The CDH Registry and Study Group
Past, Present and Future
At my age
I need glasses.
CDH Registry

- Background of the Registry
- Current Status
- Major Publications
- Future Plans
EXTRACORPOREAL LIFE SUPPORT ORGANIZATION
Charter Meeting
October 1-3, 1989 Ann Arbor, Michigan
EXTRACORPOREAL LIFE SUPPORT ORGANIZATION
Charter Meeting
October 1-3, 1989 Ann Arbor, Michigan
Members in attendance:

NAME

- Lucienne Sanchez
- Kevin Lally
- Jim Atkinson
- Charles Breaux, Jr.
- Karen West
- Billie Lou Short
- William Engle
- Jill Kernaghan for W.P. Kanto
- Michele Walsh-Sukys
- David P. Meagher, Jr.
- Gerald M. Haase
- Jay Wilson
- Desmond Bohn
- Kyle Walker
- P. Pearl O’Rourke

CENTER

- CNMC, Washington, D.C.
- Hermann Children’s/Houston
- CHLA/Los Angeles
- Children’s of Alabama
- Riley Hospital/Indpls IN
- CNMC, Washington, D.C.
- Riley Hospital/Indpls IN
- Med College of Georgia
- Rainbow Babies, Cleveland
- Children’s Hospital, Denver
- Children’s Hospital, Denver
- Boston Children’s
- Hospital For Sick Children
- Johns Hopkins Hospital
- Children’s Hospital/Seattle

• 5 Neonatologists
• 7 Pediatric Surgeons
• 3 Intensivists
CDH STUDY GROUP

MINUTES OF CHARTER MEETING 9/12/91

The meeting was scheduled to begin at 15:30, and began shortly thereafter. It lasted for approximately one hour. Items of import discussed were as follows:

* There was universal agreement of a need for such a study group. The goals of the group were not completely defined, however 2 main goals were cited:

1) **Universal data collection of CDH patients.**

2) **Collective attempt to answer questions regarding CDH patients.** There was universal agreement that no single individual or institution had found "the answer" to the ubiquitous problem of CDH infants. There were numerous expressions of willingness to work together and attempt to put aside previous biases and large egos to collectively address CDH patient management and outcome.
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CDH Registry

- Existing data forms collated and modified
- Voluntary collection
- A priori plan to limit total amount of data
- Data collection begun 1995
- Data in secure, anonymized database
- Some PHI – DOB, DOS
The Congenital Diaphragmatic Study Group
Versions of the CDH Registry

• Version 1 1995-2000
  - Defining the problem - medications, ventilator strategies, ECLS use
CONGENITAL DIAPHRAGMATIC HERNIA DATA FORM

Hospital:___________________ DOB:____/____/____ Time of Birth:____
Initials:_________________ Hosp. #:______ Admission Date:____/____/____ Time:____
Inborn Outborn Group (Circle one):  No ECMO ECMO Pre-Repair ECMO Post-Repair
Sex: M F Race: Black White Hispanic Asian Other __________
Birthweight____Kgs EGA(Exams)____weeks
Prenatal Diagnosis: Yes No If Yes EGA@Dx(wks):____ Polyhydramnics Yes No
Stomach in Chest: Yes No Left Ventricular mass index (if known) ______
Liver in Chest Yes No Prenatal Repair Yes No Pregnancy terminated: Yes No
Delivery Data: Apgar(1/5/10) _____/____/____ Early death (<24 hrs) Yes No
Immediate Distress: Yes No CPR: Yes No Age at Dx: Date:____/____/____ Time:____
Age at Intubation: Date:____/____/____ Time:____

Associated Anomalies
Cardiac: Yes No If Yes: Hypoplastic Heart/TOF/TAPVR/VSD/ASD/Other:________________________
Chromosomal: Yes No If Yes:___________ Neural tube Anomaly: Yes No
Omphalocele: Yes No Other:________________________

PHARMAOCOLOGIC DATA
Surfactant given: Yes No If Yes: Hours of Life:____/____/____
If Yes: Survanta Exosurf Infasurf Other
Drug Strategy (Circle)
Vasopressors Yes No Complications
Intravenous Vasodilators Yes No
Inhaled Vasodilators Yes No Don't Know
Hydroxyd Yes No
Sedation Yes No
Alkalization Yes No
Neuromuscular Blockade Yes No
Version 1
Versions of the CDH Registry

• Version 1 1995-2000
  o Defining the problem - medications, ventilator strategies, ECLS use

• Version 2 2001-2006
  o Understanding the details - delivery, oxygen/carbon dioxide, discharge status, cardiac anomalies
CDH Registry – Why it has worked
Management (2000 – 2019)
CONGENITAL DIAPHRAGMATIC HERNIA FORM
(To be used for patients born 10/1/2000 – 12/31/2006)

Year of Birth: ________ Center: ________ Patient: ________

Patient Date of Birth: ____/____/____ Time of Birth: __________
- Indom
- Outborn: Admission Date: ____/____/____ Time: __________

Sex: M/F
Race: Black / White / Hispanic / Asian / Native American / Other: ________
Birthweight: ________ kg Head Circ: ________ cm Length: ________ cm

EGA (at birth): ________ wks APGAR (1/5/10): ________ ________ ________

Method of delivery: Vaginal (Spontaneous) Vaginal (Induced)
- C-Section (Elective) C-Section (Urgent or Non-Elective)

Immediate Distress: Yes / No CPR Given: Yes / No
Prenatal diagnosis of CDH: Yes / No If Yes, diagnosis made at ________ weeks gestation
Prenatal steroids given: Yes / No / Unknown
If Yes, steroids given at gestational ages (in wks): ________ ________ ________

Associated Non-Cardiac Anomalies (Check all that apply and please provide DX if known):
- Chromosomal – If Yes, please describe: __________________________
- Neural Tube Defect – If Yes, please describe: ______________________
- Omphalocele
- Other Anomalies – If Yes, please describe: _________________________

Associated Structural Cardiac Anomalies (Check all that apply):
- ASD
- VSD
- AVSD (AV Canal)
- Pulmonic Stenosis
- Pulmonary Ateriesia
- TOF (Truncus Arteriosus)
- Coarctation of Aorta
- TGV (Transposition of Great Vessels or Transposition of Great Arteries)
- Truncus Arteriosus
- Complex Biventricular anatomy (i.e. heterotaxy syndrome)
- Anomalous Pulmonary Venous Return: please describe: __________
- Single Ventricle Variant (hypoplastic left heart syndrome): please describe: __________
- Other: please describe: __________

Treatment of Cardiac Anomaly (Check all that apply):
- Prostaglandins required
- Cardiac Surgery performed
  - If Yes, type of procedure(s) and date(s) performed: __________________________
  - ECMO needed post Cardiac Surgery
Versions of the CDH Registry

• Version 1 1995-2000
  o Defining the problem - medications, ventilator strategies, ECLS use

• Version 2 2001-2006
  o Understanding the details - delivery, oxygen/carbon dioxide, discharge status, cardiac anomalies

• Version 3 2007-2014
  o Staging - classifying defect size, pulmonary hypertension
Pulmonary Hypertension (PHTN):

First Echo on date: __/__/____

PHTN: ○ None ○ < 2/3 systemic ○ between 2/3 and systemic ○ > systemic

Ductus: ○ Open ○ Closed
Ductal Shunt: ○ L to R ○ Bidirectional ○ R to L
Atrial Shunt: ○ Yes ○ No
Tricuspid regurgitation: ○ Yes ○ No

Last Echo on date: __/__/____

PHTN: ○ None ○ < 2/3 systemic ○ between 2/3 and systemic ○ > systemic

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Tricuspid regurgitation: ○ Yes ○ No

Treatment of Pulmonary Hypertension:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Date Started</th>
<th>Date Ended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled Nitric Oxide</td>
<td><strong>/</strong>/____</td>
<td><strong>/</strong>/____</td>
</tr>
<tr>
<td>Maximum dose: ppm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silodosin</td>
<td>Oral</td>
<td>iv</td>
</tr>
<tr>
<td>Endothelial Receptor Blockade</td>
<td>/ / /</td>
<td>/ / /</td>
</tr>
<tr>
<td>Prostaglandin</td>
<td>/ / /</td>
<td>/ / /</td>
</tr>
<tr>
<td>Alprostadil (PGE1)</td>
<td><strong>/</strong>/____</td>
<td><strong>/</strong>/____</td>
</tr>
<tr>
<td>Milrinone</td>
<td>/ / /</td>
<td>/ / /</td>
</tr>
<tr>
<td>Other (specify)</td>
<td>/ / /</td>
<td>/ / /</td>
</tr>
</tbody>
</table>

Ventilation:

Intubated at: __/__/____, time: __:__
Extubated at: __/__/____ (Never extubated)

Actual Values in the first 24 hours of life (pre-ECMO):

<table>
<thead>
<tr>
<th>Highest pre-ductal PaO2</th>
<th>mm Hg</th>
<th>O2 sat %</th>
<th>Not available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest post-ductal PaO2</td>
<td>mm Hg</td>
<td>O2 sat %</td>
<td>Not available</td>
</tr>
</tbody>
</table>

Highest PaCO2 | mm Hg | Not available

Lowest PaCO2 | mm Hg | Not available

Highest Lactate in first 24 hours: _____ mmol/L
Highest Lactate in first 72 hours: _____ mmol/L

Version 3
Side of Diaphragmatic Hernia: [ ] Left [ ] Right [ ] Bilateral/Central

[ ] No Repair

Reasons repair not done (select best):

[ ] Patient fell to be non-survivable / not candidate for ECMO:
  [ ] PaO₂ never greater than _____
  [ ] PaCO₂ never lower than _____
  [ ] Anomaly: Cardiac / Chromosomal / Other
  [ ] Parents requested no further therapy
  [ ] Other: _______________

[ ] Patient fell to be survivable / not candidate for ECMO:
  [ ] Prematurity / low birth weight
  [ ] IVH or cerebral hemorrhage pre-ECMO
  [ ] Parents requested no further therapy
  [ ] Other: _______________

[ ] Patient fell to be survivable / placed on ECMO but no repair done:
  [ ] IVH or cerebral hemorrhage on ECMO
  [ ] Other ECMO complication:
  [ ] Parents requested no further therapy
  [ ] Unable to wean off ECMO
  [ ] Late diagnosis of anomaly: Cardiac / Chromosomal / Other
  [ ] Other: _______________

[ ] Patient came off ECMO but was not repaired:
  [ ] Refractory hypoxia
  [ ] Refractory hypercarbia
  [ ] Anomaly: Cardiac / Chromosomal / Other
  [ ] Parents requested no further therapy
  [ ] Multi-system organ failure
  [ ] Sepsis
  [ ] Other: _______________

[ ] Repair Done

Diaphragm Defect: [ ] A [ ] B [ ] C [ ] D

Type Repair: [ ] Primary [ ] Patch

If Patch, type patch: [ ] PTFE [ ] Surgisis [ ] Mesh plug [ ] Alloderm [ ] Other

Hernia Size: [ ] Yes [ ] No

Liver: [ ] Yes [ ] No

Approach: [ ] Subcostal [ ] Thoracic [ ] Both [ ] Thoracoscopic [ ] Laparoscopic [ ] Other: _______________

Abdominal Closure: [ ] Primary [ ] Ventral hernia [ ] Silo [ ] Patch [ ] Other: _______________

Chest Tube: [ ] Yes [ ] No
Versions of the CDH Registry

• Version 1 1995-2000
  o Defining the problem - medications, ventilator strategies, ECLS use

• Version 2 2001-2006
  o Understanding the details - delivery, oxygen/carbon dioxide, discharge status, cardiac anomalies

• Version 3 2007-2014
  o Staging - classifying defect size

• Version 4 2015-present
  o The role of the heart and PH, prenatal dx
Issues addressed by version 4

• Timing of surgical repair when receiving ECLS
• Cardiac dysfunction in CDH
• CDH-associated pulmonary hypertension
• Prenatal diagnosis / prediction in CDH
85 Centers/17 countries/12,000 Patients
Hernia Side

79% Left
20% Right
1% Bilateral
Operative Approach

1995-1996
- Subcostal: 90%
- Thoracic: 6%
- Other: 4%

2017-2018
- Thoracoscopic: 82%
- Laparoscopic: 14%
- Thoracoscopic: 2%
- Other: 1%
Patch Used In Repair

1995-1996:
- Yes: 51%
- No: 49%

2017-2018:
- Yes: 58%
- No: 42%
Repair On ECMO (Of all ECMO)

1995-1996
- Yes: 23%
- No: 77%

2017-2018
- Yes: 52%
- No: 48%
Time of Day For Repair

1995-1996
- 0600-1200: 2%
- 1200-1800: 40%
- 1800-2400: 10%
- 2400-0600: 48%

2017-2018
- 0600-1200: 4%
- 1200-1800: 45%
- 1800-2400: 51%
- 2400-0600: 4%
Timing of Operation (No ECMO)

- 0-24: 38 cases
- 24-48: 14 cases
- 48-72: 10 cases
- 72-96: 11 cases
- 96-120: 8 cases
- >120: 19 cases

Hours of Age

1995-1996
Timing of Operation (No ECMO)

Hours of Age

- 0-24: 7
- 24-48: 12
- 48-72: 18
- 72-96: 18
- 96-120: 13
- >120: 32

2017-2018
Publications

- Data available only to CDHSG members
- Authored by writing committee on behalf of CDHSG
- 55 publications
- Multiple studies in progress
Defect Size Determines Survival in Infants With Congenital Diaphragmatic Hernia
The Congenital Diaphragmatic Hernia Study Group
Pediatrics 2007;120;e651-e657
DOI: 10.1542/peds.2006-3040
Defect Size

Primary repair

Patch - no agenesis

Patch - Agenesis
Size Does Matter!
Defect Size

It became apparent that not all CDH were created equal and that size of defect was important

Version III designed to quantitate size of defect
Standardized Reporting for Congenital Diaphragmatic Hernia
An International Consensus
Methods
Factors Evaluated

- Defect class
- Cardiac anomalies
- Chromosomal anomalies
- Birthweight / Gestational age
- Apgar Scores
**CDHSG Staging**

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
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<tbody>
<tr>
<td>Frequency</td>
<td>13%</td>
<td>44%</td>
<td>30%</td>
<td>13%</td>
</tr>
<tr>
<td>Survival</td>
<td>99%</td>
<td>96%</td>
<td>78%</td>
<td>58%</td>
</tr>
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</table>

Congenital diaphragmatic hernia: Defect size correlates with developmental defect

The Congenital Diaphragmatic Hernia Study Group

Methods

- V. 3 of Registry
- Grouped by defect size
- Compared for associated anomalies
Congenital Diaphragmatic Hernia Defect Size and Infant Morbidity at Discharge
Methods

- V. 3 of Registry
- Evaluated recorded morbidity at d/c
- Correlated degree of morbidity to defect
- Analysis between groups and time
Conclusions

- Defect correlated with morbidity as well as mortality
- Overall improving morbidity
- No major changes in large defect patients
Is aggressive surgical management worth it?
Is aggressive surgical management worth it?

Harting et al, Ann Surg, 2018
Conclusions

- Aggressive approach leads to highest survival
- It is costly
- Morbidity is high
Evaluation of Variability in Inhaled Nitric Oxide Use and Pulmonary Hypertension in Patients With Congenital Diaphragmatic Hernia
What about Nitric Oxide?

Putnam et al, *JAMA Pediatrics*, 2017
What about Nitric Oxide?

Putnam et al, *JAMA Pediatrics*, 2017
What about Nitric Oxide?

Putnam et al, *JAMA Pediatrics*, 2017
What about Nitric Oxide?

Putnam et al, *JAMA Pediatrics*, 2017
Treatment with iNO was associated with a 15% higher absolute mortality
Conclusions

- iNO use highly variable between centers
- > 1/3 patients w/o CDH-PHTN received iNO
- Little data to support iNO benefit in CDH
- iNO use is *associated* with worse outcome
- iNO use in patients with CDH needs re-evaluation
TRADITION

JUST BECAUSE YOU’VE ALWAYS DONE IT THAT WAY DOESN’T MEAN IT’S NOT INCREDIBLY STUPID.

www.despair.com
25 Years – Any Progress?

- Centers with at least 22 years of continual participation
- Grouped by 5 year intervals
- Evaluated Overall Survival
- Looked at O:E survival
25 Years – Any Progress?

- Significant increase in survival over years
- Current overall survival is 73% for all comers
- Surgical survival is 85%
- Remains a large variation amongst centers
The CDH Study Registry

PROs

• Ability to study infrequent problems
• Data on very large number of patients
• Individual centers can compare themselves with others
• Demonstrate changes over time of management and outcome
The CDH Study Registry

CONs

- Observational data
- Inability to evaluate long-term sequelae
- Difficult to collect complicated information
- Wide spectrum of patients and treatment philosophies
The “Gold Standard”

Randomized Clinical Trial

• Expensive ($500k-$3 million+)
• Labor intensive
• Takes a long time (5-10 years)
• Requires consent / challenges of recruitment
• Requires multi-institutional cooperation
• Answers a single question
• Nearly impossible to achieve appropriate sample size in CDH
The future of the CDHSG

- Ongoing evolution of versions to address current questions
  - Version 5 – Breakout session this meeting
- Management standardization
- Long term data collection
- Novel statistical analysis
John Roesler – DOB 11/26/2019
The secret of enjoying a good wine:

1. Open the bottle to allow it to breathe.

2. If it does not look like it's breathing, give it mouth-to-mouth.