Neurodevelopmental Problems and Congenital Heart Disease

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Disclosures

- I am addressing the issue as developmental/behavioral pediatrician, not a pediatric cardiologist.
- I am a subspecialist in neurodevelopmental testing, treatment, and follow-up.
- I will quote some of the literature in these areas.
- I will emphasize basic concepts, not management.
- I am a promotional speaker for McNeil and Novartis pharmaceutical companies.
Brief History of Congenital Heart Disease Care

- 1\textsuperscript{st} 1/3 20\textsuperscript{th} century understand the pathology
  all patients with complex anatomy died
- 2\textsuperscript{nd} 1/3 20\textsuperscript{th} century initial operative repairs
  most patients with complex anatomy died
- Last 1/3 20\textsuperscript{th} century most patients with complex anatomy lived
  - End of the 20\textsuperscript{th} century to the early 21\textsuperscript{st} century death is rare (1%)
  - Now outcomes impact quality of life and long term neurodevelopmental issues
Syndromes associated with CHD

- >30% of infants with CHD have a genetic syndrome
- Some syndromes are associated with a particular cardiac lesion
- Prenatal diagnosis allows continuity of care with attention to other involved organ systems.
- It also allows parents time to process, grieve and reorganize the family around the child’s needs
- It allows the prenatal team and chosen pediatric specialists to help support the family
Microdeletions and Duplications

- Common Genomic disorders
- On microarray testing, about 20% of people with CHD have a *copy number abnormality*
- Syndrome examples: Williams Syndrome, DiGeorge Syndrome (Velo-Cardio-Facial Syndrome), Dup 7q11.23
Chromosome MicroArray Analysis

- Genotyping arrays utilize high density single nucleotide polymorphisms (SNP’s) or oligonucleotides spaced along the chromosomes
- Detect copy number variations
- Are there 2 copies (normal), 3 copies (one extra) or 1 (one missing)?
Velocardiofacial Syndrome
Shprintzen Syndrome

- Incidence/ Genetics
- 1/2000
- Chromosome 22q11.2 deletion
- Often associated with conotruncal heart defects
Down Syndrome

- John Langdon Down 1866 clinical description: “Observations on an Ethnic Classification of Idiots

- Trisomy 21 discovered in 1959
- 40-50% have heart disease, most of which require surgery
Chromosome 22 Deletion

- Angelo DiGeorge (1921- October 11 2009) endocrinologist 1960
- Robert Shprintzen speech pathologist 1970s
- de la Chapelle 1981 chromosome 22 deletion association
- Affects development, immune system, heart
Chromosome 22 Deletion

- FISH (Fluorescent in situ hybridization)
  autosomal dominant
Chromosome 22 Deletion
Syndromes-Summary

- Often associated with CHD
- Should be identified as early as possible - Chromosomes & FISH Chromosome 22 on amniotic fluid sample
- Microarray (Comparative Genomic Hybridization) can be performed on infant while in nursery
- Baseline neurodevelopmental problems related to specific syndromes
- CHD, especially cyanotic, intra-operative or bypass events can magnify neurodevelopmental issues (e.g., stroke, bleed, IVH)
CHD and Neurodevelopment Intrinsically Linked With or Without an Underlying Syndrome

- In utero
- CHD can lead to impaired hemodynamics and oxygen delivery to organs
- Impaired hemodynamics and O2 delivery can lead to impaired brain development
In Utero

- Group at CHOP showed retrograde flow to fetal brain in hypoplastic left heart (HLH) (Kaltman)

- Group at Cincinnati Children’s Hospital showed decreased head circumference growth and diffuse white matter injury in fetuses with HLH
In Utero

- Group in Columbus Ohio showed newborns with HLH, coarctation, tetralogy of Fallot without a syndrome more commonly had microcephaly.
  Barbu Am J Obstet Gynecol 2009; 201: 43

- Recommended close antenatal surveillance and possibly earlier delivery.
In Utero

- Prenatal detection CHD
  - Historically, > 2/3 not detected
CHD and Neurodevelopment Intrinsically Linked

- Postnatal and preoperative
  - Lack of prenatal detection of CHD can lead to serious consequences
  - Baby presenting in shock can effect long term neurodevelopmental outcome
  - Stabilization prior to surgery
Postnatal and Preoperative

- Lack of prenatal detection prevents prenatal delivery planning
- Metabolic consequences: Acidosis
- Hypoxia
- Heart failure
- PGE (prostaglandins) needed for PDA flow including blood flow to brain
- Stabilize sick newborn prior to a catastrophic incident
CHD and Neurodevelopment
Intrinsically Linked

- Intraoperative
  - Cardiopulmonary bypass is necessary for repair
  - Cardiopulmonary bypass may be another factor in long term neurodevelopmental outcome
Intraoperative-Cardiopulmonary Bypass
Intraoperative

- Bypass complications
  - Embolism
  - Inflammation
  - Bleed (IVH, other areas of brain)
- Related to duration
Intraoperative

- Brain protective measure with bypass (?)
  - Cooling
  - Managing flow and perfusion
  - Steroids
  - Others
Intraoperative

- CNS Monitoring
  - Transcranial doppler
  - Continuous EEG
  - Near infrared spectroscopy for cerebral oxygen saturation
CHD and Neurodevelopment
Intrinsically Linked

- Postoperative
  - Impaired cardiopulmonary function and metabolic abnormalities can occur
  - Delayed feeding and aversive oral experiences
  - Such aberration can add to long term problems
Postoperative
CICU Drama

QuickTime™ and a decompressor are needed to see this picture.

- Samuel Jonah (my grandson)
- Post-op TGA
The only available touchpoint

QuickTime™ and a decompressor are needed to see this picture.

- But he does have a Red Sox blankie
Postoperative

- Effects of narcotics
- Skin-to skin contact not possible
- Careful Monitoring
  - Acid base
  - Oxygenation
  - Perfusion
  - Cardiac output
  - Parental reaction/acceptance
- ECMO
  - Predictor of poor neurologic outcome
Postoperative

- Possibly helpful
  - Early feeding (Allow mother to pump and save colostrum and breast milk)
  - Appropriate interaction and stimulation, including parent involvement
  - Pediatric OT/PT with parent instruction (Hypotonia is frequent)
  - Explanation of and smooth transition to early intervention
Postoperative

- Use of discharge planning MRI
  
  Sherlock Stroke 2009; 40: 327-332

  - Despite prevention a problem may have occurred
  
  - May provide markers related to long term outcome
CHD and Neurodevelopment Intrinsically Linked

- Beyond the newborn
  - Additional procedures (e.g., cardiac cath) frequently needed and residual cardiac impairments possible
  - Parent-child attachment issues
  - Difficult breast feeding
  - Nosocomial Infections
  - These factors also play roles
Beyond the Newborn

- Syndromes may be missed
  - CHOP found about 25% of patients 1 year after newborn surgery were not previously diagnosed with a syndrome. Fuller Eur J Cardiothorac Surg 2009; 36: 40-47

- Prompt recognition leads to early intervention BEFORE delays occur. Part H of PL 99-457 (IDEA) as interpreted in NV allows eligibility because of a “condition that predisposes to developmental delays,” I.E., CHD.
Beyond the Newborn

- CHOP group study of 5-10 year olds after newborn complex CHD surgery  
  Shillingford Pediatrics 2008; 121: e759-767
- Inattention
- Hyperactivity
- Poor school performance
Smile, laugh, giggle

QuickTime™ and a decompressor are needed to see this picture.

Sam with Grandma L.
Run Jump & Play
THANK YOU!

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