

1. Clinical Genetics and Dysmorphology

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Laurie Demmer, MD

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2. Clinical Genetics

Clinical Genetics

The diagnosis, counseling and
care of individuals and families
with inherited, teratogenic, or
sporadic 'genetic' conditions

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3. When to Consult Genetics

When to consult genetics....

- Infant with one or more birth defects, an unusual appearance, or a chromosome anomaly
- Child or adult with unusual appearance, growth or developmental delay, or history of birth defects
- Family history of birth defects or inherited condition
- Prenatal test showing abnormalities
- Infertility or multiple miscarriages
- Strong family history of cancer

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4. Why make a genetic diagnosis?

Why make a genetic diagnosis?

- Defines the gamut of abnormalities present (what should and should not be expected)
- Prognosis for the future
- Can help to explain why the condition occurred
- Allows for genetic counseling of all family members re: recurrence risk

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5. Overview of Clinical Genetics

Overview of Clinical Genetics

- Review history and examine patient
- Obtain family history
- Derive a general impression
- Recommend diagnostic testing
- Determine best diagnosis
- Counsel individual and family re: disease, prognosis, options, treatment, recurrence

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6. Definitions

Definitions

- Birth Defect: a condition present by one year of age which required medical, surgical or cosmetic intervention.
 - Diagnosed in 3% of children at birth
 - By 1 year of life, 4% of children will have some type of birth defect
 - Ex. Congenital heart disease, polydactyly, neural tube defect

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7.

Clinical Dysmorphology

Clinical Dysmorphology

- Look for mild dysmorphic features
 - features found in a relatively small percentage of the entire population
 - or features which have been found to occur more commonly in genetic syndromes
 - 3 or more dysmorphic features strongly correlate with a possible genetic syndrome

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8.

Definitions

Definitions

- **Syndrome**: a recognizable pattern of multiple anomalies thought to be pathogenetically related
 - Ex. Down Syndrome, Neurofibromatosis, Russell-Silver Syndrome

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9.

Definitions

Definitions

- **Association**: a non-random occurrence in two or more individuals of multiple anomalies
- usually the pathogenesis is unknown
 - VATER association
 - CHARGE association

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10.

VATER (VACTERL) Association

VATER (VACTERL) Association

- **V**: vertebral
- **A**: anal anomalies
- **C**: cardiac
- **TE**: tracheo-esophageal fistula
- **R**: renal anomalies
- **L**: limb anomalies

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11.

CHARGE Association

CHARGE Association

- **C:** colobomas of the eye
- **H:** hear defects
- **A:** atresia choanae
- **R:** retarded growth and development
- **G:** genital hypoplasia
- **E:** ear anomalies including hearing loss

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12.

Definitions

Definitions

- **Sequence:** a pattern of multiple anomalies derived from a single known or presumed prior anomaly or mechanical factor
 - Pierre Robin sequence
 - Potter sequence

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13.

Definitions

Definitions

- **Malformation**: a morphologic defect of an organ, part of an organ, or a larger region of the body resulting from an intrinsically abnormal developmental process
- Ex. Cleft lip

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14.

Definitions

Definitions

- **Deformation**: an abnormal form or position of a part of the body caused by non-disruptive mechanical forces
- Ex. Congenital Dislocation of the Hip or Club foot from an abnormal intrauterine position

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15.

Definitions

Definitions

- **Disruption**: a morphologic defect resulting from a breakdown of, or interference with, an originally normal developmental process
- Ex. Amniotic band syndrome resulting in amputation of a finger

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16.

Definitions

Definitions

- **Dysplasia**: Abnormal cellular organization or function within a specific tissue type throughout the body, resulting in clinically apparent structural changes
- Ex. Hemangioma or skeletal dysplasia such as osteogenesis imperfecta

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17.

Causes of Birth Defects

Causes of Birth Defects

- Chromosomal anomalies
- Single gene defects (Mendelian Disorders)
- Imprinting
- Multifactorial
- Sporadic/field defects
- Mitochondrial defects
- Prenatal teratogen exposure
- Idiopathic

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18.

Teratogens

Teratogens

- Substances encountered during pregnancy which can lead to birth defects
 - Infectious (rubella, syphilis, CMV)
 - Medications (thalidomide, accutane)
 - Drugs of abuse (cocaine, alcohol)
 - External Agents (radiation, hyperthermia)
 - Maternal Disorders (diabetes, lupus, PKU)
- The effect on the fetus is highly dependent on the gestational age at time of exposure

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19.

Diagnostic Evaluation

Diagnostic Evaluation

- Pregnancy History
- Birth History
- Medical History
- Developmental History
- Family History
- Physical Examination

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