
  - Upper extremities
  - Lower extremities
- Asymmetry of the face





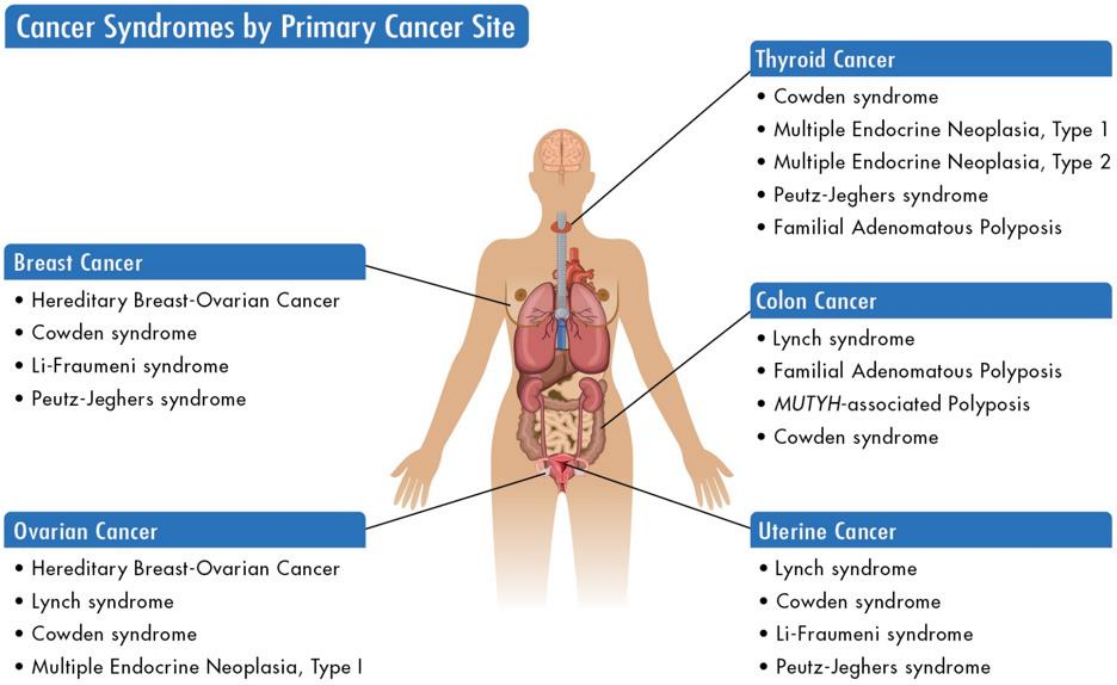




(Images from Google Images)

Hereditary Cancer

- Breast
- Ovarian
- Prostate
- Gastric
- Pancreatic
- Colon
- Retinoblastoma
- Glioblastoma
- Melanoma
- Among others…



Schneider 2012

Abnormal Newborn Screen

- Inborn errors of metabolism
- Endocrine disorders
- Hemoglobin disorders
- Hearing loss
- Cystic Fibrosis

Disorder *	Screening Result
Amino Acid Disorders	Normal
Fatty Acid Disorders	Normal
Organic Acid Disorders	Normal
Galactosemia	Normal
Biotinidase Deficiency	Normal
Hypothyroidism	Normal
CAH	Normal
Hemoglobinopathies	Normal
Cystic Fibrosis	Normal

Other/Unexplained Issues

- Epilepsy/seizures
- Hearing loss
- Hypotonia
- Spasticity
- Hypermobility
- Craniosynostosis
- Nystagmus
- Optic atrophy
- Neural tube defects
- Rhabdomyolysis/muscle aches/weakness
- Contractures
- Hypertrophic cardiomyopathy
- Aortic root dysfunction
- Cardiac arrhythmias
- More…

Referral Process

- A referral is typically needed by the primary care provider or any specialist
- A referral can be made by BabyNet* or the Department of Disabilities and Special Needs (DDSN)

*South Carolina's interagency early intervention system for infants and toddlers under three years of age with developmental delays, or who have conditions associated with developmental delays

The Genetics Team

- PAs
- Genetic Counselors
- MD Clinical Geneticists
- Nurses
- Psychologists
- Dietitians
- PhD Laboratory Geneticists

Primary Goal

- Accurate Diagnosis
  - Natural history and prognosis
  - Support
  - Management
  - Surveillance
  - Treatment
  - Recurrence risk
  - Prenatal diagnosis options

Getting an Accurate Diagnosis

- Reviewing all medical records
- Obtaining a thorough history
- Physical exam
- Genetic studies

The Genetics Evaluation

- Pregnancy History
- Perinatal History
- Medical History
- Developmental History
- Family History
- Physical Exam
- Ordering genetic studies, if indicated
- Genetic Counseling

Pregnancy History

- Maternal and Paternal age
- Gravida, Para (G1P0 versus G5P1)
- Gestation (single versus twin versus multiple)
- Degree of fetal activity
- Amniotic fluid levels
- Maternal weight change
- Maternal illnesses/complications
- Maternal exposures
- Prenatal ultrasounds
- Prenatal diagnostic testing

Perinatal History

- Gestational age
- Labor (spontaneous, induced, prolonged)
- Type of Delivery (vaginal, assisted, C-section)
- Delivery complications (fetal distress, cord issues)
- Birth weight
- Birth length
- Birth head circumference
- Newborn complications (jaundice, feeding, breathing)
- Congenital anomalies (heart anomaly, extra fingers/toes)
- Length of hospitalization

Medical History

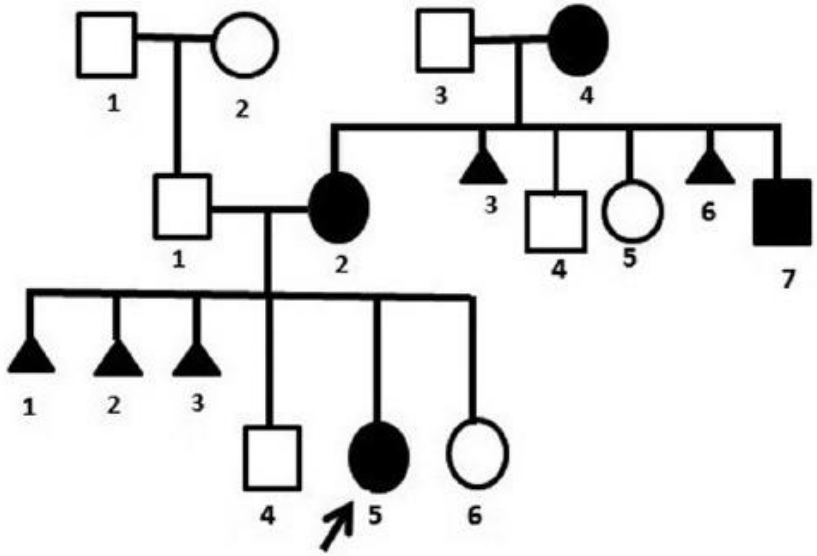
- Health concerns
- Hospitalizations
- Surgeries/Procedures
- Major injuries
- Specialist evaluations
- Genetic testing
- Imaging studies
- Medications
- Allergies

Developmental History

- Developmental issues (DD, ID)
- Developmental milestones (on time versus delayed)
- Regression (loss of skill)
- Behavior (hyperactivity, anxiety)
- Socialization
- Feeding
- Sleeping
- Psychoeducational testing (IQ testing)
- Autism screening/testing (MCHAT, ADOS-2, DSM-5)
- Therapies (speech, occupational, physical)
- School (grade level, resource, needs extra help)

Family History

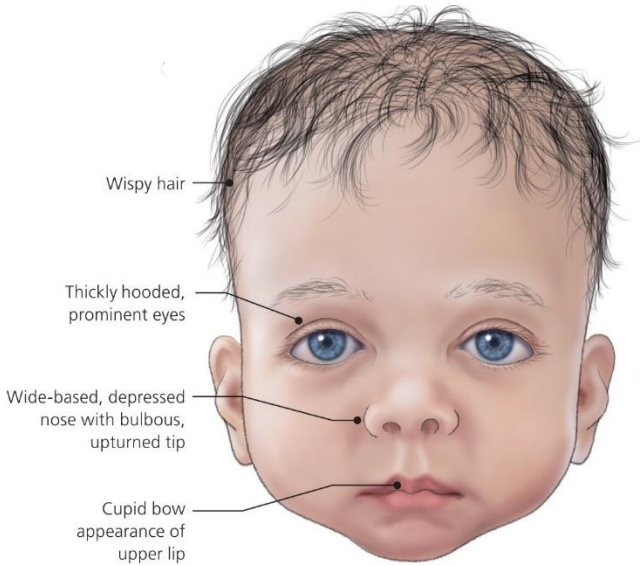
- Three-generation pedigree
- Siblings
- Mother and maternal side
- Father and paternal side
- Consanguinity
- Ethnicity



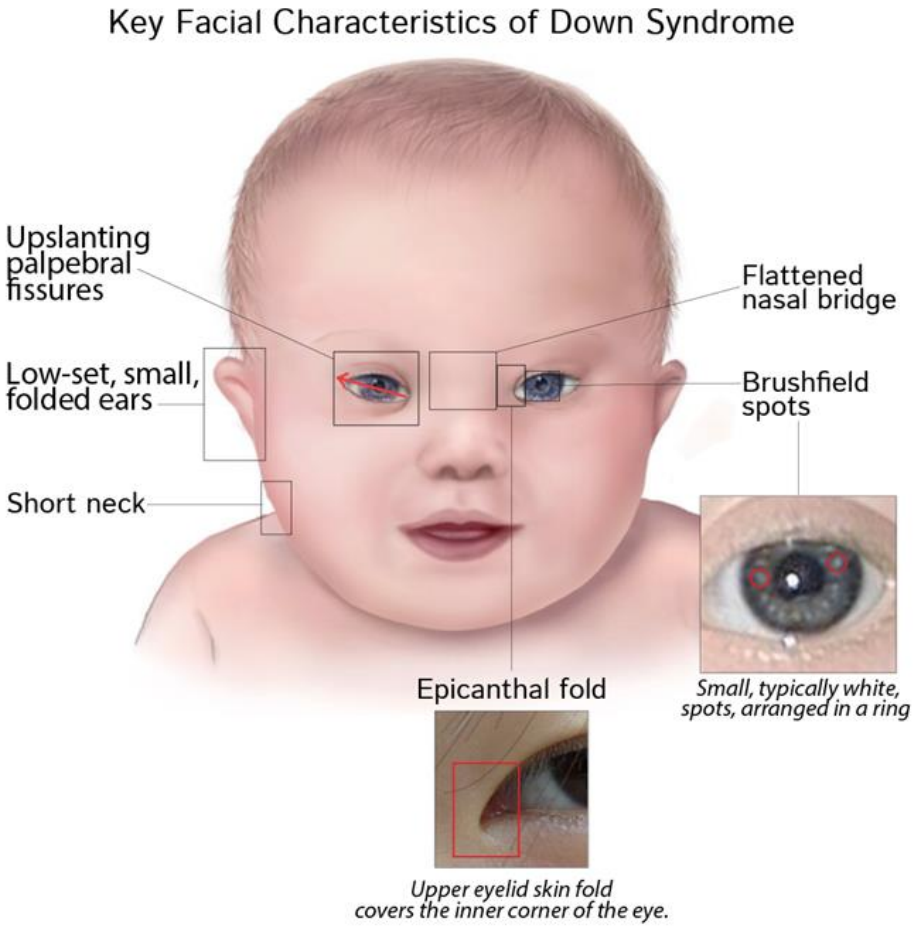
Physical Exam

- Measurements
- A good head-to-toe exam
- Dysmorphology exam

Key Facial Characteristics of Noonan Syndrome

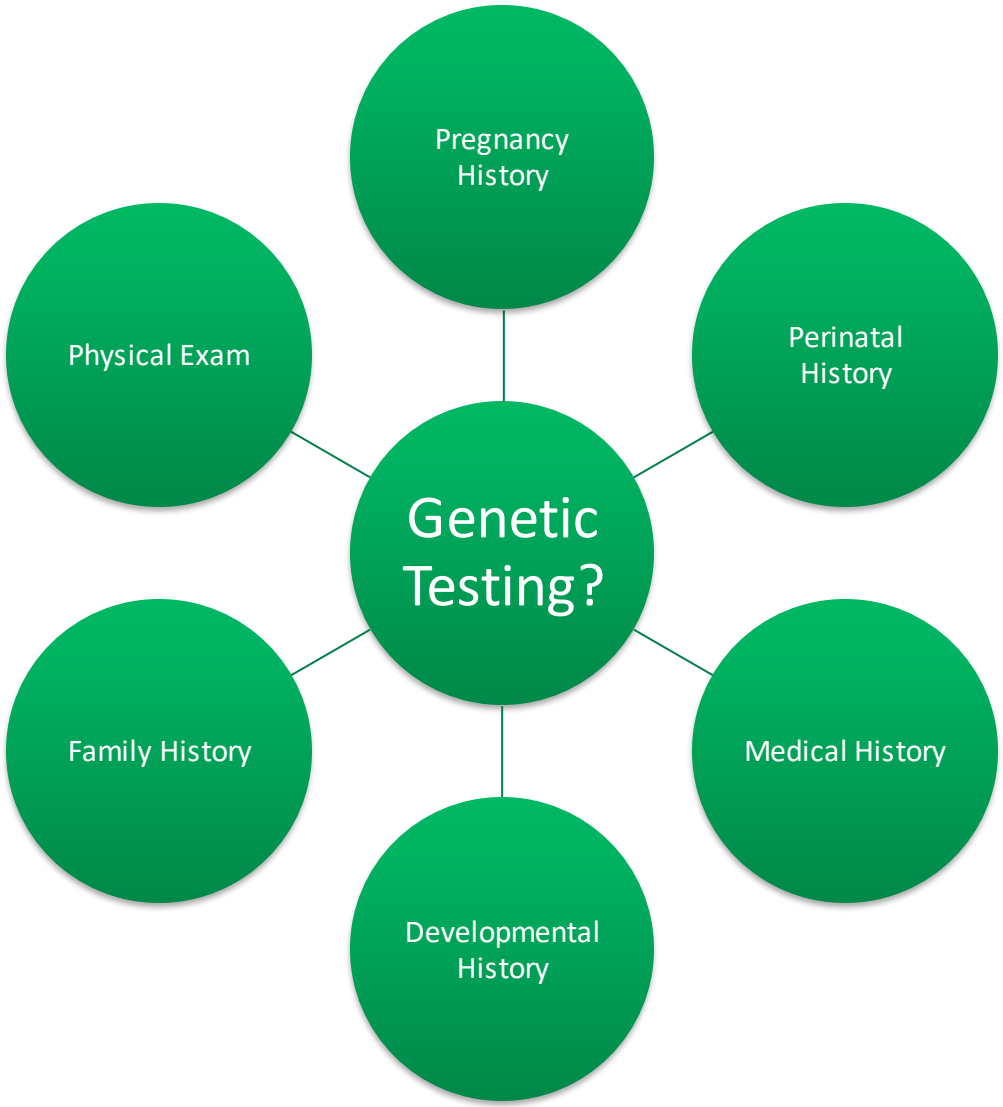


American Academy of Family Physician



(Image from Google Images)

Putting It All Together



Genetic Testing

- Targeted – known diagnosis or familial variant
- Focused/Single Gene – suspected diagnosis
- Panels – suspected disease type/area
  - Ex. Patient with seizures -> epilepsy panel
- Broad
  - Cytogenetics – microarray
  - Molecular Genetics – whole exome sequencing/whole genome sequencing

Genetic Counseling

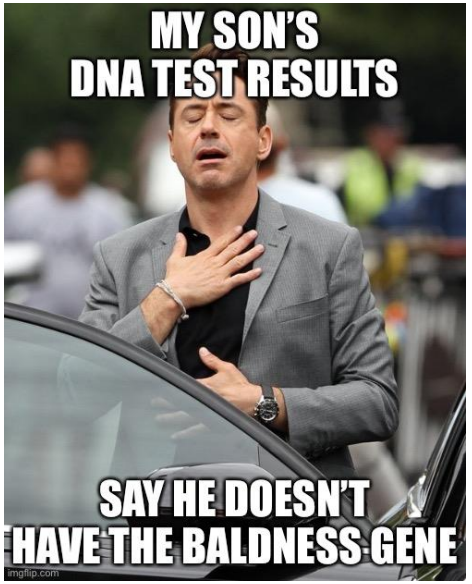
- Genetic counselors are health professionals with specialized graduate degrees and experience in the areas of medical genetics and counseling

- The National Society of Genetic Counselors strongly advises pre-test counseling that facilitates informed decision-making, elicits patient preferences regarding secondary and/or incidental findings if possible, and formulates a plan for returning such results before testing occurs

https://www.nsgc.org/

Genetic Testing Results

- Interpret genetic testing results
- Discuss the results with the patient and family
- If a diagnosis is made:
  - Natural history and prognosis
  - Support
  - Management
  - Surveillance
  - Recurrence risk
  - Prenatal diagnosis options
  - Order additional labs or imaging, if warranted
  - Coordinate care with other providers
- If a diagnosis is not made:
  - Discuss next steps



Find Genetics in Your Area

- American College of Medical Genetics and Genomics (ACMG)
  - https://clinics.acmg.net/
- National Society of Genetic Counselors (NSGC)
  - https://findageneticcounselor.nsgc.org/

Genetic Resources

- GeneReviews®
- MedlinePlus (formerly Genetics Home Reference)
- Genetics and Rare Disease Information Center (GARD)
- Online Mendelian Inheritance in Man (OMIM)
- Orphanet

Take Home Points

- Usually two or more congenital anomalies warrants a genetics referral
- Any individual with unexplained ID or ASD should undergo a genetics evaluation
- Genetic Counselors can be utilized as a resource for patients and providers regarding genetic health

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Huge Thanks to My GGC Family

Questions?

- Contact: wpatterson@ggc.org
- SPAGG website: https://spagg.wildapricot.org/