Name That Syndrome!

Catherine J. Goodhue, MN, CPNP
Nurse Practitioner II
Division of Pediatric Surgery

Goodhue
Disclosure

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Pedro Sanchez, MD - Pediatric Geneticist

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Objectives

- Discuss characteristics of common genetic syndromes
- Describe diagnostic criteria and/or testing for common genetic syndromes
- Identify current guidelines for primary and specialty care for common genetic syndromes
Name That Syndrome!

• 1 month old female
• Normal birth history
• Some feeding problems
• PE:
  – Small mouth and ears
  – Redundant neck folds
  – Noisy breathing
  – Somewhat hypotonic

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Common Physical Features

- Brachycephalic
- Epicanthic folds
- Flat nasal bridge
- Upward slanting palpebral fissures
- Brushfield spots
- Small mouth

- Small ears
- Excessive skin at nape of neck
- Single transverse palmar crease
- Short fifth finger with clinodactyly
- Hypotonia
Newborn Period

- Feeding problems
- 60% have eye disease
- 75% have hearing loss
- ↑ incidence of URI’s; 50-75% have OSA
- 50% have cardiac defects → need echo
- 12% develop obstructive bowel anomalies
- 15% have thyroid disease; 1% congenital
- Hypotonia
- Importance of early intervention
Infancy

• 50-70% develop serous OM
  – Behavioral audiogram at 1 year
• Check for strabismus, cataracts, nystagmus
  – Peds ophthalmology by 6 months of age
• Repeat thyroid function screen at 6 and 12 months then annually
• Routine immunizations – consider Synergis
Early Childhood

• Growth and development
• If unable to visualize TM’s audiogram every 6 months up to 3 years – ENT referral
• Annual vision screening → refer to ophtho for exam every 2 years
• Cervical x-ray at 3-5 years
• Review s/s OSA & refer to ENT prn
• Screen for celiac disease at 2-3 years
• Dental screening every 6 months
Late Childhood

- Assess growth and development
- Annual audiologic evaluation
- Annual ophthalmolologic evaluation
- Annual thyroid screening
- Review skin problems prn
Adolescence – Early Adulthood

• Physical exam
  – CBC
  – Thyroid function test
• Annual audiologic evaluation
• Annual ophthalmologic evaluation
• Recommend routine gynecologic care
• Transfer to adult medical care
Diagnostic Testing for Down

- Prenatal screening
  - Nuchal translucency
  - Nuchal thickness
  - Triple screen
  - Quadruple screen
- Prenatal & Post-natal testing
  - Chromosomes

Copied from Counselling Aids for Genetics, 3rd edition, produced by Greenwood Genetic Centre
Robertsonian Translocation

Maternal age as effect on Trisomy 21

<table>
<thead>
<tr>
<th>Mother's age</th>
<th>Risk of Down Syndrome in live births %</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>0.1</td>
</tr>
<tr>
<td>25</td>
<td>0.1</td>
</tr>
<tr>
<td>30</td>
<td>0.2</td>
</tr>
<tr>
<td>35</td>
<td>0.5</td>
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<tr>
<td>40</td>
<td>3.6</td>
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<td>45</td>
<td></td>
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</tbody>
</table>

American Family Physician: Aug 15, 2000

46, XX, dic(21;21) (q22.2;q22.2)

100% recurrence risk
Resources for Down Syndrome

• Growth Charts
  – http://adc.bmj.com/cgi/content/full/87/2/97

• AAP Health Supervision Guidelines

• For parents
  – http://www.dsala.org
Name That Syndrome!

- 3 year old female just moved here from Mexico
- No significant birth hx
- PE
  - Short stature
  - Heart murmur
Turner Syndrome Care

- Evaluate cardiac anatomy - echo
- Evaluate renal anatomy - UTZ
- Monitor blood pressure
- Thyroid function
- Refer to Endocrine

- Evaluate hearing
- Evaluate vision
- DDH & scoliosis common
- Predisposed to obesity
- Short stature
- 90% gonadal failure
- ↑ risk for keloids
Diagnostic Testing for Turner

- Chromosomes

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Resources for Turner Syndrome

• www.turnersyndrome.org
Name That Syndrome!

- 4 month old male
- Prenatal history
  - Cardiac rhabdomyoma now resolved
- Mom describes some strange posturing
  - Baby bends in two
- PE
  - See photo
Diagnostic Criteria – Tuberous Sclerosis

- Major features
  - Facial angiofibromas
  - Ungual or periungual fibroma
  - Hypomelanotic macules
  - Shagreen patch
  - Cortical tuber
  - Subependymal nodule
  - Subependymal giant cell astrocytoma
  - Multiple retinal nodular hamartomas
  - Cardiac rhabdomyoma
  - Lymphangiomyomatosis
  - Renal angiomyolipoma

- Minor features
  - Multiple randomly distributed pits in dental enamel
  - Hamartomatous rectal polyps
  - Bone cysts
  - Cerebral white-matter “migration tracts”
  - Gingival fibromas
  - Nonrenal hamartoma
  - Retinal achromic patch
  - “Confetti” skin lesions
  - Multiple renal cysts
# Diagnostic and Surveillance Screening in TSC

<table>
<thead>
<tr>
<th>Test</th>
<th>CHILD</th>
<th>ADULT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fundoscopic Examination</strong></td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td><strong>Brain MRI</strong></td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td><strong>Brain EEG</strong></td>
<td></td>
<td>✗</td>
</tr>
<tr>
<td><strong>Cardiac EKG and ECHO</strong></td>
<td></td>
<td>✗</td>
</tr>
<tr>
<td><strong>Renal MRI, CT or Ultrasound</strong></td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td><strong>Dermatologic Screen</strong></td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td><strong>Neurodevelopmental Testing</strong></td>
<td></td>
<td>✗</td>
</tr>
<tr>
<td><strong>Pulmonary CT</strong></td>
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</table>

<table>
<thead>
<tr>
<th>Notes</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
</table>
| ✗     | With a negative physical examination, computed tomography is recommended.  
|     | Every 1 to 3 years.  
|     | Probably less frequently than in children.  
|     | Unless seizures are suspected, generally not useful in diagnosis.  
|     | As clinically indicated.  
|     | Unless needed for diagnosis.  
|     | Every 6 months to 1 year until involution or site stabilization.  
|     | Ultrasound generally recommended due to cost although local imaging expertise may vary.  
|     | Every 3 years until adolescence.  
|     | Generally for children only.  
|     | Recommended for children at the time of beginning 1st grade.  
|     | For women at age 18.  

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Diagnostic Testing for TS

- TSC1 Gene
- TSC2 Gene
Resources for Tuberous Sclerosis

• www.tsalliance.org
Name That Syndrome!

- 2 year old male new to your practice
- Negative birth hx
- PE:
  - Macrocephalic
  - Mild hypotonia
  - See photos
Diagnosing NF1

• Must have 2 or more of the following:
  – 6 or more CLMs
  – 2 or more neurofibromas or 1 plexiform NF
  – Axillary or inguinal freckling
  – 2 or more Lisch nodules
  – Distinctive bony lesions
  – Affected first-degree relative
Axillary Freckles

Café au lait macules

Neurofibromas

Plexiform neurofibroma

Subcutaneous skin changes
Management of NF1

• Evaluate for new neurofibromas and progression of lesions
• Monitor blood pressure
• Evaluate neurodevelopmental progress
• Evaluate for skeletal changes
• Yearly ophthalmologic evaluations
• 40-50% have learning disabilities
Complications of NF1

- Direct involvement by neurofibromata
- Optic gliomas
- Hypertension
- Scoliosis/kyphosis
- Learning disabilities
- Hypertension
- Risk for malignancies

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Diagnostic Testing for NF1

• Clinical diagnosis

• Gene sequencing or FISH for deletion
Must differentiate from Legius Syndrome (SPRED1 gene) if the patient has no neurofibromas
Clinical features include:
- Multiple Café au lait macules
- Axillary freckling
- Macrocephaly
- Autosomal dominant

**NO RISK OF NEUROFIBROMAS OR SKIN TUMORS**
Usually requires genetic testing for mutations in the SPRED1 gene
Resources for NF1

- www.ctf.org
- www.nfinc.org
- Growth charts
Name That Syndrome!

- 6 month old female
- Birth hx normal
  - 9 lb 14 oz
- PDA ligation 4 weeks
- Off the charts for weight, height, hc
- On PE:
  - Bilateral OM
  - Corneal clouding

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Common Characteristics for MPS

- Coarse facial features
- Short stature
- Dysplastic bones
- Thickened skin
- HSM
- Hernias
- Progressive joint stiffness
- Recurring respiratory infections
- OSA
- Heart disease
- Corneal clouding
- Some mental retardation/dev delays
- Hearing loss
Diagnostic Testing for MPS

• Screening if suspect MPS
  – Urinary GAG

• More definitive testing depends on which type of MPS is suspected
Resources for MPS

• http://www.mpssociety.org/
Name That Syndrome!

- 4 year old male
- Birth history normal
- In speech therapy
- Mild mental retardation
- PE
  - Large ears
  - Prominent jaw
Characteristics of Fragile X

- Physical features
  - Prominent jaw
  - Large ears
  - Large testes
- Connective tissue
  - Double jointed
  - Flat feet
- Mitral valve prolapse

- Cognitive delays
- Behavioral challenges
  - ADHD
  - Hand flapping
- Sensory integration problems
- Living skills problems
- Speech & language problems
Diagnostic Testing for Fragile X

• Fragile X DNA
  – Suspect in any male with mental retardation
  – Suspect in any autistic male
Resources for Fragile X

• http://www.fragilex.org/
Name That Syndrome!

- 2 month old male
- Birth history
  - Spent a few days in NICU for NG feeds
- PE:
  - hypotonia
Diagnostic Criteria

• Major
  – Infantile central hypotonia
  – Infantile feeding problems and/or FTT
  – Rapid weight gain age 1-6 years
  – Narrow bifrontal diameter, narrow nasal bridge, down-turned mouth
  – Hypogonadism
  – Developmental delay/MR

• Minor
  – Infantile lethargy
  – Sleep disturbance or apnea
  – Short stature (teen)
  – Hypopigmentation
  – Small hands and feet
  – Narrow hands with straight ulnar border
  – Esotropia/myopia
  – Thick viscous saliva
  – Skin picking
Evaluation

• Management of hypotonia/poor feeding
• Evaluation for hypogonadism and/or hypopituitarism – refer to Endocrine
• Management of obesity
  – Risk for Type II diabetes
• Monitor for scoliosis
• Behavioral interventions
• Nutritional evaluation
Diagnostic Testing for PWS

- Methylation Studies
Table 1 Nutritional phases in Prader-Willi syndrome

<table>
<thead>
<tr>
<th>Phases</th>
<th>Median ages</th>
<th>Clinical characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Prenatal to birth</td>
<td>Decreased fetal movements and lower birth weight than sibs</td>
</tr>
<tr>
<td>1a</td>
<td>0–9 months</td>
<td>Hypotonia with difficulty feeding and decreased appetite</td>
</tr>
<tr>
<td>1b</td>
<td>9–25 months</td>
<td>Improved feeding and appetite and growing appropriately</td>
</tr>
<tr>
<td>2a</td>
<td>2.1–4.5 years</td>
<td>Weight increasing without appetite increase or excess calories</td>
</tr>
<tr>
<td>2b</td>
<td>4.5–8 years</td>
<td>Increased appetite and calories, but can feel full</td>
</tr>
<tr>
<td>3</td>
<td>8 years to adulthood</td>
<td>Hyperphagic, rarely feels full</td>
</tr>
<tr>
<td>4</td>
<td>Adulthood</td>
<td>Appetite is no longer insatiable</td>
</tr>
</tbody>
</table>

Modified from Am J Med Genet A.3

Figure a & b: without Growth hormone
Bottom c & d WITH Growth hormone treatment

Resources for Prader-Willi

• www.pwsausa.org
Name That Syndrome!

- 1 year old female
- Hx feeding problems
- No words yet
- Not walking yet
- 1st episode tonic-clonic seizure
Characteristics of Angelman

- Severe developmental delay
- Speech impairment
- Ataxia
- Behavioral uniqueness
  - Laughter
  - Hand flapping
  - ↑ excitability
- Typical facies
  - Flat occiput
  - Prognathia
  - Almond-shaped eyes
  - Wide mouth
- Suck/swallow disorder
- Strabismus
- Sleep disturbance

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Diagnostic Testing for Angelman

- Methylation studies
Resources for Angelman

- www.angelman.org
- www.international.angelmansyndrome.org
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