Neonatal Critical Congenital Heart Disease screening

Sophia Tsakiri, MD
Objectives

• Review of the fetal and neonatal circulation
• Overview of critical congenital heart diseases [CCHD]
• Review of CCHD outcomes
• Screening for CCHD
• Screening for CCHD with pulse oximetry
Cardiovascular system

One-way direction of blood flow
Fetal circulation

Placenta: gas and nutrient exchange
Parallel pulmonary and systemic circulations
Fetal shunts: atrial, ductal, hepatic
Neonatal circulation

Removal of the placenta
Closure of fetal shunts: atrial, ductal, hepatic
Establishment of one-way direction of blood flow
Critical periods of development for various organ systems and the resultant malformations

<table>
<thead>
<tr>
<th>Embryonic Period (in weeks)</th>
<th>Fetal Period (in weeks)</th>
<th>Full Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
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<tr>
<td>Period of dividing zygote, implantation, and bilaminar embryo</td>
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<td>3</td>
<td>4</td>
<td>5</td>
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<td>Usually not susceptible to teratogens</td>
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</tbody>
</table>

- Critical periods of development (red denotes highly sensitive periods)
  - Heart
  - Arms

- Central nervous system
- Prenatal death
- Major morphologic abnormalities
- Physiologic defects and minor morphologic abnormalities

© Elsevier 2005
Cardiac embryology

- Fusion
- Bending
- Rotation
- Looping
- Partitioning
- Shunts
Risk for Congenital Heart Disease (CHD)

• 8 out of 1000 babies have CHD
• Most are mild
• 2/1000 are critical

• Higher risk for CHD, if a family member w/ CHD
• Recurrence risk in the family 2-15%

• More than 2 million Americans with CHD
• ~5,000 infants born each year with CHD in US
• Leading cause of death in 1st year of life
Causes of CHD

- Unknown
- Genetic syndrome: eg. Trisomy 21, 18, 13
- Single gene defects
- Maternal illness: Diabetes, SLE, obesity, PKU
- Environmental exposure:
  - Infections: Rubella, Enterovirus
  - Alcohol
  - Drugs: Thalidomide, Anti-acne meds, Valproic acid, Lithium
Congenital heart disease

A heart abnormality that is present from birth

Structural defects

- Hypoplasia
- Obstruction
- Septal defects
- Complex anatomy

Functional defects

- Infections
- Metabolic cardiomyopathy
- Arrhythmias
Critical Congenital Heart Disease (CCHD)

An abnormality in the structure or function of the heart
- that exists at birth,
- causes severe life-threatening symptoms,
- and requires medical intervention within the first few hours, days or months of life
CCHD pathology

- **Hypoplasia:** Hypoplastic left ventricle
  Single ventricle

- **Obstruction:** Pulmonary atresia with intact septum
  Tricuspid atresia
  Pulmonary stenosis
  Aortic arch atresia, hypoplasia or interruption
  Coarctation of Aorta

- **Septal defects:** Atrial septal defect
  Ventricular septal defect
  Atrioventricular septal defect

- **Complex anatomy:** Tetralogy of Fallot
  Total Anomalous Pulmonary Venous Return
  Transposition of great arteries
  Truncus arteriosus communis
  Double outlet right ventricle
  Ebstein’s anomaly
CCHD pathophysiology

Ductal-dependent systemic circulation:
- eg. HLHS, CoA, interrupted Ao arch
- Shock, if the ductus closes

Ductal-dependent pulmonary circulation:
- eg. Pulmonary atresia, TOF
- Severe hypoxia, if the ductus closes

Complex pathophysiology
- eg. TAPVR, truncus, TGA
- Combination of cardio-respiratory insufficiency, if the ductus closes
CCHD pathophysiology

Interrupted aortic arch

Pulmonary atresia

TAPVR
Presentation of CHD

• CCHD patients can look healthy at birth

• Within hours or days after birth they can have serious complications and even die

• Some patients will be asymptomatic for months or years
Symptoms of CHD

- Cyanosis or mild hypoxia
- Low blood pressure
- Breathing difficulty or tachypnea at rest
- Feeding difficulty
- Poor growth
- Sleepiness or irritability
- Sweating
- Murmur on exam
- **Sudden death**: 1/3 of first year cardiac deaths
Outcomes of CHD

85% of children diagnosed with CHD will survive into adulthood

Survival rates vary by disease complexity:

<table>
<thead>
<tr>
<th>CHD complexity</th>
<th>CHD examples</th>
<th>Long-term survival [&gt;20 years]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple</td>
<td>ASD, VSD, valve d/o</td>
<td>95%</td>
</tr>
<tr>
<td>Moderate</td>
<td>CoA, AVC, TOF</td>
<td>90%</td>
</tr>
<tr>
<td>Great</td>
<td>Truncus, TGA, single ventricle</td>
<td>80%</td>
</tr>
<tr>
<td>Specific complex disorders</td>
<td>HLHS</td>
<td>60-70%</td>
</tr>
</tbody>
</table>

Marino BS et al. Circulation 2012; 126: 1143-1172
Neurodevelopmental delay in CHD

The prevalence and severity of NDD increases with the complexity of CHD

NDD in the areas of intelligence, language, attention, motor skills, visual processing, executive function and psychosocial adjustment

Marino BS et al. Circulation 2012; 126: 1143-1172
Determinants of outcome of fetal cardiac disease

Late detection or lack of diagnosis

\[ \rightarrow \]

Closure of the ductus arteriosus and physiologic increase of the pulmonary vascular resistance

\[ \rightarrow \]

Cardiogenic shock, multiorgan failure and hypoxic ischemic brain injury

\[ \rightarrow \]

Morbidity

Neurodevelopmental delay

Death


Donofrio MT et al. Circulation 2014; 129: 2183-2242
Improved outcome of fetal cardiac disease

Early detection and risk stratification

Delivery at an appropriate birthing center

Early disease-specific treatment

Multidisciplinary medical care

Social support

Donofrio MT et al. Circulation 2014; 129: 2183-2242
Marino BS et al. Circulation 2012; 126: 1143-1172
Critical CHD screening

- CCHD screening of the fetus
- CCHD screening of the high risk fetus
- CCHD screening of the ill newborn
- CCHD screening of the well newborn
Fetal echocardiography

Specificity nearly 100%

Fetal CHD diagnosis is usually accurate

Sensitivity of the basic ECHO views 49%

Sensitivity of the advanced ECHO protocols and of the 3\textsuperscript{rd} trimester screening can be up to 85%

Fetal ECHO may miss up to 50% of CHD

Zhang YF et al. Medicine 2015; 94(42): e1759
Fetuses at high risk for CHD

- Maternal diabetes mellitus
- Phenylketonuria
- Family history of CHD
- Maternal infections
- Maternal Lupus and Connective tissue d/o
- Teratogen exposure
- Assisted reproductive technology
- Known or suspected chromosomal abnormality
- Monochorionic twins
- Hydrops fetalis
- Arrhythmias
Work up and diagnosis of CCHD in the ill neonate

- Clinical exam
- Blood pressure
- Pulse oximetry
- Electrocardiogram
- Chest radiograph
- Hyperoxia test
- Echocardiography
- Cardiac catheterization
- Genetic and other testing
CCHD screening: the evidence

Case-control study of pulse oximetry measurements

- 2,876 healthy newborns
- 32 newborns with CHD

Hoke TR et al. Pediatr Cardiol 2002; 23: 403-409
CCHD screening: the evidence

Meta-analysis of pulse oximetry screening for CCHD in asymptomatic newborns:

• 13 studies included
  (12 cohort & 1 case-control studies)
• 229,421 newborns

• Sensitivity 76.5%
• Specificity 99.9%
• False positive rate 0.14%

• The false positive rate was lower, if the screen was conducted at >24 hours of life

Pulse oximetry screening

- Easy
- Rapid
- Non-invasive
- Indirect measure of blood oxygen saturation
- Targets the primary CCHD
- May detect the secondary CCHD

Texas Pulse Oximetry Project
Primary screening targets

**Hypoplasia:** Hypoplastic left ventricle

**Obstruction:** Pulmonary atresia with intact septum  
Tricuspid atresia

**Complex:** Tetralogy of Fallot  
Total Anomalous Pulmonary Venous Return  
Transposition of great arteries  
Truncus arteriosus communis
Secondary screening targets

Hypoplasia: Single ventricle defect

Obstruction: Pulmonary stenosis/atresia
Aortic arch atresia/hypoplasia
Interrupted aortic arch
Coarctation of Aorta

Septal defects: Atrial septal defect
Ventricular septal defect
Atrioventricular septal defect

Complex: Double outlet right ventricle
Ebstein’s anomaly
Cost-effectiveness of CCHD screening

Texas Pulse Oximetry Project:
• The CCHD screening is cost-effective, with a cost estimated at $3-6 per asymptomatic newborn screened

Peterson 2014:
• The average cost of screening per newborn was $13.50 in the US [$6.68 cost of labor + $6.83 in equipment]
• The incremental cost for detecting one of 1,189 estimated newly diagnosed newborns with CCHD per year was $20,862
• The favorable cost-effectiveness estimate of averting up to 20 infant deaths per year was $42,385 per life-year gained

❖ Texas Pulse Oximetry Project
Pulse oximetry screening

Oakley 2015:
• 6329 babies had post-ductal pulse-oximetry
• 14 had abnormal screen
  ➢ 7/14 had CCHD
  ➢ 3/14 had non-critical CHD
  ➢ 4 had undiagnosed respiratory illness or sepsis

Jawin 2015:
• 5247 babies had post-ductal pulse-oximetry
• 15 had abnormal screen
  ➢ 2/15 had CCHD
  ➢ 2/15 had sepsis
  ➢ 11/15 had undiagnosed respiratory illness

All babies with low saturations had identifiable pathology

❖ Jawin V et al. PLoS One 2015; 10(9); e0137580
Screening recommendations

- US Health and Human Services Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children recommended in 2010 that CCHD screening be added to newborn screening panel

- The recommendation was endorsed in 2011 by the Secretary of Health Kathleen Sibelius
ALL STATES SHOULD SCREEN NEWBORNS FOR CRITICAL CONGENITAL HEART DISEASE (CCHD)

18/10,000 babies are born with CCHD

Delayed diagnosis of CCHD can lead to infant death

CCHD can cause impaired speech and motor function

CCHD is a group of 7 abnormalities.

Babies should be screened 24 hours after birth but before they leave the hospital.

$6.00

AVERAGE COST PER SCREEN

31 STATES

REQUIRE NEWBORN SCREENING FOR CCHD

5 MINUTES

SCREENING IS QUICK AND PAINLESS

CCHD can be added to state newborn screening requirements by legislation, regulation, or adoption as a standard of practice.

American Academy of Pediatrics

Dedicated to the health of all children

1-800-433-4010, x27991

dpsedits@aap.org
Newborn CCHD Screening Progress
Click on a state for additional details.
Critical CHD screening in Texas

- House Bill 740, 2013 added CCHD to the required Texas newborn screening panel

- The Texas Department of State Health Services developed the Texas Administrative Code rules for CCHD [Title 25, Chapter 37]

- Screening for CCHD of all newborns at a birthing facility, before they become symptomatic, is mandatory in Texas since September 1st, 2014
“CCHD toolkit”

• Developed for the Texas Pulse Oximetry Project from UTHSC San Antonio, Baylor College of Medicine and the Texas DSHS

• Educational effort with a goal to facilitate the implementation of the rules for CCHD screening and of the reporting of documented cases of CCHD

  ➢ https://www.dshs.state.tx.us/newborn/cchdtoolkit/
  ➢ Algorithm for screening
  ➢ Documentation
  ➢ Sample policy
  ➢ CCHD reporting form

Texas Pulse Oximetry Project
Critical CHD screening in Texas

• Screening for CCHD with pre- and post-ductal pulse oximetry measurements to detect mild hypoxemia

• Interpretation of results, according to the most current published AAP screening algorithm

• The pulse oximeter used for the screening should meet the FDA standards

Texas DSHS, Texas administrative code, Title 25, Chapter 37
Critical CHD screening in Texas

• Screening for CCHD with pulse oximetry measurements of the right hand and one foot in parallel or one after the other

• Infant should be calm and awake

• Perform before the discharge from the nursery and after 24 hours of age

• If an early discharge is planned, CCHD screening should be done as close to discharge as possible
Pulse oximetry screening for CCHD

Pre-ductal measurement: right hand
Post-ductal measurement: one of the feet
Critical Congenital Heart Disease
Newborn Screening Algorithm

Pulse ox on right hand and foot after 24 hours

- ≥95% in right hand or foot and ≤3% difference between right hand and foot → PASS
- 90% - 94% in right hand and foot → Indeterminate
  - Repeat screen in 1 hour
- < 90% in right hand or foot → POSITIVE (FAIL)
  - Notify MD/NNP

Remind parents that CCHD newborn screening may not find all types of problems in a baby’s heart.
Passing scores

- 100% and 100%
- 100% and 97%
- 99% and 96%
- 98% and 95%
- 97% and 94%
- 96% and 93%
- 95% and 92%

Critical Congenital Heart Disease
Newborn Screening Algorithm

Pulse ox on right hand and foot after 24 hours

- ≥95% in right hand or foot and ≤3% difference between right hand and foot
- 90% - 94% in right hand and foot
- < 90% in right hand or foot

PASS

Repeat screen in 1 hour

Indeterminate

Notify MD/NNP

POSITIVE (FAIL)

Repeat screen in 1 hour

Indeterminate

POSITIVE (FAIL)

Remind parents that CCHD newborn screening may not find all types of problems in a baby's heart.
Virginia Department of Health

**Mueller CCHD Screening Table**

Green = Negative Screen (PASS)
Yellow = Rescreen in 1 hour
Yellow for 3 consecutive screens = Positive Screen (FAIL)
* Red = Automatic Positive Screen (FAIL)

<table>
<thead>
<tr>
<th>Right Hand</th>
<th>Foot</th>
<th>&lt;90</th>
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<tbody>
<tr>
<td>100</td>
<td>96</td>
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<td>&lt;90</td>
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Created by Cynthia Mueller BSN, RN - Anne Arundel Medical Center

**Screen all babies after 24 hours, before discharge.**
The next steps for a failed screen

- Pulmonary evaluation
- Infectious etiology evaluation
- ECHO
- Referral to a Pediatric Cardiologist
Reporting of confirmed CCHD cases

All confirmed cases of CCHD need to be reported to the DSHS via the CCHD Reporting Form

CCHD Program
Mail: DSHS Newborn Screening Genetics Branch
PO Box 149347, MC 1918
Austin, Texas 78714-9347
Fax: CCHD Program
(512) 776-7593
Exemption from CCHD screen

- Parent declines screening
- Previously diagnosed newborn with CCHD
- Newborn has had a post-natal ECHO
- Newborn was discharged from birthing facility by 10 hours of life with referral to another birthing center, physician or healthcare provider
- Newborn was transferred to another facility before the screening

Texas DSHS, Texas administrative code, Title 25, Chapter 37
Medical, Social & Financial impact of CHD

• CHD is a “lifelong” condition: even patients with “repaired” CHD, will need lifelong highly specialized care

• Associated conditions:
  • Congestive heart failure
  • Pulmonary hypertension
  • Arrhythmias
  • Endocarditis
  • Developmental delay

• Prolonged & repeated hospitalizations
• Long follow up and treatment

• Extensive financial resources
• Emotional and financial strain for the family
Screening and timely diagnosis of CCHD means decreased morbidity and mortality