Down Syndrome
2011 Health Supervision Guidelines

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Dr. Roizen has no conflicts of interest to report

Objectives:

1. To describe AAP guidelines for health supervision for children with Down syndrome and the recent changes.
2. To practice medicine in a way to set the optimal clinical trajectory for children with Down syndrome.

Are YOU Doing Your Part?
**CHANGES:**

Much more prescriptive  
More discussion state of evidence  
More anticipatory counseling  
Evaluation symptoms  
Added: hg, sleep study  
Do not use DS growth charts

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“Life is not a matter of holding good cards, but of playing a poor hand well.”

Robert Louis Stevenson

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Jack who has DS and ADHD was born with feeding problems that resulted in *failure to thrive* necessitating tube feeding. Ventricular septal defect was corrected surgically at less than a year of age. His congenital glaucoma was corrected at 10 months of age. Recently, he had to be *sedated for much needed ophthalmic and dental examinations*. At 29 years of age, Jack *works in a sheltered workshop that would like his father to give him medication for his ADHD*. He likes to listen to music and on weekends bowls with a friend with DS.

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Sandy at 38 years of age has *not had significant health problems*. He attended early intervention and graduated from special education at 21 yrs of age. He *uses public transportation to his full time job as a mail clerk*. He is actively involved in his church, plays piano, and swims regularly.
Organization of Care for DS

EVALUATION: cardiac, vision, hearing, sleep apnea, birth TMD
MONITOR: thyroid, hgb, growth
SYMPTOMATIC: atlanto-axial subluxation, celiac, sleep apnea, feeding/swallowing problems
VIGILANCE: arthritis, constipation, diabetes, GE reflux, GI obstruction, leukemia, renal, seizures
PREVENTION: gingivitis, obesity

Down Syndrome: CHD

Survey of 1469 cases 44% with CHD
43% VSD
42% ASD
39% AV septal defect
6% TOF
1% aortic coarctation
3% other
(Freeman et al., 2008)

Evaluation

Cardiac
Hearing
Vision
Sleep Apnea
Birth TMD

CHD: DS – Evaluation

• PE (+ O₂ sat) vs ECHO
  – Positive predictive value- abn PE 78%
  – Positive predictive value – nl PE 59%
  – 15 w/nl PE & abn ECHO – 9 required sx
    (McElhinney et al., 2003)
• PE & EKG (n=49) detected 78%
  hemodynamically significant
    (Shashi et al., 2002)
Cardiovascular Disease = DS

- HR response to exercise = low physical work capacity + cardiorespiratory fitness
- Low prevalence of coronary artery disease in DS – worth looking for protective factors

“Perform an echocardiogram to be read by a pediatric cardiologist. Regardless of whether a fetal echocardiogram performed. Refer if abnormal to a pediatric cardiologist.”

(Bull. AAP Committee on Genetics. Pediatrics. 2011;128: 393-406)

Hearing Loss: DS

Cross sectional studies 38-78%

Sensorineural HL/or mixed 4-20%

Hearing-ABR-(n=52 ears)

- Normal hearing both ears 32%, unilateral loss 22%, bilateral loss 46%
- Without loss 43%, conductive 11%, mixed 19%, sensorineural 27%
- Range of loss – mild 25%, moderate 42%, severe 6%

(Roizen et al., J Peds 1993; 123: s9-11)
Every 6 Month ENT Visit

- 48 children with DS <24 mo
- ENT & audiogram q 6 mo
- Follow-up 18 mo – 2 yr later
- 40 had PE tubes – 45%x1, 43%x2, 7.5%x3, 5%x4
- 4/48 – normal audiogram w/out antibiotics or PE tubes
- 1 abnormal hearing (2%)
- After 2 years (7% HL)

(Shott, SR et al. 2001 Int. J Ped Otol 61:199-205)

1. NB hearing screen and follow up
2. Audiology eval:
   a. every 6 mo from 6mo-5yr
   b. every year 6yr-21 yr
3. Behavioral audiogram & tympanometry until
4. Bilateral ear specific testing possible.
5. Abnormal results refer to otolaryngologist

(Bull. AAP Committee on Genetics. Pediatrics. 2011;128: 393-406)

Visual Disorders (n=77)

- Total with disorders 60%
- Total with disorders and normal PE 35%
- 2-12 months 38%
- 5-12 years 80%

Specific Visual Disorders (n=77)

- Refractive disorders 35%
- Stabismus 27%
- Nystagmus 20%
- Ptosis 5%
- Congenital cataracts 4%
- Spasmus nutans 3%
- Acquired cataracts, congenital glaucoma, congenital stationary night blindness, choreoretinal coloboma, and retinal detachment 1%

(Roizen et al. DMCN, 1994; 36: 594-600)
**OPHTHALMOLGY RECS**

Evaluate for cataracts at birth
0-6 months pediatric ophthalmology eval
1-5 yrs annually
5-13 yrs q 2 yrs
13-21 yrs q 3 yrs
(Bull. AAP Committee on Genetics. Pediatrics. 2011;128: 393-406)

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**Vigilance vs Monitor**
**Obstructive Sleep Apnea - DS**

- Contributing factors: mid-face & mandibular hypoplasia, large tonsils and tongue, glossoptosis, small upper airway, obesity, secretions, hypotonia
- 50% at 3 yr with OSA
- Parental reports: 60% DS with abnormal sleep studies report no sleep problems
(Shott, 2006)

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**OSA – Abn Sleep Studies**

- \( \text{O}_2 \) supplement with CPAP
- T&A - < 50% successful
- T&A with pharyngoplasty – same
(Merrell & Shott, 2007)

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By 4 years of age sleep study or polysomnogram
**Leukemia – AMKL- DS**

- Transient myeloproliferative disease (TMD) occurs in 4-10% of newborns with DS
- 20% with TMD develops DS-AMKL (acute megakaryocytic leukemia) w/in 4 years
- GATA 1 mutation (x-chromosome) regulates megakaryocyt differentiation
- N=134: 88% of TMD + GATA 1 mutation
  - 85% w/ myeloid leukemia + GATA 1 mutation
  (Alford K. et al., Blood. 2011 ;118 :2222-38)

**Leukemia – AML-DS**

- AML in DS >4 years negative for GATA1 mutations
- Prognosis does not differ form AML w/out DS

**HEME RECS**

Birth : CBC to r/o TMD & polycythemia

(Bull. AAP Committee on Genetics. Pediatrics. 2011;128: 393-406)

**Leukemia – ALL- DS**

- 20 fold higher vs general population
- Clinically & cytogenetically linked to “common” ALL
- 10 year survival
  - disease free: 55% (DS) vs 73%
  - event free: 56% (DS) vs 74%
- Separate into hi risk DS and low risk DS
  (Malinge S et al. BLOOD. 2009;113:2619-28)
**Thyroid ABN: DS**

- Congenital hypothyroidism
- Primary hypothyroidism
- Autoimmune thyroiditis
- “Subclinical” hypothyroidism
- Hyperthyroidism

**Monitor: Thyroid- DS**

1:128 nb screen abnormal (28-54 x gen pop) 4-54% with /DS w/age

Study of 1257 children w/DS 10.8% at 1-18 yr of age tx thyroxine
Most frequently: < 3 yr of age & between 12-18 yr
(Carroll et al., 2008)

**Iron Deficiency & Iron Deficiency Anemia (n=114)**

- Iron deficiency 10% (n=12)
- Iron deficiency anemia 3% (n=3)
- Not dx w/ RBC indicators 86% (13/15)
- Low transferrin saturation 100% sensitivity 85% specificity

• Obtain Hg at 1 yr & annually
• If at risk for iron deficiency or Hg < 11 g: serum ferritin & CPR or CHr

(Bull. AAP Committee on Genetics. Pediatrics. 2011;128: 393-406)

**SYMPTOMATIC:**

• Atlanto-axial subluxation
• Celiac
• Feeding & swallowing
• Obstructive sleep apnea

**Symptomatic: Atlantoaxial Instability**

• Lax ligaments – atlanto-axial joint C1-2
• Definition – atlanto-dens interval > 4.5 mm (on lateral neck at 3-5 year)
• 15% with DS – but 2% develop spinal cord compression (0.3%)
• Symptoms: loss of motor skills, stiff neck, change in bowel & bladder fx changes neurological exam, quadriplegic

“If signs or sx of myelopathy:”

1. Obtain neutral position spine films;
2. If normal, obtain flexion & extension films;
3. Refer to pediatric neurosurgeon or orthopedic surgeon
4. w/ expertise in evaluating and treating atlanto-axial instability.”

(Bull. AAP Committee on Genetics. Pediatrics. 2011;128: 393-406)
Celiac Disease: DS

1: 133 general population
1: 20-66 (5-15%) – European & US w/DS
Symptoms: diarrhea, bloating, poor growth, weight loss
• Symptomatic to asymptomatic: gen pop 1:8
  DS 4:8

1-21 yrs: check for celiac if + symptoms transglutaminase IgA and quantitative IgA

(Bull. AAP Committee on Genetics. Pediatrics. 2011;128: 393-406)
**SYMPTOMATIC:**

“Radiographic swallowing assessment if marked hypotonia, slow feeding, choking with feeds, recurrent or persistent respiratory sx, FTT”

(Bull. AAP Committee on Genetics. Pediatrics. 2011;128: 393-406)

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**Rheumatoid Arthritis: DS**

- 8.7/1000 vs .2-1/1000 in general population
- Symptom onset (6.3 years) with average delay of 2 years
- Morning stiffness 72%
- Polyarticular disease (57%) & oligoarticular disease (43%) but of these 54% progresses to polyarticular
- LABS: 72% elevated sed rate; 23% positive ANA; 6% positive rheumatoid factor
- 26% subluxation of involved joints;
- 32% respond to first line drugs

(Juj H & Emery H. J Peds. 2009;154:234-8)

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**Vigilance**

- Arthritis
- Diabetes
- GI malformations
- Seizures
- Renal diseases

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**Vigilance – Type 1 Diabetes**

- General population 0.12-0.17%
- DS 1% (1.4-10.6%)
- 54% with DS (7/13) take 1 dose insulin/day vs. 2-3 without DS

(Gillespie et al., 2006)
GI Malformations

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenal stenosis/atresia</td>
<td>3.9%</td>
</tr>
<tr>
<td>Imperforate anus</td>
<td>1.0%</td>
</tr>
<tr>
<td>Hirschsprung disease</td>
<td>0.8%</td>
</tr>
<tr>
<td>TE fistula/esophageal atresia</td>
<td>0.4%</td>
</tr>
<tr>
<td>Pyloric stenosis</td>
<td>0.3%</td>
</tr>
<tr>
<td>Other</td>
<td>0.3%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>6.7%</strong></td>
</tr>
</tbody>
</table>

(Freeman et al., Clinical Genetics, 2009. 75, 180-186)

NY State Congenital Malformation Registry
Renal & Urinary Tract Anomalies

<table>
<thead>
<tr>
<th>Group</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS (n=3832)</td>
<td>3.2%</td>
</tr>
<tr>
<td>Non-DS (n=3.4 million)</td>
<td>0.7%</td>
</tr>
<tr>
<td>OR 4.5</td>
<td></td>
</tr>
</tbody>
</table>

(Kupferman, Druschel, & Kupchik, Pediatrics, 2009. 124: e615-21)

PREVENTION

Dental

Obesity

- Proportional at birth
- 0-30 months light for height
- Lower resting metabolic rate
- >BMI than typical population
- Adults with more access to social and recreational activities and friendship have lower BMI
- Goal is to prevent obesity

DO NOT PLOT ON DS SPECIFIC GROWTH CHARTS
Plot on National Center Statistics or WHO
Calculate weight-for-height or BMI

ALL VISITS DISCUSS
Spine positioning esp w/ anesthesia, surgery
Risk some contact sports and trampolines
Review signs and symptoms of atlantoaxial instability, sleep apnea, feeding, and swallowing

Discuss:
CAM
How to tell siblings
Support groups, resources, EI
Genetic risk/future pregnancies

Behavior Problems
Psychopathology 18-23%
ASD 10%
ADHD 6-8%
ODD/CD 10-15%

(Dykens, MRDDRR, 2007)
Age at Regression with Autism With & Without DS (n=12)

<table>
<thead>
<tr>
<th></th>
<th>Single word</th>
<th>Language loss</th>
<th>Skill loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autism</td>
<td>14.9 mo</td>
<td>19.7 mo</td>
<td>19.5 mo</td>
</tr>
<tr>
<td>Autism w/ DS</td>
<td>40.6 mo</td>
<td>61.8 mo</td>
<td>46.2 mo</td>
</tr>
<tr>
<td>P-value</td>
<td>.005</td>
<td>.01</td>
<td>.006</td>
</tr>
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Comparison of Function in DS with & without Autism (n=23)

With Autism & DS: more poorly on receptive & expressive language skills, cognitive skills and adaptive skills. (p<0.0001)

History of Seizures: 7 with ASD and 1 w/out ASD (p=0.01)

Adjusting for ID: ADI-R diagnostic algorithm: Reciprocal Social Interactions, Communication and Restricted, Repetitive and Stereotyped Behaviors (p<0.0001)

Organization of Care for DS Summary

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