ENT Considerations in Down’s Syndrome

Prasad John Thottam, DO
Pediatric Otolaryngology Fellow
Children’s Hospital of Pittsburgh of UPMC
Outline

* General information/ definitions/ considerations
* Otologic manifestations
* Airway and sleep considerations
* General surgical and management pearls
History

* Identified as a syndrome in 1886 by John Landon Down
  * Microgenia, macroglossia, epicanthal folds, upslanting palpebral fissures, shorter limbs, single transverse palmar crease, poor muscle tone, mental retardation and learning disabilities
  * Originally described as “Mongolian idiocy” until 1961 Lancet publication changing name to Down’s Syndrome

* Chromosomal abnormality/ chromosome 21 trisomy was identified in 1959 by Jerome Lejeune
Genetics

- Trisomy 21 (47 chromosomes; 3- chrms 21)
  - 94% of Down’s
  - Risk increases with maternal age
- Robertsonian translocation involving chrm 21
  - 3-4% of cases
  - Not associated with maternal age
- Trisomy 21 Mosaicism
  - 1-2% of cases
Most common congenital chromosomal abnormality

1 of 700 live birth\(^1\)

Massive gains life expectancy over the past 40 years

- Life expectancy in 1983 – 25 years\(^2\)
- Life expectancy in 2014 – 50 to 60 years\(^3\)
- Primary reasoning – congenital heart surgical advancement\(^2,3\)

> 50% report seeing an otolaryngologist regularly\(^4\)
Predisposition to ENT related Problems

* **Anatomical**
  * Midface hypoplasia
  * Shortened palate
  * Relative Macroglossia
  * Narrowed oropharynx and nasopharynx
  * Hypotonia
  * Paranasal sinus abnormalities

* **Systemic**
  * Immunologic deficiency
  * Ciliary dyskinesia
Comorbidities

- Congenital heart disease
- Pulmonary hypertension
- GERD
- Subglottic stenosis
- Cervical instability
<table>
<thead>
<tr>
<th>Condition</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing problems</td>
<td>75</td>
</tr>
<tr>
<td>Vision problems</td>
<td>60</td>
</tr>
<tr>
<td>Cataracts</td>
<td>15</td>
</tr>
<tr>
<td>Refractive errors</td>
<td>50</td>
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<tr>
<td>Obstructive sleep apnea</td>
<td>50–75</td>
</tr>
<tr>
<td>Otitis media</td>
<td>50–70</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>40–50</td>
</tr>
<tr>
<td>Hypodontia and delayed dental eruption</td>
<td>23</td>
</tr>
<tr>
<td>Gastrointestinal atresias</td>
<td>12</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>4–18</td>
</tr>
<tr>
<td>Seizures</td>
<td>1–13</td>
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<tr>
<td>Hematologic problems</td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>3</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>10</td>
</tr>
<tr>
<td>Transient myeloproliferative disorder</td>
<td>10</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>5</td>
</tr>
<tr>
<td>Atlantoaxial instability</td>
<td>1–2</td>
</tr>
<tr>
<td>Autism</td>
<td>1</td>
</tr>
<tr>
<td>Hirschsprung disease</td>
<td>&lt;1</td>
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Otologic Manifestation

- EAC stenosis
- High incidence of otitis media
- High incidence of chronic ear disease
- Secondary hearing loss
- Ossicular abnormalities
- Inner ear dysplasia
Present in 40-50% of DS newborns

Generally resolves via natural progression and not an obstacle by 2-3 years of age

Important because: PCP examination/ infection and hearing monitoring

Recommendation: Follow-up every 3 months for microscopic evaluation
Otitis Media/ Chronic Ear Disease

- Reduced immune system: T&B cell reduction; IgG4 reduction; defective neutrophil chemotaxis\textsuperscript{6,7}
- Midface hypoplasia = narrowed ET and nasopharynx
- Adenoid tissue encroachment
- ET cartilage collapse and decreased tensor veli palatini function
- Mastoid aeration
- Possible histopathologic changes of ME mucosa
Midface Hypoplasia/ Nasopharynx

*The Skull Base & Nasopharynx in DS in Relation to Hearing*\(^8\)

- 28 DS/ 33 non-syndromic: age & sex matched
- All underwent pneumatic otoscopy, audio, lateral x-ray
- DS patients demonstrated smaller nasopharyngeal area & less acute angle between skull base & hard palate
- Resulted in soft tissue encroachment and less acute angle in children with DS and hearing loss
**Congenital anomalies of the ET in DS: Histopathology**

- DS ET smaller, collapsed in midcartilaginous, isthmus and poorly developed lateral cartilage

**Temporal bone morphometric study on ET & assoc. structures in patients with chromosomal aberrations**

- Chromosomal aberration patients had smaller volume of lateral lamina cartilage, reduced tensor veli palatini m. attachment
- Chrom. aberration patients reduced LL to ML ratio
Examined patients undergoing tympanoplasty DS & Non-DS for history of COM

- Otorrhea 60% of DS vs 27.2% Non-DS (p<0.05)
- Mastoid pneumatization index
  - 50.8 mm² DS vs 291.3 mm² Non-DS (p<0.05)
- No statistical significant difference in mastoid pneumatization regardless of tube history
Otitis media in a mouse model for Down syndrome

Fengchan Han*, Heping Yu*, Jiangping Zhang*, Cong Tian*, Cecilia Schmidt†, Casey Nava*, Muriel T. Davisson† and Qing Y. Zheng*

*Department of Otolaryngology-HNS, Case Western Reserve University, Cleveland, OH, USA and †The Jackson Laboratory, Bar Harbor, ME, USA

- Animal model
- Ts65Dn mice (TrisomyChrm >80% homologous with Human 21) compared to wild type
- ABRs/ Histological exam of ME/ Bacterial Cultures

Results
- ABR required higher mean threshold in Ts65Dn due to effusions
- Ts65Dn mice demonstrated higher density of goblet cells
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Hearing Loss

- Higher prevalence of hearing loss in DS regardless of CHL/ Mixed/ SNHL\textsuperscript{12}

- Estimated 50-90\% of DS children dx with hearing impairment vs 4-9\% general population\textsuperscript{12,13}

- Monitoring is paramount as hearing loss can be dismissed as natural course/ intellectual impairment
Hearing loss in Chinese school children with Down syndrome

Bradley McPherson\textsuperscript{a}, Sandy Pui-Shan Lai\textsuperscript{a}, Kevin Kwong-Ki Leung\textsuperscript{a}, Iris Hoi-Yee Ng\textsuperscript{b,*}

- Designed as study to examine need for amplification in specialized schools
- 92 DS children with mild – moderate intellectual impairment enrolled in special need schools
- Perceived hearing impairment asked
- Otologic exam; Tympanogram; TEOAE’s; PTA conducted
- 90% of participants had at least >25 dB HL in one ear
- 19.1% had Type B tympanogram in at least one ear
<table>
<thead>
<tr>
<th>Table 1</th>
<th>Sample characteristics of the screening group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>49 (53.3%)</td>
</tr>
<tr>
<td>Female</td>
<td>43 (46.7%)</td>
</tr>
<tr>
<td>Intellectual impairment</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>26 (28.3%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>66 (71.7%)</td>
</tr>
<tr>
<td>Previous hearing test</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>81 (88.0%)</td>
</tr>
<tr>
<td>Yes</td>
<td>11 (12.0%)</td>
</tr>
<tr>
<td>History of middle ear infection</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>86 (93.5%)</td>
</tr>
<tr>
<td>Yes</td>
<td>6 (6.5%)</td>
</tr>
<tr>
<td>History of hearing loss</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>78 (84.8%)</td>
</tr>
<tr>
<td>Yes</td>
<td>14 (15.2%)</td>
</tr>
<tr>
<td>Use of hearing aid</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>86 (93.5%)</td>
</tr>
<tr>
<td>Yes</td>
<td>6 (6.5%)</td>
</tr>
<tr>
<td>Cerumen level (Sullivan scale)</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>23 (25.6%)</td>
</tr>
<tr>
<td>1</td>
<td>25 (27.8%)</td>
</tr>
<tr>
<td>2</td>
<td>30 (33.3%)</td>
</tr>
<tr>
<td>3</td>
<td>12 (13.3%)</td>
</tr>
<tr>
<td>Left</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>20 (22.2%)</td>
</tr>
<tr>
<td>1</td>
<td>29 (32.2%)</td>
</tr>
<tr>
<td>2</td>
<td>28 (31.1%)</td>
</tr>
<tr>
<td>3</td>
<td>13 (14.5%)</td>
</tr>
</tbody>
</table>
Hearing loss is masked by various delays seen in DS (speech; intellectual)\textsuperscript{14}

- Early detection and associated maintenance critical
- Effect of hearing loss is greater on children with developmental delay compared to non-delayed (critical)\textsuperscript{14}
Clinical Report—Health Supervision for Children With Down Syndrome

- ABR/OAE screening at birth
- Hearing screening every 6 months up to age 3 depending if ear specific behavior audiometry can be established and is normal
- Once ear specific audiometry established – testing performed annually
Surprisingly controversial

Short-term efficacy of tympanostomy tubes for secretory OM in children with DS\textsuperscript{15}

* 24 DS vs 21 non-DS/ All with secretory OM and CHL/ Age matched
* Audiogram performed 6-9 wks post BMT
* 60% of DS vs 91% in non-DS reported improvement
* NOTE: all patients over the age of 6 -> delay of treatment
Prospective study examining DS/OME/BMT over time
* All enrolled under the age of 2 with 81% CHL
* Followed by ENT every 3-6 months
* Treated with BMT and replacements
* At 2 years 93% had normal hearing
* Aggressive management of DS OME = 3.6x’s higher rate of normal hearing compared to age matched non-aggressive treatment
Age requiring first set of tubes
Relationship of otitis media and language impairment in adolescents with DS\textsuperscript{14}

* Examined language scores in DS adolescents now with normal hearing
* Kids with history of tubes had higher language scores than DS with no tubes who had >3 known childhood infxns

Conclusion
* Temporary hearing loss may play role in language deficits
* Hearing loss effects can be present long after disease course
Facts for parents tubes in DS

* Tubes may be placed early in children with DS
* Expect child to require multiple sets
* Need closer monitoring and audiology visits
* Risks:
  * Otorrhea, persistent perforation, cholesteatoma

* Tube re-insertion should be counseled as a continuation of treatment **NOT** a failure of treatment
Obstructive Sleep Apnea

* Estimated as high as 80% in DS vs 1-2% non-syndromic\textsuperscript{15,16}
* Many predisposing factors that contribute
* Single modality treatment often not curative
* Can lead to further neurocognitive delay in the already delayed
* Pulmonary HTN in children predisposed to cardiac anomalies
Predisposing Factors

- Midfacial and mandibular hypoplasia
- Relative macroglossia
- Glossoptosis
- Smaller upper airway prone to adenotonsillar encroachment
- Lingual tonsil hypertrophy
- Laryngomalacia
- Increased secretions
- Increased obesity
- Generalized hypotonia
Fig. 1. Sagittal cut of healthy child (A) and child with Down Syndrome (B) highlighting anatomic differences. 1: Retrognathic mandible, 2: midface hypoplasia, 3: relative macroglossia, 4: obstructing adenoid pad and 5: higher rates of subglottic stenosis.
Trisomy 21 and Facial Developmental Instability

John M. Starbuck\textsuperscript{1,*}, Theodore M. Cole III\textsuperscript{2}, Roger H. Reeves\textsuperscript{3}, and Joan T. Richardsmeier\textsuperscript{1,4}

\textsuperscript{1}Department of Anthropology, The Pennsylvania State University, University Park, PA 16802

\begin{itemize}
  \item Prospective; age matched; 4 group study design
  \item Facial analysis of DS to Siblings to both age matched samples (n=55 in each group)
  \item Examined facial points for fluctuating asymmetry (FA) between all groups
\end{itemize}
Conclusions:

- DS sample had fluctuating facial asymmetry when compared to other groups
- When compared to siblings, DS had 2.7 to 6.9 fold number of significant differences in facial features/regions
- Frontal prominence was most stable
- Mandibular prominence most unstable/underdeveloped followed by maxillary prominence
Relative rather than absolute macroglossia in patients with Down syndrome: implications for treatment of obstructive sleep apnea

Carolina V. A. Guimaraes • Lane F. Donnelly • Sally R. Shott • Raouf S. Amin • Maninder Kalra

- Examine if DS patients have true macroglossia
- 16DS compared to age matched non-DS patients
- All O-AHI > 5
- MRI examined tongue size & bony confines

Conclusion
- DS tongue **smaller** than control (p=0.02)
- DS bony confines **smaller** than control (p<0.001)
- **THUS** Tongue size relative to bony confines larger than control (p<0.001)
Table 1  Measurements of tongue size on MRI in the Down syndrome and control groups.

<table>
<thead>
<tr>
<th>Tongue parameter</th>
<th>Down syndrome group (n=16)</th>
<th>Control group (n=16)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area (mm²)</td>
<td>2,431.9±432.3</td>
<td>2,767.4±326.6</td>
<td>0.02</td>
</tr>
<tr>
<td>Volume (mm³)</td>
<td>81.1±20.3</td>
<td>96.2±11.8</td>
<td>0.02</td>
</tr>
<tr>
<td>AP diameter (mm)</td>
<td>48.2±6.2</td>
<td>54.4±4.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2  Measurements of the bony confines of the pharynx on MRI in the Down syndrome and control groups.

<table>
<thead>
<tr>
<th>Craniofacial parameter</th>
<th>Down syndrome group (n=16)</th>
<th>Control group (n=16)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermandibular distance (mm)</td>
<td>69.8±4.3</td>
<td>80.15±1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mental-spine distance (mm)</td>
<td>64.2±7.6</td>
<td>74.9±5.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mental-clivus distance (mm)</td>
<td>82.1±4.5</td>
<td>98.1±4.6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Thought to be secondary narrowing of nasopharynx and oropharynx

Contribution by relative hypotonia

Adenotonsillectomy only curative 27% of DS patients

Ongoing CHP study on TA, PSG and DS (Thottam, Choi, Kitsko)

- CSA decrease post TA (p=0.02)
- 88% reduction in disease severity (p<0.001)
- TA size correlated with surgical response (p=0.02)
A Case-Control Comparison of Lingual Tonsillar Size in Children With and Without Down Syndrome

Ahmad R. Sedaghat, MD, PhD; Renee B. Flax-Goldenberg, MD; Bob W. Gayler, MD; George T. Capone, MD; Stacey L. Ishman, MD, MPH

* Retrospective case control study lateral xray
* Examined lingual tonsillar size in patients (105 DS & 89 non-DS)
* Lingual tonsillar size was significantly larger in DS (p=0.0008)
* Lingual tonsillar size correlated with increasing age in DS (p<0.0001)
* Concluded: Lingual tonsillar hypertrophy more common in DS and increases with age in DS
Examined DS & age control non DS patients without OSA

* Underwent MRI evaluations of airway volume & measurements

**Conclusion**

* Airway volume in DS 18% smaller/ 16% oropharynx
* Smaller bony parameters (mid-lower face)
* DS without OSA had smaller tonsil & adenoids compared to controls & similar BOT and parapharyngeal soft tissue
* Likely soft tissue crowding at sites causing OSA
So, who needs to be evaluated and when?
Obstructive Sleep Apnea

Should All Children With Down Syndrome Be Tested?

Sally R. Shott, MD; Raouf Amin, MD; Barbara Chini, MD; Christine Heubi, BS; Stephanie Hotze, BS; Rachel Akers, MPH

* DS underwent overnight PSGs after exam & questions
* Parental questionnaires on OSA signs/ symptoms, physical and history

Results
* 69% (24/35) parents reported no sleep problems **BUT** 54% (13/24) of this group demonstrated OSA on PSG
* 60% of kids with negative histories had abnormal PSGs

Concluded: All DS children between ages 3-4 years of age should get overnight baseline PSG to have objective data
So what kind of study?

* **HAS TO BE OVERNIGHT STUDY**

* Nap studies tend to underestimate severity\(^\text{18}\)
* Nap studies have demonstrated less sensitivity (75%) of patients with OSA; compared to full night (100%) in previous study\(^\text{18}\)
SO why get a PSG in DS

* **CLINICAL PRACTICE GUIDELINE**<sup>19</sup>
  * All children with DS get PSG before undergoing TA

* “Parents just don’t understand” – it’s under reported
  * Give them objective evidence

* May require more than just a TA
  * Can follow results and progression (baseline)
Surgical Treatment DS & OSA

- Adenotonsillectomy alone initially
- No data to support more aggressive surgery initially\(^\text{20}\)
  - \textit{TA+lateral pharyngoplasty vs TA alone}\(^\text{20}\)
    1. No statistical difference in OSA post-operatively with roughly 50-60% both having residual OSA

- Next place to look -> BOT/ lingual tonsils
  - \textit{Genioglossus advancement + BOT coblation post TA}\(^\text{21}\)
    1. 63% of DS patients AHI < 5 post procedure
Points for Parents on OSA/DS/Surgery

- PSG needed before surgery
- TA often not curative so often set realistic goals
  - 25% cure rate but a much higher reduction rate\(^\text{22}\)
  - Reduce CPAP settings/ increase compliance
- If obese BMI reduction always helps
- Increased risk and have to stay overnight\(^\text{23,24}\)
  - Longer hospital stay; decreased PO; 5x’s increase in respiratory event
- Increased risk of VPI and hypernasal speech\(^\text{24,25}\)
  - High arched palate, hypotonia, Levator dysfunction
- More surgery/ further interventions and PSG’s are common
General Operative Consideration

* Subglottic Stenosis
  
* Atlanto-axial instability
  * (def) increased mobility at the articulation of the first & second cervical vertebrae
  * Due to generalized ligamentous laxity of any of or all the 3 ligaments of the C1-C2 joint
Subglottic Stenosis and DS\textsuperscript{26}

- 4% of DS population required LTRS vs. 0.15% of non-DS
- Secondary to congenital narrowing and acquired

LTP for SGS in DS: The Cincinnati Experience\textsuperscript{27}

- Higher rate of intubation secondary to cardiac surgery
- Severe respiratory infections requiring intubation
- The above occurs at a young age = increased risk of SGS
Down Syndrome: Analysis of Airway Size and a Guide for Appropriate Intubation

Sally R. Shott, MD

- Prospectively evaluated DS airway size in DS (42) compared to control (32)
- Leak tests and MRIs (evaluate diameter)
- **Concluded**
  - DS kids required ETT 2-3 sizes smaller

- **Recommended:** ETT in DS be 2 sizes smaller for intubation and critical to check for air leak at 10-30 cm H20
AA Instability in DS

* Was first brought to wide attention in 1983 Special Olympics
* Incidence reported to be around 14% BUT only 1.5% determined to symptomatic
* Catastrophic injury can occur at extension and rotation BUT has been demonstrated in patients with long standing history of signs (abnormal gait; limited neck mobility etc)

* **Recommendations:**
  1. History of neurological signs greater priority than radiography
  2. Support head with rotation for BMT and limited extension
* For stenotic ear canals hearing and cerumen should be monitored closely
* DS child should undergo behavioral audiologic testing q6 months or q3 if canals are stenotic until able to tolerate ear specific testing
* Treat OME aggressively & prepare for multiple tubes
* High rate of OSA & get PSG at 3-4 y/o regardless
* TA is first treatment but only 25% successful
* Intubate with tube 2 sizes smaller
* Careful when turning head and history is most important
Thank You