Down Syndrome: Otolaryngologic Manifestations
Past, Present, and Future
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USA incidence: 1 in 800 live births in the USA
Spain incidence: 1 in 10,000 live births due to pre-natal diagnosis and termination of pregnancy
Occurs in all cultures, ethnic groups, geographic areas

Risk
Increased risk maternal age over 40 years
80% born to women less than 35 years
Increases with maternal age
15-29 years 1:1500
30-34 years 1: 800
35-39 years 1: 270
40-44 years 1: 100
older than 45 1: 50
Recurrence rate = 1%

History
Originally described by John Langdon Down in 1866
Chromosomal basis of syndrome described by Lejuene in 1959
Incorrectly assumed racial ethnology: Mongolism
This term no longer used
Early 20th century- DS were largest population of institutionalized patients
Down Syndrome - Legal Aspects
Baby Doe 1981 Bloomington, Indiana
Child with DS + TEF
Hospital initially denied treatment
Parents sued to obtain full care for their child
Child Abuse Amendments 1984
All disabled infants must receive full care
Exceptions
Irreversible coma
Treatment would prolong dying
Treatment is futile or inhumane
Down Syndrome in 2013
Not institutionalized – Part of the family
100 families currently on waiting list hoping to adopt a child with DS
Life expectancy 60 years
Level of developmental delay is variable
Inclusive education – various degrees
Better accepted by others with disabilities
Families have high goals

Down Syndrome - Physical Exam
Flattened, hypoplastic midface
Anterior/posterior flattening of the skull
Short, flat nasal bridge
Epicanthal folds
Shortened external ears
Shortened phalanges
Trisomy 21: An Aberrant Chromosomal Disorder
Chromosomal studies confirm diagnosis
Assess risk of future children
Inherited translocations
Sporadic translocations
1% risk of recurrence in most cases

Down Syndrome - Associated Anomalies
Cardiovascular
Anomaly in 40-50%
Cardiac evaluation by a cardiologist needed at birth
Echocardiogram
Gastrointestinal
Congenital duodenal atresia – 300 times more common than general population
Gastroesophageal reflux
Hirschsprung’s disease
Celiac disease
Thyroid
Hypothyroidism more common
Hypothyroidism in approx. 50% of adults with DS
Test at birth and yearly
Hematologic – Neonatal
Polycythemia in neonates
Increases risk of thromboembolism
Increased risk of leukemia
10-30 times higher risk
Pulmonary
Chronic hypoxemia due to:
Recurrent pulmonary infections
Obstructive sleep apnea
Hypoventilation due to decreased muscle tone
Increased incidence of pulmonary hypertension due to:
Chronic hypoxemia
Impaired development of alveoli and pulmonary vasculature

Otolaryngologic Manifestations
History of ENT knowledge and literature on DS
Retrospective and descriptive
No intervention given – Just “part of DS”
Relied on parental reports to determine outcomes
No objective data on response to interventions
Few evidence-based recommendations
• “Otolaryngologic Manifestations of DS”
  Emily Ann Hayes Research Fund
  Cincinnati Children’s Hospital Medical Center
  Provide “state of art” care
  • ie. care all the other children would be getting
• 5 year prospective study
• 65 consecutive children with DS
  Had to be no older than 2 yo when first enrolled
• Need to establish new ‘norms’ and increase expectations
• Cannot accept ‘it’s just part of DS’
• Chronic Ear Disease - WHY?
  Anatomic anomalies of eustachian tube
  • Shaped differently
  • Collapses more easily
    • Due to decreased function of tensor veli palatini muscle of the soft palate
    • Decreased cartilage cell density
  • Sits in a contracted nasopharynx
  • Poor muscle function
    • GER with pepsin in MEE (?)
• Chronic Ear Disease - WHY?
  Overall immaturity of the immune system:
  • Granulocytes normal in number but structurally and functionally abnormal
  • Humoral (B cell) response to some antigens is decreased
  • More upper respiratory infections (URI’s)
  • Increased incidence of leukemia (1%)
  • EAC stenosis
  • Small, stenotic external ear canals in 50%
  • Makes diagnosis of otitis media difficult – if you can’t see it, you can’t diagnose it!
  • Hearing loss from canal collapse
  • From cerumen impactions
• Chronic otitis media / Hearing loss - What we know:
  • Chronic ear infections are common
    • 3x higher incidence of COM and secondary hearing loss compared to other children with developmental delays
    • High incidence of inadequate medical and surgical treatment of the chronic ear disease (Roizen et al Clin Pediatr 1994)
  • Infections last longer
    – the children are less likely to grow out of the COM
    • Multiple sets of PET’s are frequently needed
    • Repair of tympanic membrane perforations should be done at an older age
    • Ossicular reconstruction has poor results
  • Sensorineural hearing loss
    • 4-20% incidence with SNHL or mixed hearing loss
• “True” SNHL or due to consequences of untreated chronic OM?
• Long term studies needed on children who received appropriate intervention of their COME
• Higher incidence of inner ear anomalies

• Inner ear dysplasia and hypoplasia of inner ear structures seen in children with DS
• Compared to normal hearing “typical” children
• Statistically significant differences in 55% of inner ear measurements done
• No actual correlation to DS hearing levels done
• Hearing loss
  Previous published studies on incidence of hearing loss: 40-75%
  • Is this the true incidence?
  • Why is even mild hearing loss so important?
  • Mild hearing loss will effect those with developmental delay more
  Studies show greater effect on those with DS
• Hearing loss - Hypothesis
  • High incidence of hearing loss in DS is due to consequences of poor medical surveillance and lack of aggressive medical and surgical intervention
  • Diligent and aggressive treatment of chronic ear disease will result in better hearing levels

• Otitis media – Study Protocol
  (Now part of routine care)
  • Children seen every 6 months
  • If ear canals stenotic, seen every 3 months
  • Audiograms every 6 months
  • Appropriate medical and surgical management of OM
  • PET Placement
  • 90% required PET’s
  • Most needed repeated PET’s
    • 46% PET’s x 1
    • 40% PET’s x 2
    • 11% PET’s x 3
    • 3% PET’s x 4
  • Worst vs Best Audiogram
    Prior to treatment
    • 81% had abnormal hearing levels
    • Range from borderline normal/mild loss to severe loss
  • After treatment
    • 90% normal to borderline normal hearing levels
    • 7% mild loss
    • 2% moderate loss
  Children with PET’s in place had a 3.6 times higher chance of normal hearing compared to audiograms done with PET’s not in
  • Of the 87 who failed NBS:
    • 16 subsequently had normal hearing
    • 25 of 33 with conductive hearing loss had normal hearing after treatment
    • 41 of 87 in normal hearing group
    • 9% with persistent conductive hearing loss
    • 5.7% with SNHL: moderate to profound
    • 3% mixed HL

• Efficacy of PET’s in DS
    • 40% continued hearing loss after PET’s
    • Minimal improvement and should only be used if severe hearing loss or severe pathological changes to TM
    • Why Such Poor Results?
  • Selikowitz study
    • Patients 6 to 15 years old
    • No previous PET’s
    • 6 to 15 years of inadequate treatment?
  • Iino study
    • Also delay in PET placement
    • Doesn’t differentiate ‘tubes in’ and ‘tubes out’ at time of hearing evaluation
    • Almost half were without PET’s
    • They conclude that since COME returned once tubes extruded, tubes are a “failure”

• Conclusions
  • Hearing loss less common in children with Down syndrome IF:
    • Aggressive medical and surgical care
    • Diligent examination with microscope
    • Frequent follow-up exams
    • Early PET placement
    • PET replacement may be needed …

• Questions That Still Need Answers:
  • What will happen to this group’s hearing levels over time?
  • How long and how many PET’s will be needed?
  • What will be the consequences of repeated PET’s?
  • COME in DS - Treatment

• If the ear drums cannot be seen by the Pediatrician, parents should request referral to ENT doctor
• Offer this service to your referring physicians

• Medical treatment of otitis media
  • Antibiotics
  • GER treatment (?)
  • Eliminated risk factors
    • Day care – only 6-8 children per group
    • Cigarettes

• Surgical Treatment
  • PET’s – ventilation tubes
  • Indications fall outside of standard published indications
  • Similar, but sooner
  • Indications
    • Recurrent ear infections
    • Persistent middle ear fluid
    • Failure of an acute episode of otitis to improve on antibiotics
  • PET’s and Adenoidectomy
  • Assessment of Hearing
    • Initial assessment – ABR, OAE
    • Hopefully before the child goes home from hospital

• Health Care Guidelines for Individuals With DS
  • Published originally in Down Syndrome Quarterly
  • Now through the American Academy of Pediatrics
  • Audiologic testing New AAP recommendations August 2011
  • Newborn screen or within 3 months of age
  • Continue testing every 6 months until ear specific testing is achieved
  • Then yearly, if hearing is normal
  • Follow up testing depends on presence or absence of hearing loss and ear disease
  • CCHMC Study data
    • Using this current recommendation:
      • Only 14% were able to do ear specific testing by end of 3rd year of age
      • Only 41% were able to do ear specific testing by end of 4 year of age
    **Soundfield testing alone could miss unilateral hearing loss

• Amplification of Hearing – Hearing Aides/Cochlear Implants
  • Obstructive Sleep Apnea Syndrome (OSAS)
  • Episodes of partial or complete airway obstruction during sleep
  • Usually assoc. with decrease in oxygen saturation or hypercarbia
• **Prevalence:** 2% or 500,000 children with OSAS in the USA

• Peak age is 2 to 5 years (developmental peak of T&A hypertrophy)

• Second peak in middle to late adolescence (more ‘adult’ symptoms)

• Children male = female

• Adolescent male > female

• **Down Syndrome**

• Higher probability of developing OSA

• Even if asymptomatic

• Higher risk due to:
  - Midface hypoplasia
  - Narrow nasopharynx
  - Large tongue
  - Muscular hypotonia
  - Increased URI's
  - Small larynx and trachea

• 50% will also have a cardiac anomaly

• Cor pulmonale more likely

• Underlying pulmonary anomalies and hypotonia contribute to hypoventilation and chronic hypoxemia associated with OSAS

• **Incidence of OSAS in DS**

• Marcus et al (1991) Retrospective study
  - 53 children – Ages 4 weeks to 51 years (Mean age 7 years)
  - 100% abnormal sleep studies

• Dyken et al (2003) Prospective study
  - 19 patients - Ages 3 to 18 (Mean 9 years)
  - Abnormal AHI in 79%

• Shott et al (2004) Prospective study
  - 48 patients - Ages 3-4 years
  - 57% abnormal AHI

• **Down Syndrome – OSAS** Why is it overlooked?

• Many sequelae of OSA are disorders associated with DS:
  - Failure to thrive
  - Pulmonary hypertension
  - Behavioral problems

• After 1984: Cardiac surgery done on all children with DS

• Still higher than expected incidence of pulmonary hypertension

• WHY??

• OSA!!

• **Parents Of Children With DS Underestimate Severity Of Their Child’s Sleep Abnormalities**

• Marcus et al. (1991)
  - In children with DS, 68% of parents reported no symptoms of obstruction
  - 100% had abnormal studies

• Brouillette et al. (1984)
  - In normal children with proven OSA, parents reported sleep difficulties correctly 96% and correctly reported apnea 78%

• Parents assume this is “normal for DS”

• No obvious snoring, but:

• Sleep with head hyperextended

• Sleep in sitting position, or bent forward at the waist

• Found sleeping, sitting up on the floor

• Up several times during the night

• Is daytime sleepiness being mistaken for learning disabilities??

• Is daytime sleepiness being mistaken for behavior disorders??

• **Indications For Sleep Study In Children With DS**

• Parental concerns of obstruction

• Poor sleep habits, frequent waking or unusual sleeping positions

• New AAP Guidelines: Baseline sleep study obtained at age 4 years, even if no obvious symptoms

• New AAO Guidelines: Pre-op T&A

• **Sleep studies in children with developmental delays**

• Need to go to Pediatric Sleep Lab

• Success rate much higher

• At Cincinnati Childrens Hospital, extra sleep tech present

• Parents need to be prepared
  - If parents get frustrated, child gets frustrated

• **Pediatric Sleep Studies**

• Need to use ‘pediatric’ definitions

• Important to assess normal and abnormal values used when evaluating test results and published literature

• **Obstructive Index**

• Number of obstructive apneas and hypopneas per hour of sleep

• Normal                       <1

• Mild abnormal (mild OSA)                     1-5

• Moderate abnormal (mod OSA)             5-10

• Severe abnormal (severe OSA)               >10

• **Hypoxemia**

• Important to look at AHI along with presence or absence of oxygen desaturations

• Sustained oxygen sats < 93%

• Intermittent oxygen sats <90%

• **Hypoventilation Syndrome**

• Occurs if end tidal CO > 50 mm Hg for greater than 10%-25% of the time

• Hypercarbia associated with increased risk of hypertension, abnormal cardiac variability, increased sleep fragmentation

• **Treatment of OSA – Medical**

• Treat upper airway congestion

• Saline spray, hypertonic saline irrigations

• Antibiotics – full course and maintenance

• Eliminate risk factors, esp. cigs!!

• Allergy treatment

• Steroid spray, antihistamine sprays

• **Oxygen during sleep**
  - Very young children
• Only option other than trach
• Need to monitor for respiratory depression and hypoventilation
• **Weight loss if patient is obese or has had a recent weight gain**
• Pre-teen years
• Oral appliances
  • Palate expanders — around age 8
  • Oral dental splints — post-puberty
    • Bennett DDS: 4 young adults with DS successful with oral mandibular appliances
• **CPAP – BiPAP** Continuous positive airway pressure
  • Requires child’s cooperation
  • Not tolerated well, but it does work
  • Nasal delivery may be more successful ("No mask" or nasal pillows)
  • Higher success if able to admit child for CPAP training
  • Need yearly repeat sleep study to confirm that settings are correct
  • Concerns of facial sores and facial growth effects

OSAS - Surgical Treatment: T&A
• T&A - most common Rx for OSA in children
• Usually successful because T&A most common source of obstruction
• May improve obstruction, but not always successful in DS
  • 37 patients with DS
  • Ages 3-4 years
  • 43% had normal post-op AHI
  • If AHI, hypoxemia and hypercarbia are all evaluated: Only 29% had normal sleep study after T&A
• Shete et al. 2010: 11 patients with DS
  • Mean age 8.4 years
  • Only 18% had normal post-op AHI
• OSAS - Surgical Treatment
  • Important to get post-T&A sleep study

**More important than pre-op study**
• After T&A fails, what do you do??
• Treatment is dependent upon appropriate diagnosis of source and level of the obstruction

• Causes of persistent obstructive sleep apnea despite previous T&A in children with Down syndrome as depicted on static and dynamic cine MRI  

27 patients — Mean age 9.9 years
• Macroglossia 74%
• Glossoptosis 63%
• Recurrent adenoids 63%
• Enlarged lingual tonsils 30%
• Hypopharyngeal collapse 22%
• **What if T&A fails?**Define the level of obstruction
• Lateral neck xray — Regrowth of adenoids?
  • Seen in 63%
• Flexible endoscopy in the supine position
• Cine MRI
• Flexible Endoscopy for evaluation of OSA
  • **Advantages**
    • Awake or asleep
    • Evaluate for adenoid regrowth, nasal obstruction, base of tongue
    • Includes evaluation of larynx and trachea
  • **Disadvantages**
    • General anesthesia level required for instrumentation of airway may exacerbate collapse of airway and give false positive findings
    • Can only evaluate one level of the airway at a time
• Cine MRI
• High resolution, dynamic examination of the airway
• 128 images over 2 minutes
• Obtained with snoring or oxygen drops
• Done with sedation but less than what is needed for airway instrumentation (dexmedetomidine)
  • Useful especially in those with complex airways
• (Patient examples)
  • Allows assessment of multiple levels of airway at the same time
• THE UPPER AIRWAY CENTER at Cincinnati Children’s Medical Center — opened Jan 2013

OSAS – Further surgical options:
• Depends on level(s) of residual obstruction
  • Base of tongue collapse
  • Oropharyngeal collapse
  • Nasopharyngeal collapse
  • Hypopharyngeal collapse
• Base of tongue obstruction
  • Lingual tonsillectomy
• Genio-glossus advancement
  • Midline osteotomy: Pull segment of jaw bone forward
  • Genioglossus advancement suspension technique
• Resection of wedge of base of tongue
• Midline posterior glossectomy with coblation
• Mandibular — maxillary distraction surgery
• In most children with Down syndrome, it is a combination of both macroglossia and glossoptosis
- **Oropharyngeal Stenosis:**
  - 49 of 104 patients multilevel, single-stage surgery – all included lingual tonsillectomy
  - 4/49 patients developed OPS - 8.2%

- **OSA – Surgical Options - Tracheotomy**
  - Consider if all else fails and there is evidence of cor pulmonale, pulmonary hypertension
- **OSAS - Follow up Sleep Study**
  - Post-surgical sleep study should be done 2-3 months after surgery
  - Allows for resolution of surgical edema and maximal surgical improvement
  - Especially if severe pre-op OSA
  - Long term monitoring in high risk children is appropriate

THE FUTURE: Dynamic computational modeling of obstructive sleep apnea in Down syndrome (DYMOSA) NIH RO1HL105206-01

- **Etiologies of Sinusitis in Down Syndrome**
  - Midface hypoplasia
  - Contracted nasopharynx
  - Adenoid hypertrophy
  - Immature immune development
  - Paranasal sinus anomalies
    - hypoplasia
  - Assessment
    - Rule out upper airway obstruction, especially nasal obstruction
    - Question for risk factors, especially cigarettes!!
    - Xray assessment – both plain films and CT scans
    - Immune work up
    - Allergy testing
  - **Down Syndrome – Sinusitis Conservative Treatment**
    - Nasal irrigations
    - Maintenance antibiotics
  - Allergic rhinitis treatment:
    - Antihistamines, especially Zyrtec and nasal steroids – Very successful!!
    - Singulair
  - Allergy evaluation
  - Surgical Intervention
    - Adenoidectomy
    - Functional Endoscopic Sinus Surgery (FESS)
    - Palatal expansion – increases nasal airway
  - Anesthetic Concerns
    - Cardiac problems
    - Pulmonary hypertension
  - Thyroid disease
  - Sensitivity to drugs commonly used in anesthesia, esp. cardiac sensitivity
  - **Cervical Spine Concerns**
    - Special precautions should be taken with neck positioning in surgery
    - This is especially a concern for T&A and ear surgery
  - **Cervical Spine Abnormalities**
    - 25% have atlantoaxial joint instability (AAI)
    - Odontoid hypoplasia
    - Laxity of transverse ligament
    - Abnormal fusion of cervical spine
    - Hyperextension of neck → compression of spinal cord
  - 89% with AAI are asymptomatic
  - **Cervical spine X-rays:** No longer recommended by AAP Guidelines
    - Xrays can miss diagnosis
    - Physical exam is more sensitive
  - Assume everyone has it and protect the neck during surgery from hyperflexion and hyperextension
  - **Down Syndrome - Subglottic Stenosis**
    - Common practice to intubate with 1 size (0.5mm) smaller ETT
    - Is this adequate?
    - Children with DS have smaller subglottic/tracheal airways
    - Intubate with 2 sizes smaller ETT
  - **Oral and Dental Abnormalities**
    - Macroglossia – usually, more of a “relative” macroglossia
    - Tongue thrusting : Neurologic vs OSA
    - Fissured tongue
    - Enlarged taste buds
    - Missing teeth 50%
    - Poor occlusion