Overview of Chromosome Abnormalities

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Objectives

- Explain the genetic basis of chromosome abnormalities
- Review the signs and symptoms of common chromosome abnormalities
- Discuss the challenges in taking care of students with chromosome abnormalities and provide useful web-based resources

Normal Karyotype

Female

Male
Chromosomal Microarray

Chromosome Microarray

Can detect microdeletion and microduplication

Types of chromosome abnormalities

**Numerical:**
- Aneuploidy: autosome or sex chromosomal
  - Monosomy: Turner syndrome-45;XO
  - Trisomy: 21, 18, 13
- Polyploidy: Tr-, Tetraploidy

**Structural:**

- Duplication
- Inversion
- Deletion
- Insertion
- Translocation
Down syndrome

Genetics of Down Syndrome

- Nondisjunction (95%)
- Translocation (3-4%)
- Mosaicism (1-2%)

Nondisjunction

- Standard Trisomy 21
- 47,XY,+21
- 47,XX,+21
Cognitive Features

- Intellectual disability, degree variable, most often within mild-to-moderate range (IQ 35-70), rarely IQ<35
- Global Developmental Delay
- Problems with learning
- Speech/Language
- Short and long-term memory
- Well-documented risk of early onset Alzheimer's disease (~30 years)

Medical Issues

<table>
<thead>
<tr>
<th>Medical Concern</th>
<th>% Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Heart Disease</td>
<td>50%</td>
</tr>
<tr>
<td>Hearing Loss</td>
<td>66-89%</td>
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<tr>
<td>Ophthalmic Conditions</td>
<td>60%</td>
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<tr>
<td>Gastrointestinal</td>
<td>5%</td>
</tr>
<tr>
<td>Endocrine (i.e. Hypothyroidism)</td>
<td>15-40%</td>
</tr>
<tr>
<td>Dental conditions</td>
<td>60-100%</td>
</tr>
<tr>
<td>Orthopedic anomalies</td>
<td>15%</td>
</tr>
<tr>
<td>Seizures</td>
<td>5-10%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.6%</td>
</tr>
</tbody>
</table>

Physical features

Pt PIC
Summary of Referrals

- Cardiology
- ENT
- Dentist
- Ophthalmology
- PCP – thyroid checked
- Developmental and Behavioral Pediatrician
- Babies Can’t Wait
- Others as necessary

Resources

- LOCAL
  - Down syndrome Association of Atlanta (DSAA)
  - New Parent Seminar put on by DSAA
  - Parent to Parent of Georgia (www.p2pga.org)
  - Corrigan Cares (CorriganCares.org)
  - Babies Can’t Wait
  - Katie Becket Deeming Waiver – Debbie Dobbs, MS (Social Worker)
45, XO: Turner Syndrome

- Occurs in 1:2500 female births
- Appearance at birth: Variable
- Most common features at birth, if detectable
  - Cardiovascular anomalies
  - Lymphedema of hands and feet
  - Web of skin lateral neck
  - Nail deformities
  - Microcephaly
  - Small size
Characteristics of 45 XO

- Short Stature
- Immaturity
- Learning disabilities: Dyscalculia
- Social Interaction difficulties
- Fertility Issues
- Delayed sexual development
- Amenorrhea
- Anticipate adult infertility

https://www.turnersyndromefoundation.org/

22q11.2 microdeletion

![22q11.2 microdeletion diagram]
Inheritance

- 93% of cases are new mutations
- 7% are inherited from a parent

Mother and son-- pics

22q11.2 deletion
DiGeorge syndrome
Velo-cardio-facial syndrome
Conotruncal-Anomaly-Face syndrome

- Conotruncal cardiac defects: 76%
- Abnormal facies: almost 100%
  - (more difficult to assess in African American infants)
- Thymic aplasia/ hypoplasia: 77%
- Clefting/ palate abnormalities: 76%
- Hypoparathyroid - hypocalcemia: 49%
- 22q11.2 deletion

Other major presentations

- Learning disability
  - Strengths: verbal memory, reading, rote memorization
  - Weaknesses: math, visuospatial, abstract reasoning

- Behavioral/Psychiatric
  - Generalized anxiety
  - Phobias
  - ADHD
  - Autism
  - Poor social interaction skills
  - Impulsivity
  - Frank psychiatric disorders in older patients: 10–30%
    * Bipolar, autistic spectrum disorder, schizophrenia/ schizoaffective disorder
Dysmorphic features

- Hooded eyelids (25%)
  - Short and narrow palpebral fissures
- Bulbous nose (60%)
  - Deficient alae nasi
- Nasal dimple (10%)
- Micronasxia (21%)
- Microtia (12%)
- Posteriorly rotated ears (13%)
- Postaxial polydactyly (6%)

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Chromosome 22q11.2 deletion syndrome (DiGeorge syndrome/velocardiofacial syndrome).
McDonald-McGinn DM, Sullivan KE.

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Practical guidelines for managing patients with 22q11.2 deletion syndrome.

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Children's Healthcare of Atlanta
22q Multidisciplinary Clinic

Lisa Kobrynski, M.D., Medical Director

Appointments: 404-785-2490
Fax clinic notes to: 404-785-5891

Specialists available during each clinic include:
- Endocrinology
- Gastroenterology
- Genetics
- Immunology
- Sibley Heart Center Cardiology
What to offer families

“Faces of Sunshine” booklet
Dempster Foundation resources
Local Parent Support Group
Web and Educational Resources

22q Resources on the Web

- [www.22q.org](http://www.22q.org) International 22q Foundation
- [www.dempsterfamilyfoundation.org](http://www.dempsterfamilyfoundation.org) Ryan and Jenny Dempster Family Foundation
- [www.genetics.emory.edu/22q](http://www.genetics.emory.edu/22q) Southeastern Center for Excellence in 22q
- [www.kumc.edu/gec/support/](http://www.kumc.edu/gec/support/) Genetic Conditions and Rare Conditions Support Groups
- [www.parenttoparentofga.org](http://www.parenttoparentofga.org) Parent to Parent of Georgia

Challenges in taking care of students with chromosome abnormalities

- Multisystem involvements with variable presentation
- Multiple congenital defects
- Dysmorphic features
- Feeding difficulty and growth deficit
- Learning difficulty (vision and hearing concerns)
- Communication issues
- Behavior concerns

Questions?
Thank You!