18p deletions

18p Critical Regions
Newborn Physical Findings (N=31)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal complications</td>
<td>74%</td>
</tr>
<tr>
<td>Feeding Difficulties</td>
<td>42%</td>
</tr>
<tr>
<td>Respiratory Difficulties</td>
<td>29%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>29%</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>10%</td>
</tr>
<tr>
<td>Muscle tone abnormalities</td>
<td>84%</td>
</tr>
<tr>
<td>Hypotonia</td>
<td>71%</td>
</tr>
<tr>
<td>Mix abnormal tone</td>
<td>13%</td>
</tr>
</tbody>
</table>

Immediate Referral
- Early Childhood Developmental services (OT, PT, ST) - Developmental delay 100%
- Genetics evaluation and counseling - Parental chromosome analysis or FISH
- Ophthalmology evaluation
  - Strabismus 2%
  - Optic nerve abnormalities 13%
  - Congenital cataracts 6%
  - Refractive Errors 52%
  - Astigmatism 29%
  - Hyperopia 32%
  - Myopia 13%

Initial Physical evaluation for:
- Cardiac Abnormalities 29%
- Holoprosencephaly findings 13%
  - Single central incisor 10%
  - Septo-optic dysplasia 3%
- Pectus Excavatum 29%
- Hernia (Inguinal, hiatal, umbilical) 29%

Monitor and Refer
- Seizures 16%
- Nystagmus 6%
- Kyphosis/ Scoliosis 19%
- Reflux 13%
- Constipation 32%
- Growth hormone deficiency 35%
- Panhypotuitarism 6%
- Thyroid abnormalities 16%
- Hearing loss 22%
- Recurrent ear infections 61%

Findings reported in more than 25% of this population include:
- Muscle tone abnormalities 88%
- Transient neonatal complications 63%
- Chronic otitis media 56%
- Refractive errors 53%
- Findings on the holoprosencephaly spectrum 31%
- Constipation 31%
- Strabismus 31%
- Cardiac anomalies 25%
- Growth hormone deficiency 25%

Other less common findings include seizures, scoliosis, pectus excavatum, ptosis, hearing loss, and thyroid abnormalities.
### Behavior in 18p-(cen) Adults

**BASC-2**  
\( n=15 \)

**Common Problems:**
- Poor social skills 40%
- Avoiding social contact 40%

**No problems identified:**
- Overly active and acting without thinking
- Engaging in anti-social and rule-breaking behaviors
- Incapacitating sadness or stress
- Easily distractible and unable to concentrate

### Executive Functioning in 18p-(cen) Adults

**BRIEF-A**  
\( n=16 \)

**Common Problems:**
- Moving from one situation to another 69%
- Keeping track problem solving successes/failures 50%

**No problems identified:**
- Inability to inhibit, resist, or not act on an impulse

### Social Impairment in 18p-(cen) individuals

**Adults**  
\( n=17 \)

**SRS-2**

**Common Problems:**
- Picking up on social cues 54%
- Repeating behaviors/obsessing same routines 53%
- Expressing social communication 53%

**Less common problems:**
- Interpreting social cues once they are picked up 47%
- Motivation to engage in social behavior 35%

### Behavior in 18p-(non-centromere) Adults

**BASC-2**  
\( n=17 \)

**Common problems:**
- Inability to adapt readily to changes 53%
- Inability to work with others for a common goal 50%

**Less common problems:**
- Nervous, fearful and worrisome tendencies 18%
- Easily distractible and unable to concentrate 12%
- Hostile and threatening behavior 6%
- Anti-social and rule-breaking behaviors 6%

### Executive Functioning in 18 p-(non-centromere) Adults

**BRIEF-A**  
\( n=16 \)

**Common problems:**
- Tracking of problem solving successes/failures 75%
- Moving from one situation to another 75%
- Keeping work and living spaces orderly 63%
- Managing current and future oriented tasks 56%
- Remembering information to complete a task 56%
- Beginning a task or independently generate ideas 50%
- Modulating emotional response 50%

**Less common problems:**
- The inability to inhibit, resist, or not act on impulse 19%

### Social Impairment in 18p-(non-centromere) individuals

**Adults**  
\( n=15 \)

**SRS-2**

**Common problems:**
- Repeating behaviors and obsessing over routines 67%
- Interpreting social cues 67%
- Picking up on social cues 60%
- Social communication 60%
- Motivation to engage in social behavior 60%

### Social Impairment in 18p-(non-centromere) individuals

2.5–18 years  
\( n=18 \)

**SRS-2**

**Common problems:**
- Obsessing over the same routines and rituals 78%
- Pick up on social cues 72%
- Interpret social cues 67%
- Social communication 61%

**Less Common Problems**
- Motivation to engage in social behavior 44%
18p- Natural History
(>18 years)

<table>
<thead>
<tr>
<th>Living Situation:</th>
<th>n=27</th>
<th>n=27</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Live with their parents</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>• With parent in independent area</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>• Supervised independent living program</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>• Apartment alone</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>• Group home</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>• Unknown</td>
<td>8</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Highest educational level:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Did Not Complete High School</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>• Attending High School</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>• High School Graduate (certificate)</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>• High School Graduate (diploma)</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>• Attending College/University</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>• Some College/University (no degree)</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>• Associates Degree</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>• Vocational School Degree/Certificate</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>• Unknown</td>
<td>8</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Martial Status/Children:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Married (no)</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td>• Married (unknown)</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>• Separated / Divorced</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>• Children (none)</td>
<td>19</td>
<td>22</td>
</tr>
<tr>
<td>• Children (unknown)</td>
<td>8</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Work (Volunteer, Part-time, Full-time):</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Yes</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>• No</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>• Unknown</td>
<td>8</td>
<td>5</td>
</tr>
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18p-: Current Ages & Age at Death

<table>
<thead>
<tr>
<th>Deceased</th>
<th>Current</th>
</tr>
</thead>
<tbody>
<tr>
<td>13 years F</td>
<td>Brain bleed post cardiac surgery</td>
</tr>
<tr>
<td>22 years 4 months F</td>
<td>Pneumonia complicated by lupus</td>
</tr>
<tr>
<td>Goldenhar syndrome; severe GE reflux; complex congenital heart disease</td>
<td></td>
</tr>
<tr>
<td>Lupus nephritis; hypothyroid; adrenocorticotropic hormone deficiency</td>
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<table>
<thead>
<tr>
<th>Age deceased</th>
<th>Gender</th>
<th>Cause of death</th>
<th>Past medical history</th>
</tr>
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<tr>
<td>13 years</td>
<td>F</td>
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Average score = the full range of scores

The normal range = the normal IQ range

Mild ID range = the mild ID range

Severe to profound = severe to profound

At risk = “at risk” range

Problem range = problem range

18p- (cen)
continued
**SMCHD1 = FSH Dystrophy 2**
- Digeneic
- DUX4 2nd gene (small array, A allele)
- Age of onset before age 20
- Progressive muscle weakness (asymmetric); shoulders, upper arms, lower leg
- Our data: 0/21 affected (8-30 years old; ave. age 18)
- 2/83 genetically at risk

**EMILIN2 = ?? Or any of 20 genes**
- Our data: 11 18p- = poor platelet function
- & 8 Tet18p = normal platelet function

**TGIF = Holoprosencephaly**
- Our data: 6/65 (single central incisor, iris coloboma, pituitary abn.)

**PTPN2**
- Inflammatory bowel disease (IBD)
- Mice with only 1 copy of *PTPN2* have increased susceptibility to inflammatory bowel disease (IBD)
- Genetic Studies: Crohn’s Disease & Ulcerative Colitis
- Rheumatoid arthritis
- Type 1 Diabetes??
- Our data: 0/67 have IBD
- 11/67 had an autoimmune condition
  - (juvenile rheumatoid arthritis, Sjogren’s syndrome, hypothyroidism, Graves, celiac, vitiligo, psoriasis, and alopecia)

**LAMA1 = Tortuous Retinal Vasculature and keratosis pilaris**
- Our data: 1/32 had retinal vascular anomalies
- 7/79 keratosis pilaris - from chart review (common in typical population)

**GNAL = Dystonia (Muscle Cramps)**
- Age of onset: 31.3 yrs. Range 7-54 years
- Common effects: neck 82%, speech 92%
- Our data: neuro exam = 0/17 evaluated met criteria
  - medical records = 2/58 had dystonia

**AFG3L2 = Spinalcerebellar ataxia 28**
- Age of onset: 24 years Range 3-60 years
- Likelihood of diagnosis = 93%
  - Slowly progressive gait & limb ataxia - incoordination 100%
  - Dysarthria- motor speech problem with articulation 100%
- Our data: 0/15 met criteria (8-30 years old; ave. age 16)

**DLCAP1, LCCR30, ANKRD12, IMPA2 = implicated in autism**
- Our data: 8/56 clinically significant GARS scores