

## GENETICS

*Contact:* G. Bradley Schaefer (559-6800) Lori Myers- staff asst.

*When to contact:* One month prior

*Preceptors:* Bruce Buehler, M.D.; Ann Olney, M.D.; Horatio Plotkin, M.D.; G. Bradley Schaefer, M.D.; William Rizzo, M.D.,

*Where to meet:* Munroe-Meyer Institute, Hattie B. Munroe Annex room 3066

### Purpose:

Congenital anomalies play a major role in all of pediatric care. The leading cause of infant mortality in the United States is the sequelae of congenital anomalies. This exceeds the death rate for prematurity, SIDs, and other common causes of infant or neonatal death. Sixty percent of all admissions to a pediatric hospital are for conditions with a genetic basis. Three percent of all newborns have a recognizable congenital anomaly. An additional 2% of children have congenital anomalies that are not detectable in the newborn period. Finally, 3% of the United States population is mentally retarded, of which 80% is due to genetic factors. Primary care physicians involved in the provision of health care for children and adolescents need a basic understanding of how to evaluate and when to refer children with genetic disorders or other congenital anomalies.

Graduate level (medical student, resident, post doctoral fellows, graduate trainees) may elect to take a four-week elective in Human Genetics as an option separate from Rehabilitation and Genetic Medicine. On this elective, they will have a variety of experiences including:

- Clinics: the Staff of Human Genetics supports a large number of genetic and interdisciplinary clinics, utilizing genetic services both at the Munroe-Meyer Institute and at community clinics.
- Laboratory exposure can be provided in the areas of both cytogenetics and molecular genetics.
- Formal lectures will be provided for pertinent topics; as well, attendance at regularly scheduled conferences will be encouraged. Regularly scheduled conferences include a weekly clinical Case Conference and a bi-weekly cytogenetics case conference.

The Genetics rotation is strictly an **outpatient clinical rotation**. There are no inpatient duties other than consultation. The resident will have the opportunity to rotate and observe most, if not all, of the genetics clinics and interdisciplinary clinics that the genetics staff participates in here at the Munroe-Meyer Institute, UNMC, and at all hospitals in the Omaha area. Depending on the scheduling time, the students may also have the opportunity to attend Outstate Genetics Clinics in the greater Nebraska area. There will be no pre- or post-test given.

**Recommended reading list** for this rotation would include:

- Jones's book Smith's Recognizable Patterns of Human Malformations
- Jorde's Medical Genetics

"**Mini research projects**" can be designed and implemented if the student so desires to participate in a small research project during his/her time on the Genetics rotation.

### Objectives:

1. Recognize the features of the more common pediatric genetic conditions/syndromes.

2. Know unique medical and neurodevelopmental issues of the more common conditions/syndromes.
3. Be able to categorize congenital anomalies as malformation, deformation, or disruption.
4. Understand the patterns of multiple congenital anomalies (syndrome, sequence anomaly, association).
5. Appreciate the psychosocial implications for families of children with congenital anomalies.
6. Recognize urgent issues in genetic medicine and be able to rapidly identify such issues and the immediate standard interventions.

Methods:

1. Clinical participation: clinics, consultations, interdisciplinary services
2. Attendance at scheduled genetic conferences:
  - Case conferences
  - Cytogenetics conferences
  - Molecular genetics conferences
3. Presentation of a selected topic at the genetics Case Conferences
4. Recommended readings
5. Individual instruction with attending

Implementation:

The resident will be oriented to MMI on the first day of the rotation. Standard information will include:

- Call schedule
- Clinic schedule
- Conference schedule
- Expectations
- Time lines

Evaluation:

- Direct observation in clinics
- Critique and assessment of presentation
- Conference attendance
- Evidence of independent readings

**COMMON PEDIATRIC SYNDROMES**

Down (trisomy 21)  
Patau (trisomy 13)  
Edwards (trisomy 18)  
Fragile X  
Turner (monosomy X)  
Achondroplasia  
Noonan  
Beckwith-Wiedemann  
Fetal Dilantin embryopathy  
Stickler  
Marfan  
Rubinstein-Taybi  
Waardenburg  
Albright hereditary osteodystrophy  
Crouzon/other craniosynostosis syndromes

Fetal Alcohol Syndrome/Effects  
Prader-Willi  
Amniotic band disruption spectrum  
Williams  
Ehlers-Danlos  
Treacher-Collins  
Aarskog  
Sotos  
Russel-Silver  
Wolf-Hirschhorn (4p-)  
Cri-du-cat (5p-)  
Oculo-auriculo-vertebral spectrum  
(Including hemifacial microsomia, Goldenhar)

**Sequences and Associations**

VATER Association  
CHARGE Association  
MURCS Association  
Oligohydramnios sequence  
(Pierre) Robin sequence  
Arthrogryposis multiplex congenita

**Phakomatoses**

Neurofibromatosis  
Tuberous sclerosis  
Sturge-Weber

References:

1. Jacobsen et al, The twenty-five most common multiple congenital anomaly syndromes in Nebraska, *Nebraska Medical Journal* 71(3):65-67, 1986.
2. Jones (Ed.), Smith's Recognizable Patterns of Human Malformations, 5<sup>th</sup> Edition, 1997.

**URGENT GENETIC HEALTH CARE ISSUES IN CHILDREN**

- Acute Metabolic Emergencies\*
- Asphyxiating Neonatal Skeletal Dysplasias
- Syndromes/Sequences with Pulmonary Hypoplasia
- Syndromes with Invariably Lethal Outcomes
- Psychosocial Urgencies
- Stillborns/Miscarriages

\*Metabolic Emergencies

Hyperammonemias  
Hypoglycemia  
Lactic Acidosis  
Other Metabolic Acidoses

Metabolic Syndromes

Smith-Lemli-Opitz Syndrome  
Zellweger Syndrome  
X-linked Chondrodysplasia Punctata

**MAJOR TYPES OF GENETIC TESTING**

- Chromosomal Analysis (karyotype)
- Metaphase analysis, G(Giemsa) banding

- Prometaphase (high resolution) analysis
- Special stains (banding) studies
- Breakage studies
- Sister chromatid exchange

#### Molecular Cytogenetics

- Fluorescent in situ hybridization (FISH)
- Chromosome painting

#### Linkage Studies

- Restriction fragment linked polymorphisms (RFLP)
- Polymorphic microsatellite analysis
- CG repeats
- Variable number tandem repeats (VNTR)
- Chromosome polymorphisms

#### Quantification of Trinucleotide Repeats

#### Southern Blot

#### Site Specific Conformational Polymorphisms (SSCP)

#### Deletional Screening

- Point mutations

#### Protein Truncation Assay

#### Multiplex Polymerase Chain Reaction (PCR)

- Major gene rearrangements/deletions

#### Direct Sequencing

#### Biochemical Studies

#### Immunofluorescent Protein Studies

#### Combination Strategies