GENETICS

Contact: G. Bradley Schaefer (559-6800) Lori Myers- staff asst.
When to contact: One month prior
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
Human Genetics Elective Rotation

COMMON PEDIATRIC SYNDROMES

Down (trisomy 21)                  Fetal Alcohol Syndrome/Effects
Patau (trisomy 13)                 Prader-Willi
Edwards (trisomy 18)               Amniotic band disruption spectrum
Fragile X                         Williams
Turner (monosomy X)               Ehlers-Danlos
Achondroplasia                    Treacher-Collins
Noonan                            Aarskog
Beckwith-Wiedemann                Sotos
Fetal Dilantin embryopathy        Russel-Silver
Stickler                          Wolf-Hirschhorn (4p-)
Marfan                            Cri-du-cat (5p-)
Rubinstein-Taybi                  Oculo-auriculo-vertebral spectrum
Waardenburg                       (Including hemifacial microsomia, Goldenhar)
Alright hereditary osteodystrophy
Crouzon/other craniosynostosis syndromes

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

Phakomatoses
Neurofibromatosis
Tuberous sclerosis
Sturge-Weber

References:

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(Giems) 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 Confirmational 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