LIVE HYBRID ACTIVITY

15th Annual Neonatal Advanced Practice Conference

Thursday, June 19, 2025

8:00 a.m. – 5:00 p.m.

Children's Hospital Colorado | Anschutz Medical Campus – Mts. Yale/Princeton Conference Room

Jointly Provided by

Children's Hospital Colorado, Neonatal Nurse Practitioner Department
Front Range Association of Neonatal Nurses

National Association of Neonatal Nurses
Front Range Chapter

Children's Hospital Colorado

Affiliated with
University of Colorado
Anschutz Medical Campus

15th Annual Neonatal Advanced Practice Conference

Overview, Target Audience and Learner Outcome

This conference presents topics of interest to neonatal care providers, including NNPs, nurses, physicians, as well as other health care professionals working in the neonatal ICU. Speakers cover new and emerging neonatal topics, clinical presentations, as well as reviews of available evidence for current practice strategies related to the anticipation, recognition, assessment, and stabilization of acute and long- term neonates. Discussion and question sessions will follow each presentation. At the conclusion of this event, the participant will report increased knowledge and intent to change practice related to current best-practice and innovative solutions for patient care in the NICU.

Agenda

Thursday, June 19, 2025

7:30 a.m.	Breakfast and Check-in
7:50	Welcome
8:00	**Golden Hour: Where are we now. *A Comparative Look at Two Local Centers*** *Emily Grabau, NNP-BC* *Grace Krupa, BSN, RN, RNC-NIC, C-ELBW, C-NNIC*
9:00	**Fetal Fentanyl Syndrome: A Novel Embryopathy Associated with Prenatal Fentanyl Exposure** *Erica Fernandes, DO, FAAP, FACMG*
10:00	Break
10:30	**Patent Ductus Arteriosus: Current Trends in Management** *Michael W. Cookson, MD*
11:30	**Ventilation for Evolving Lung Disease of Prematurity** *Satya "Sadie" Houin, MD* *Jennifer Miller, NNP*
12:30 p.m.	Lunch (provided for in-person attendees)
1:30	**The APP Role in Telemedicine** *Valerie Beascochea, APRN, NNP-BC*
2:30	**Neonatal Surgical Emergencies** *Caroline Credille, MSN, PNP-AC*
3:30	Break
3:45	**Neonatal Seizures – Conventions and Controversies** *Andra Dingman, MD*
4:45	Wrap-up and Evaluation
5:00	Adjourn

**Children's Hospital Colorado reserves the right to modify the agenda or cancel this conference in the event of an unforeseen circumstances.*

Locations

In-person Learners

Children's Hospital Colorado
Anschutz Medical Campus
Medical Conference and Education Center – 2nd Floor
Mts. Yale and Princeton Conference Rooms
13123 East 16th Avenue, Aurora, Colorado 80045

Virtual Learners

Zoom link: https://us06web.zoom.us/j/82927656443

Continuing Education Credit

Registration, attendance, sign-in and submission of the online evaluation, including a written response to questions related to any changes in practice that you may make as a result of learning that took place at this activity, are required for successful completion and receipt of the certificate of attendance. Claim only those hours you attend.

Attendance

Learners are required to sign-in for this NCPD activity to verify participation in the program.

Signing-in: Sign-in opens 30-minutes prior to the event. There are two sign-in options:

1. Text the attendance code below to 720-790-4423 or
2. Enter the attendance code below at ce.childrenscolorado.org/code

Attendance Code: **15NAP**

Evaluation

To obtain your NCPD certificate, the on-line **evaluation must be completed by midnight, Thursday, July 3, 2025**. After completing the evaluation, you will be prompted to claim your NCPD credits. Any questions or concerns with access should be directed to ce@childrenscolorado.org.

Credit

Nursing: Children's Hospital Colorado is approved with distinction as a provider of nursing continuing professional development by Colorado Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation. This program for 7.25 contact hours is provided by Children's Hospital Colorado.

Other Care Providers: A general certificate of attendance will be available.

Financial Disclosure

Planners, faculty, and others in control of content (either individually or as a group) have no relevant financial relationships with ineligible companies.

Faculty

Valerie Beascochea, APRN, NNP-BC
Mercy Hospital and St. Catherine Hospital Neonatal APP Lead
Envision Healthcare

Caroline Credille, MSN, PNP-AC
Pediatric Nurse Practitioner
University of Colorado School of Medicine
Department of Surgery
Division of Pediatric and Fetal Surgery
Children’s Hospital Colorado

Michael W. Cookson, MD
Assistant Professor of Pediatrics
University of Colorado School of Medicine
Attending Neonatologist
Neonatal ICU
Children’s Hospital Colorado

Andra Dingman, MD
Associate Professor of Pediatrics (Child Neurology)
University of Colorado School of Medicine
Children's Hospital Colorado

Erica Fernandes, DO, FAAP, FACMG
Assistant Professor of Pediatrics
Thomas Jefferson University's Sidney Kimmel Medical College
Clinical Geneticist
Nemours Children's Hospital
Wilmington, Delaware

Emily Grabau, MSN, RN, NNP-BC
Clinical NNP
Children's Hospital Colorado

Satya "Sadie" Houin, MD
Assistant Professor of Pediatrics
University of Colorado School of Medicine
Attending Neonatologist
Medical Director of SPROUT team for severe BPD
Children’s Hospital Colorado

Grace Krupa, BSN, RN, RNC-NIC, C-ELBW, C-NNIC
Neonatal ICU Nurse
Intermountain Healthcare
St. Jospeh Hospital, Denver, CO

Jen Miller, NNP
APP SPROUT's Subject Matter Expert
Children's Hospital Colorado

Golden Hour: Where Are We Now?

A Comparative Look at Two Local Level 3 Centers

Emily Grabau, MSN, NNP-BC, Grace Krupa, DNP

What is Golden Hour?

The hour following birth, referred to as the ‘Golden Hour’ is the period of time in which medical care to prevent irreversible damage is most effective and represents the inverse relationship between elapsing minutes and likelihood of survival.

https://laerdal.com/us/products/simulation-training/obstetrics-pediatrics/premature-anne/

Golden Hour: Key Components

“The first 60 minutes of an extremely premature neonate's life consist of many competing priorities that all impact both short and long term outcomes.” (Doak & Waskosky, 2022)

- A systematic and timely approach by the NICU medical team to support fetal to neonatal transition
- Initiation of many important tasks with close attention to detail

How do we monitor our progress and timeliness?

Golden Hour: Key Components

- Short term outcomes
  - Reduced rates of hypoglycemia, hypothermia, improved efficiency with initiating IV fluids and medications
- Long term outcomes
  - Decreased risk for BPD, IVH, ROP
- Importance of standardization of practices for improved outcomes

UCH Anschutz NICU

Background:

In 2023, University of Colorado Hospital (UCH) NICU had 836 admissions

- 342 < 30 weeks gestation
- 70 < 1 kg at birth
- 41% population extremely premature and/or ELBW

https://www.cuanschutz.edu/images/librariesprovider109/social/uc-health.jpg?sfvrsn=b4da40b9_0

UCH Anschutz NICU

2024:

- 957 admissions into the UCH NICU
- 83 neonates < 1 kg birth weight

- ❖ 121 more admissions, 13% growth
- ❖ 13 more neonates < 1 kg BW, 16% increase

UCH Anschutz NICU

- Level 3b
- Average daily census 43 in 2024
- Offer resuscitation from 22 weeks and above

Daily staffing:

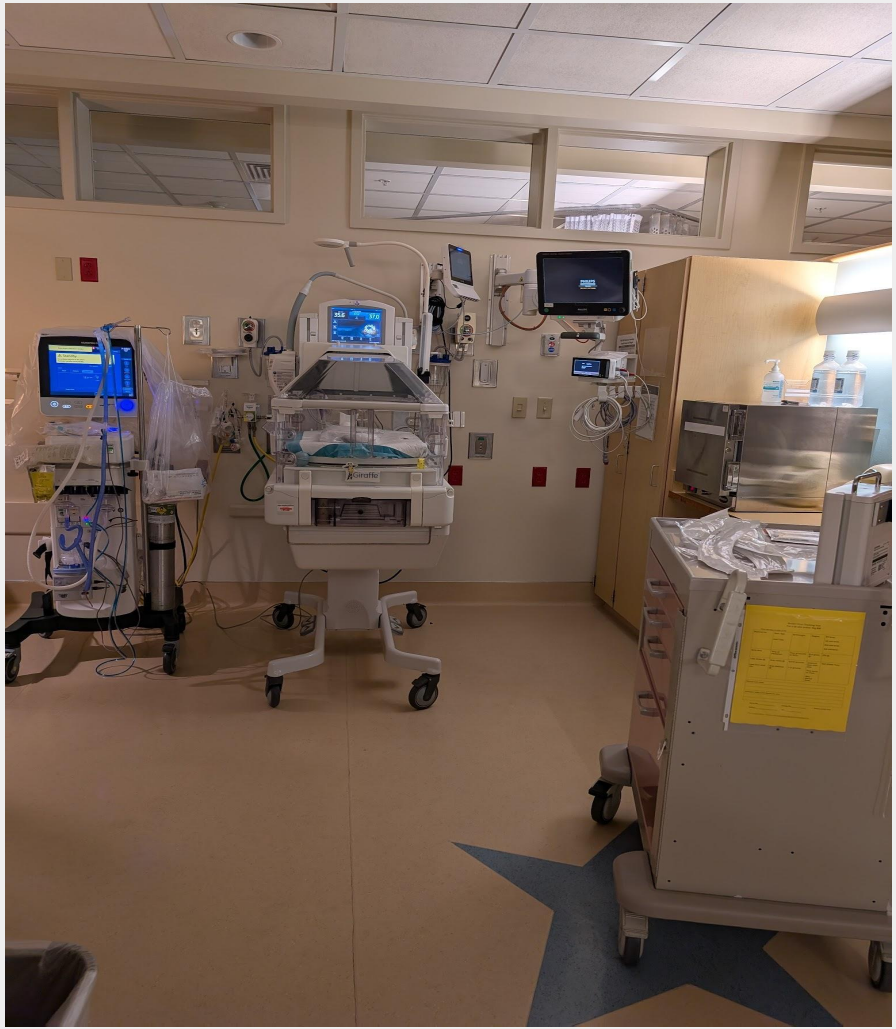
- 2 Charge RN’s day and night
- 4 NNPs during the day, 3 overnight
- Typical staffing with ~21 RNs per shift
- NICU Fellow coverage day and night plus residents
- 2 Attending MD’s Daily, 1 overnight
- 2 dedicated RTs day and night

Interdisciplinary team:

- OT/PT/SLP
- CNAs/ACPs
- PharmD
- Dietician
- Psychologist

Preparation & Training

- Readily available bed setups & planning for imminent as well as unexpected admissions
- Charge RN conducted training specific to skills & admissions
- Level 4 orientation after 1 year minimum of NICU experience
    - EPT neonates- RNs must have completed lv 4 orientation



Gathering the Data

- Fall 2023 began brainstorming methods to gather data surrounding admission tracking
- December 2023 met with charge RN group
  - Staff update on upcoming golden hour tracking
- January 2024 rolled out the golden hour tracking form
  - Tracking forms placed on each procedure cart
  - Completed forms placed in designated location in provider workroom

Golden Hour Tracking Tool
For ≤ 30 wks and/or 1kg BW

Time indicates minutes of life:

Maternal Hx:	**Gest. Age:** **Add'l Info:**	**Birthweight:**	**Apgars:**	**DR temp:** **1st unit temp:** **2nd unit temp:** **3rd unit temp:**
Birth time:	**Time of intubation:**	**Time of transfer to NICU:**	**Surf given @:**	**PIV @:**
Labs drawn @: **Labs from what site:**	**Xray called @:** **Xray obtained @:**	**Admit glucose:** **1 hr glucose:**	**Umbilical lines start time:** **Time spent on lines:** **Who placed lines:**	**TOP DOWN Time:** _____ **Were orders pended prior to delivery?** **YES or NO**

Delivery room notes:
Admission notes and/or barriers for care:

Admit RN:_____ **Charge RN:**_____ **Patient sticker here**

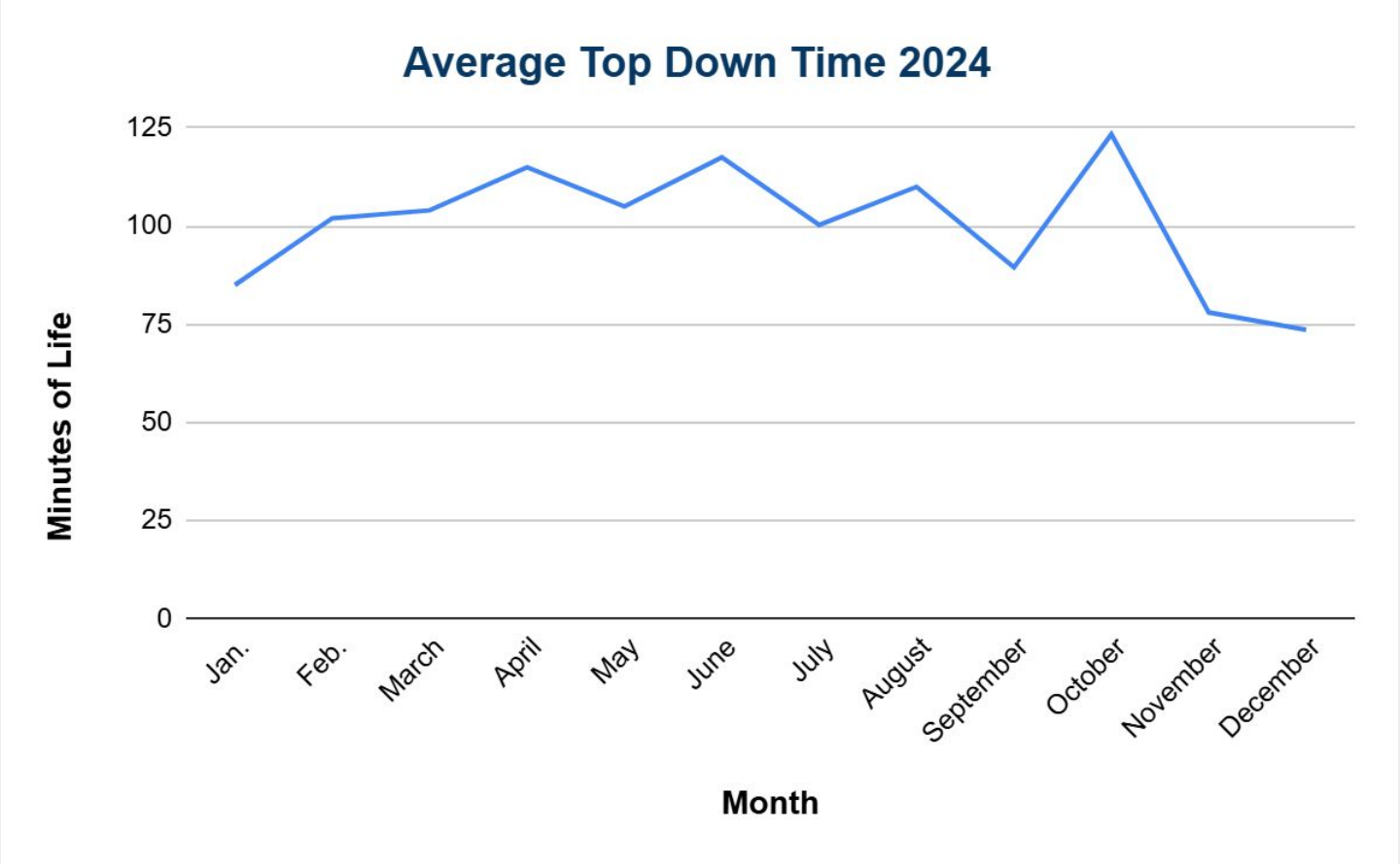
NNP(s):_____ **RT:**_____

For input/feedback, please email emily.grabau@childrenscolorado.org

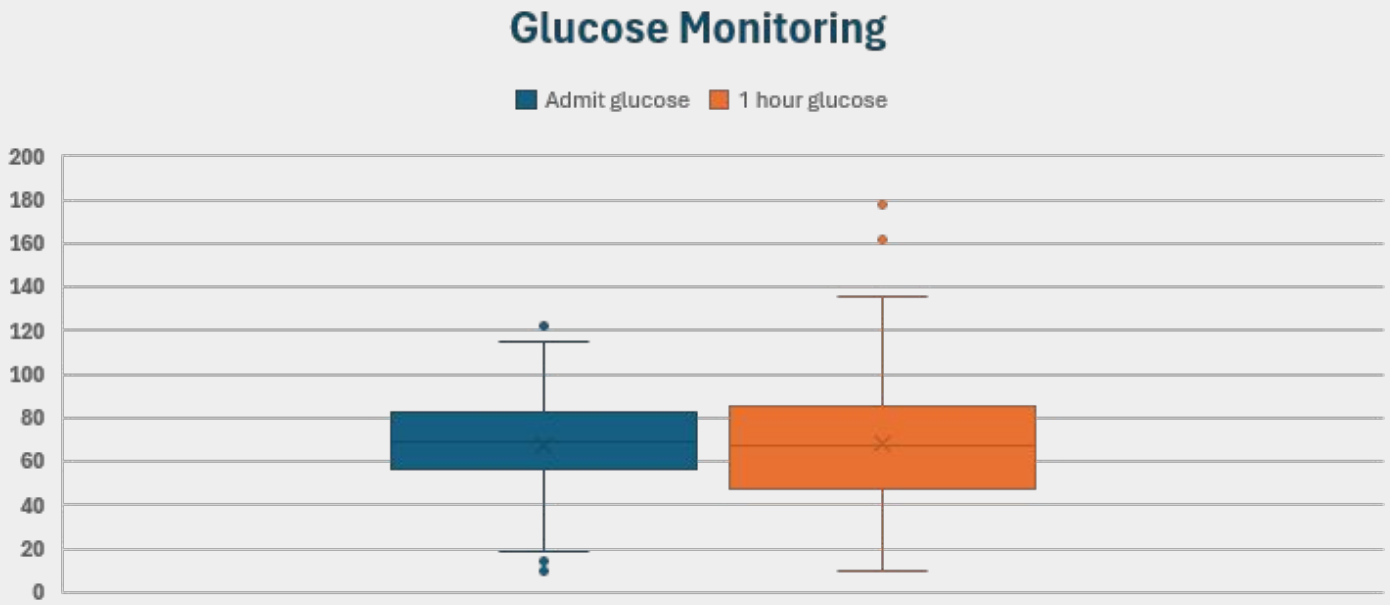
Keeping Momentum Going!

- Monthly charge group check-ins for first 6 months
  - Moved to quarterly
- Staff updates
  - Keeping the awareness & reminders

1 year of data

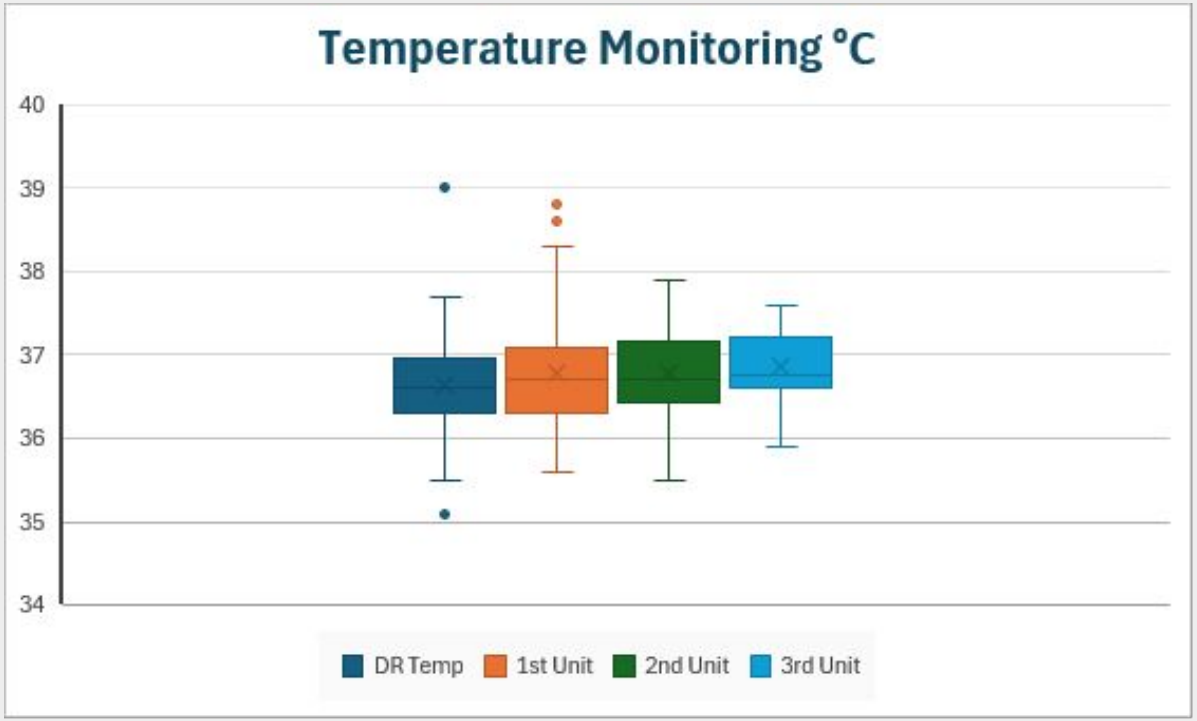


Glucose Monitoring



Average	Max	Min
67.12	122	10
68.28	178	10

Thermoregulation



Average	Max	Min
36.62319	39	35.1
36.79211	38.8	35.6
36.77679	37.9	35.5
36.85	37.6	35.9

St. Joseph Hospital NICU Statistics

- NICU Level 3b - As of August 30, we have had 420 admits with 54 of them VLBWs
- 51-bed unit
- Average census ~30
- 105 nurses
- 11 NNPs
- 10 MDs
- RTs, OTs, Speech, PharmD, Dietician
- Volunteers

Evolution of our Small Baby Team

- Started from a VON initiative in 2020/2021, then separated off into its own group
- Began educational requirement of Engage Grow Thrive program
- Created a periviability team surrounding offering of resuscitation at 22 weeks
- Provided Education to the OB team and residents
- Admission Debrief tool
- Small Baby Newsletter
- SBNQCC

Buy in from all team members

- Initially education was voluntary
- Now it is required, and 30 of the 45 credit hours, people can do at home and get reimbursement for
- We try to assign nurses to these babies based on desire of a specific stage
  - Admission
  - Min stim (first 72 hours)
  - Post min-stim until 30 weeks
  - 30 weeks and above
- We have lot of nurses on day shift who have completed EGT
- Night shift is still about 50%
- We still have about 50% of MD and NNP providers through the program
  - Their buy in is harder
- X-ray- as soon as we put in an order for a film on admission they treat it like an emergency and come up and wait for us (most of the time)

Pre-huddle paper and Role assignment

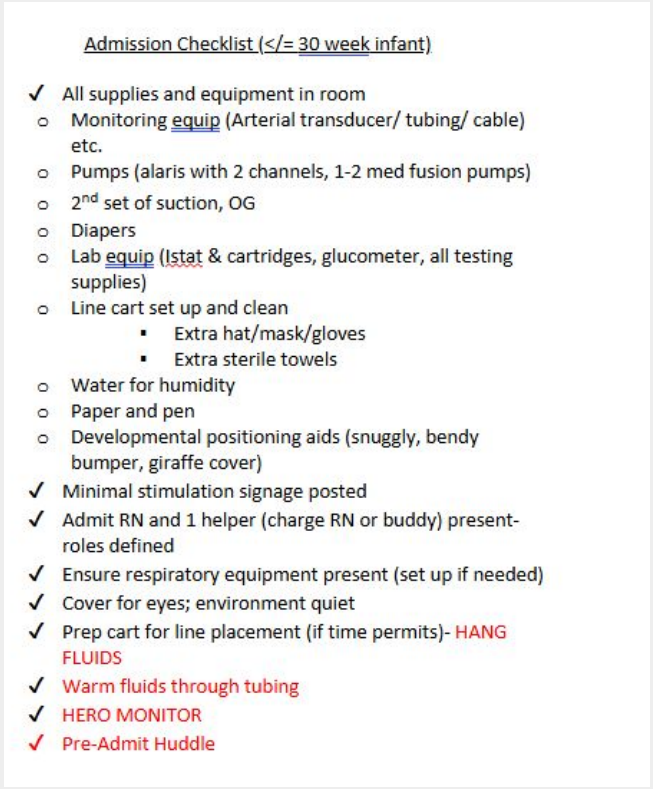
Small Baby Team Admission/ Golden Hour Roles						
Time	Provider	Charge RN	Admit RN	RT	Family Support	Runner/Buddy
Pre-Delivery	-Review maternal history for pertinent information -Consult/ Reintroduce to family/ Consent for lines -Begin admission in Neodata -Gather supplies for umbilical lines- prep if time permits PRE-HUDDLE with team	-Set up Giraffe in OR 1 -Increase OR temp -Inform admit nurse- ensure roles are covered -Plan for obtaining labs from placenta -Identify delivery room assistant (transition or admit RN?) for recording/ bands/ calling NICU PRE-HUDDLE with team	-Obtain Small Baby Admit cart -Prepare room -Run IV fluids PRE-HUDDLE with team	-Check shuttle tanks and supplies- place outside OR -Gather all intubation/ CPAP supplies -Prep CPAP securement for appropriate size -If < 28 weeks, obtain surfactant supplies -Set up Resp. equipment in room PRE-HUDDLE with team	-Identify role PRE-HUDDLE with team	-Identify role PRE-HUDDLE with team
0-10 Minutes	-Direct and oversee delivery room management -Assess respiratory status -Address respiratory needs	-If <1000 grams, place in plastic wrap and on warming mattress -Assess heart rate -Place pulse oximeter on right hand or wrist	-Assist as needed	-Manage supplies for respiratory needs/ intubation -Prepare surfactant as needed/ indicated		
10-15 Minutes	-Decide on surfactant in delivery room -Assist with measurements	-Obtain measurements (weight and OFC) and temp	-Assist as needed	-Administer surfactant as indicated -Assist with measurements		
15-20 Minutes	-Stabilize and transport to NICU with family member -Brief update to MOC and OB team	-Prepare infant and Giraffe for transport -Gather bands and recorded info -Obtain labs from umbilical cord/ placenta	-Prepare to receive infant -Ensure correct respiratory support in room (vent or CPAP)	-Gather resp. supplies -Obtain shuttle/ open tanks -Transport infant on NeoPuff with provider		
20-30 Minutes	-Prep and scrub for umbilical line placement -2nd provider places orders/ obtains line consent	-Obtain labs from umbilical cord/ placenta	-Place infant on monitor -Obtain temp/ attach skin temp control under armpit/ remove thermal mattress -Gently restrain infant for line placement	-Place on appropriate resp. support: If CPAP- may use tape on hat for temporary securement -Secure ETT and double check placement	-Introduce self to family member- provide explanations/ answer questions/ provide support	-Assist admit RN -Chart initial information -Crowd and noise control
30-45 Minutes	-Place UVC- hang pre-run fluids; Place UAC -Obtain labs/ suture lines	-Assist Admit RN and provider -Crowd and noise control	-Monitor infant vitals and skin temp -Assist provider as needed	-Monitor SpO2 and adjust FiO2 to maintain NEMO	-Continued support -Brief explanations on NICU environment	-Run labs -Call X-ray for line placement -Obtain newborn meds
45-55 Minutes	-2nd provider interprets Xray -Adjust and secure lines appropriately	-Assist Admit RN and provider -Crowd and noise control	-Prep and connect UAC fluids as indicated -Conduct brief assessment of infant	-Monitor SpO2 and adjust FiO2 to maintain NEMO	-Continued support -Brief explanations on NICU environment	-Obtain and check fluids and meds
55-60 minutes	-Update family	-Return equipment to appropriate locations	-Administer newborn meds/ other medications -Tuck infant in/ maintain midline/ top down	-Monitor SpO2 and adjust FiO2 to maintain NEMO		
Post-Admission	DEBRIEF with team	DEBRIEF with team	DEBRIEF with team	DEBRIEF with team	DEBRIEF with team	DEBRIEF with team

RN Motivation Board

- Tracks progress of people currently enrolled
- Celebrates Finishers of EGT
- Highlights new information relevant for small babies
- Encourages NCC test completion

Debrief tool

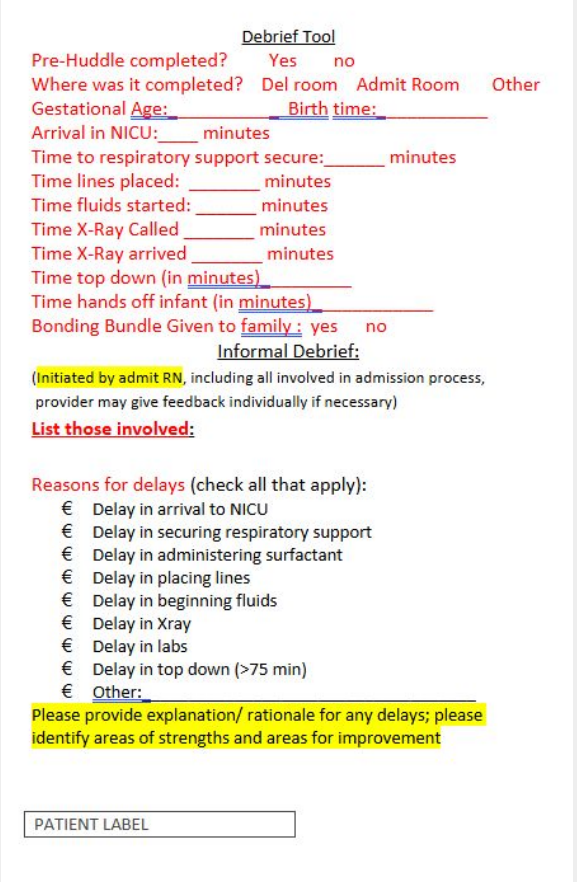
- Each member of the admission team gets together briefly after the admission to discuss what went well and what could be improved upon
- Each debrief gets discussed at the monthly Small Baby Team (SBT) meetings



Admission Checklist (</= 30 week infant)

✓ All supplies and equipment in room
- Monitoring equip (Arterial transducer/ tubing/ cable) etc.
- Pumps (alaris with 2 channels, 1-2 med fusion pumps)
- 2nd set of suction, OG
- Diapers
- Lab equip (Istat & cartridges, glucometer, all testing supplies)
- Line cart set up and clean
  - Extra hat/mask/gloves
  - Extra sterile towels
- Water for humidity
- Paper and pen
- Developmental positioning aids (snuggly, bendy bumper, giraffe cover)

✓ Minimal stimulation signage posted
✓ Admit RN and 1 helper (charge RN or buddy) present- roles defined
✓ Ensure respiratory equipment present (set up if needed)
✓ Cover for eyes; environment quiet
✓ Prep cart for line placement (if time permits)- HANG FLUIDS
✓ Warm fluids through tubing
✓ HERO MONITOR
✓ Pre-Admit Huddle



Debrief Tool

Pre-Huddle completed? Yes no
Where was it completed? Del room Admit Room Other
Gestational Age:_____ Birth time:_____
Arrival in NICU:____ minutes
Time to respiratory support secure:_____ minutes
Time lines placed: _____ minutes
Time fluids started: _____ minutes
Time X-Ray Called _____ minutes
Time X-Ray arrived _____ minutes
Time top down (in minutes)_____
Time hands off infant (in minutes)_____
Bonding Bundle Given to family : yes no

Informal Debrief:

(Initiated by admit RN, including all involved in admission process, provider may give feedback individually if necessary)

List those involved:

Reasons for delays (check all that apply):
- € Delay in arrival to NICU
- € Delay in securing respiratory support
- € Delay in administering surfactant
- € Delay in placing lines
- € Delay in beginning fluids
- € Delay in Xray
- € Delay in labs
- € Delay in top down (>75 min)
- € Other:_____

Please provide explanation/ rationale for any delays; please identify areas of strengths and areas for improvement

PATIENT LABEL

Debrief Tool Tracking-Things That we Track

- Time to Lines placed
- Time to fluids started
- How long did it take for x-ray to arrive to the bedside after they were called
- Time to top down
- Time to hands off
- Staff shout outs/Rationale for delays/Ways to improve time to top down and hands off
- Was the debrief completed?

Admission Smart note in EPIC

- Pulls in data from the charting
- Can be reviewed by a member of the SBT if the debrief form is not filled out

NICU Admission Note:

Gestational Age: 26w6d male infant arrived in NICU on [date in numbers] at [HPI MILITARY HOURS] in a/an [newborn bed type] accompanied by [NICU Staff List] on respiratory support of [NICU Admission Respiratory Support].

Lines: [NICU Admission Line] placed at [HPI MILITARY HOURS].
[NICU Admission Fluid] fluids started at [HPI MILITARY HOURS].

Surfactant [NICU Admission Surfactant Given].

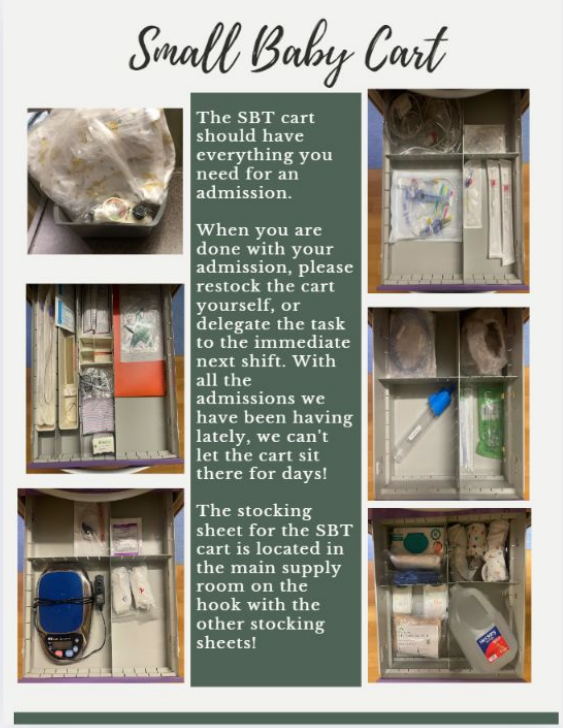
Omni bed top down at [NICU Admission Omni Bed Top Hour] hour/hours and [***] minutes after admission.

Infant bands [NICU Admission Bands Verified]. Plan of care discussed with [Guardian].

No gross abnormalities noted.

Patient Vitals for the past 24 hrs:

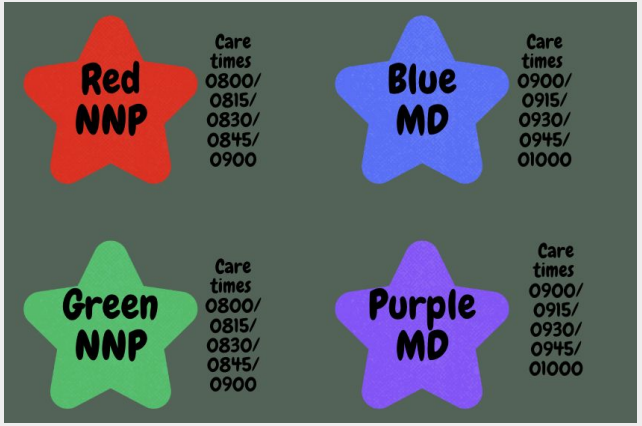
Small Baby Cart, Signage, Education, Folders

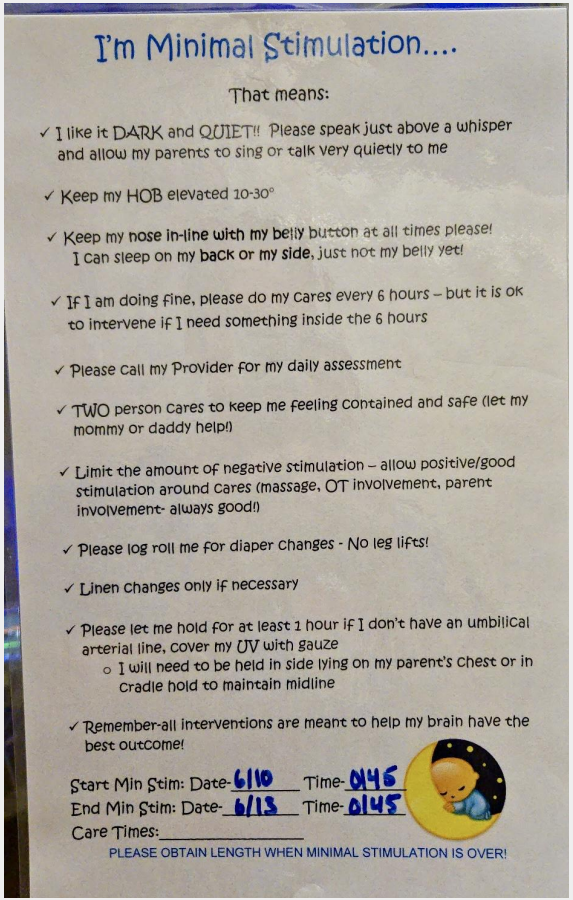


- Single baby and Twin admission
- Minimal Stimulation Signs for room
- Stars for care times
- Contains the Small Baby Orange Folder
  - Admission Debrief form
  - 2 person cares self audit tool
  - Room signage
  - Skin to skin reminders
  - FIC Modules for families
  - VON tracking sheet

Door Signage for Small Babies

- Minimal Stimulation Signage for each door for parent and staff
- Stars indicate care times, with time preferences based on MD and NNP work flow





I'm Minimal Stimulation....

That means:

- ✓ I like it DARK and QUIET!! Please speak just above a whisper and allow my parents to sing or talk very quietly to me
- ✓ Keep my HOB elevated 10-30°
- ✓ Keep my nose in-line with my belly button at all times please! I can sleep on my back or my side, just not my belly yet!
- ✓ If I am doing fine, please do my cares every 6 hours – but it is ok to intervene if I need something inside the 6 hours
- ✓ Please call my Provider for my daily assessment
- ✓ TWO person cares to keep me feeling contained and safe (let my mommy or daddy help!)
- ✓ Limit the amount of negative stimulation – allow positive/good stimulation around cares (massage, OT involvement, parent involvement- always good!)
- ✓ Please log roll me for diaper changes - No leg lifts!
- ✓ Linen changes only if necessary
- ✓ Please let me hold for at least 1 hour if I don't have an umbilical arterial line, cover my UV with gauze
  - I will need to be held in side lying on my parent's chest or in cradle hold to maintain midline
- ✓ Remember-all interventions are meant to help my brain have the best outcome!

Start Min Stim: Date- 6/10 Time- 0145
End Min Stim: Date- 6/13 Time- 0145
Care Times:_____

PLEASE OBTAIN LENGTH WHEN MINIMAL STIMULATION IS OVER!

Admission Helpers

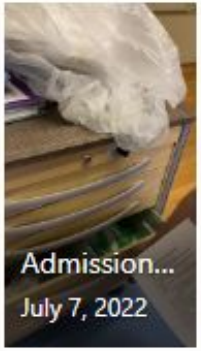
- Small baby to do list
  - In each small baby cart
- Admission playbook
- Admission Tip Sheets
- Admission Videos
  - Simulated Delivery
  - Admission for RN
  - Charge nurse duties
  - Respiratory therapy set up
  - Placing an infant on BCPAP

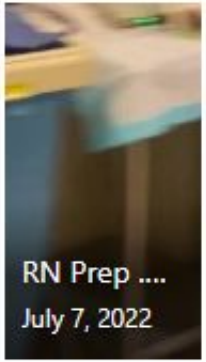
Papers that may be helpful during an admission

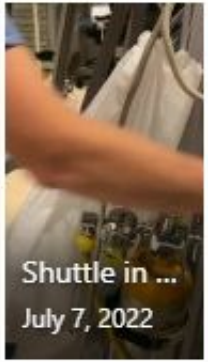
This To Do List is dry erase. After your small baby admission please wipe it down and leave it on the small baby cart for the next person!

This playbook for SBT admissions is laminated and located on all SBT admission carts. If you use it please wipe it down and leave it on the SBT Cart when you are done!

Admission Videos

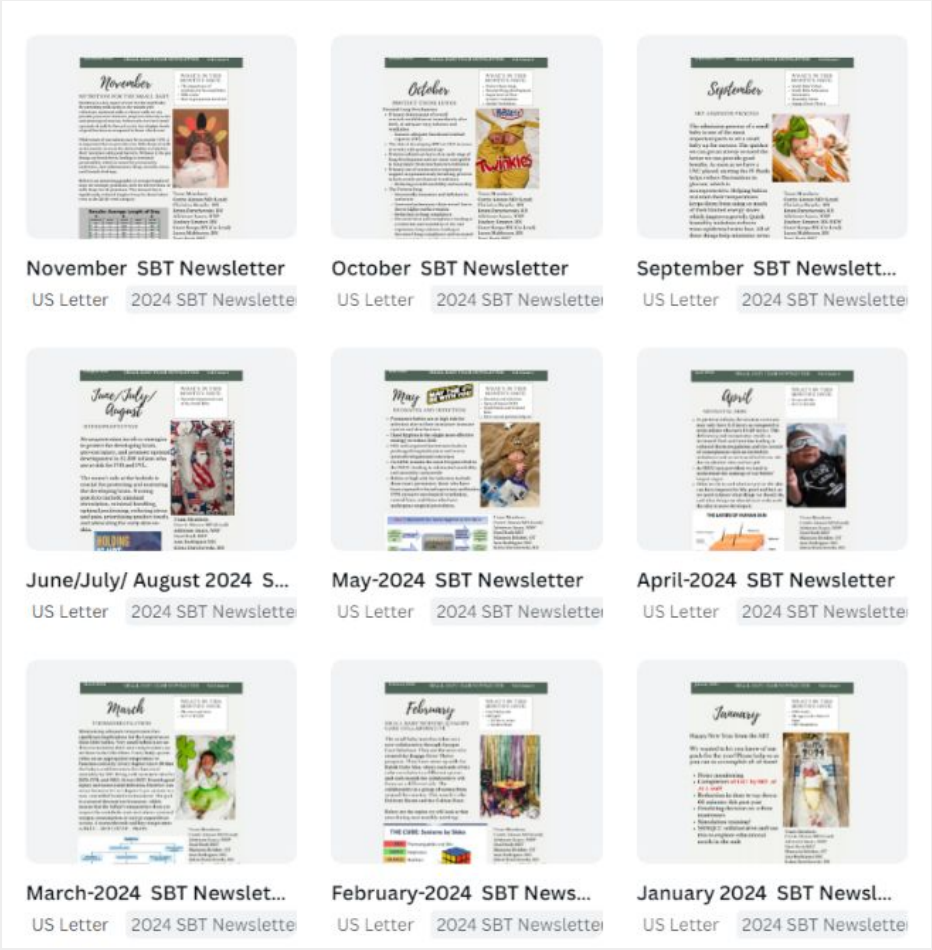






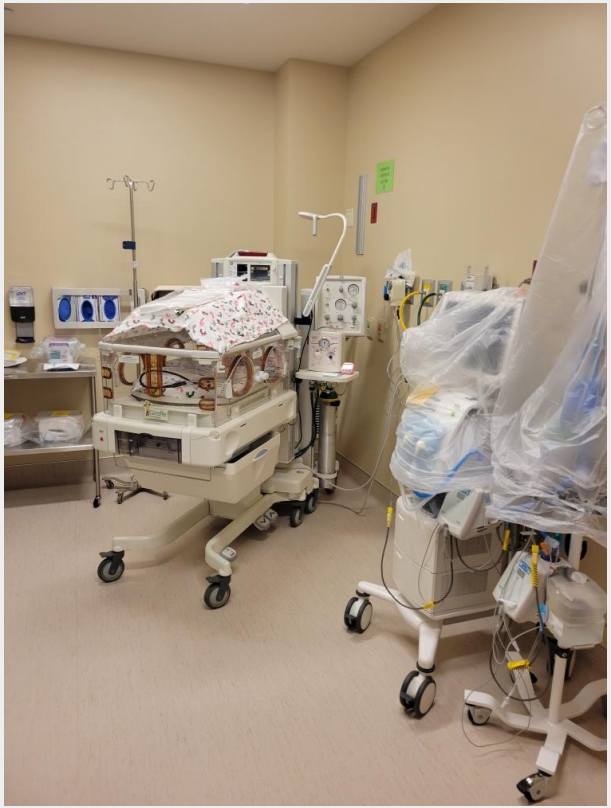
Small Baby Newsletter

- Each month has a topic ranging from neuroprotection, to respiratory support, kangaroo care, parental involvement and more



Delivery room Giraffe, with Bubble CPAP

- Always set up ready to go
- Includes bubble CPAP
- Emergency Bed
- Drager Ventilator



Engage Grow Thrive

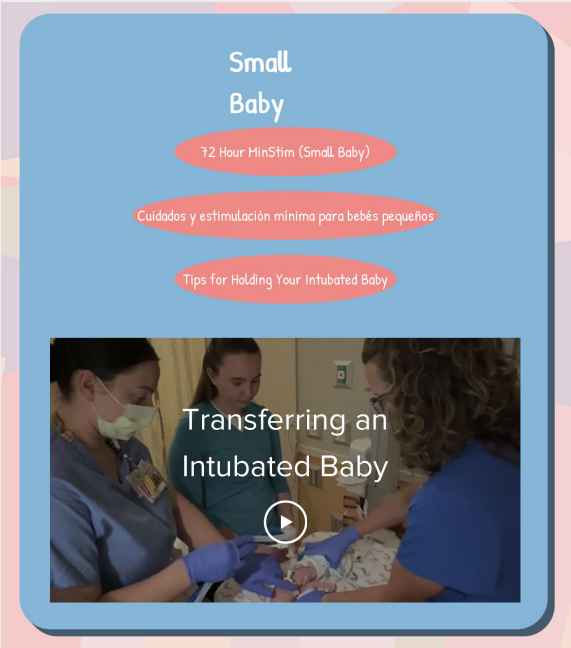
engage grow thrive
An interdisciplinary healthcare approach to improving lives

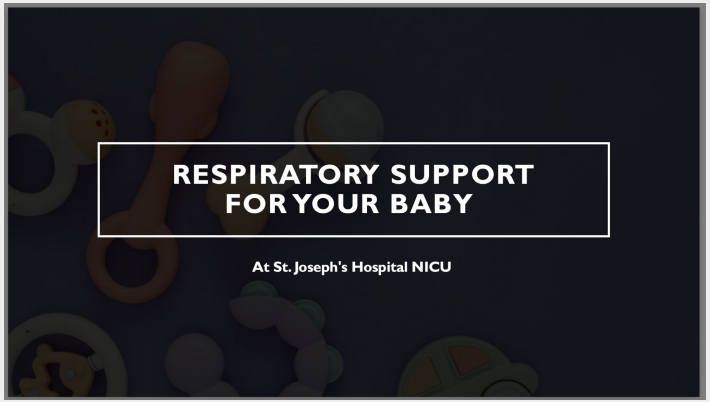
- Presentations total over 43 credit hours
- Links are given to all staff members including RN, OT/SLP, MD, NNP, and Respiratory has an abridged version
- Topics include
  - Family partnered care
  - Small baby survival and outcomes
  - Maternal role attainment
  - Communication and teamwork
  - QI process
  - Antenatal Care
  - Golden hour and stabilization
  - Thermoregulation
  - Nutrition
  - Feeding
  - Respiratory management and BPD
  - Pain
  - Positioning
  - Antibiotics
  - Skin
  - Renal
  - ROP
  - Pharmacotherapy
  - Ethics

- Customizable-we added guidelines, videos and important notes specific to our unit
- Endorsed by NANN, and has a specialty certification from the NCC

Family Integrated Care

- Minimal stimulation
- Kangaroo Care
- Respiratory modes for parents

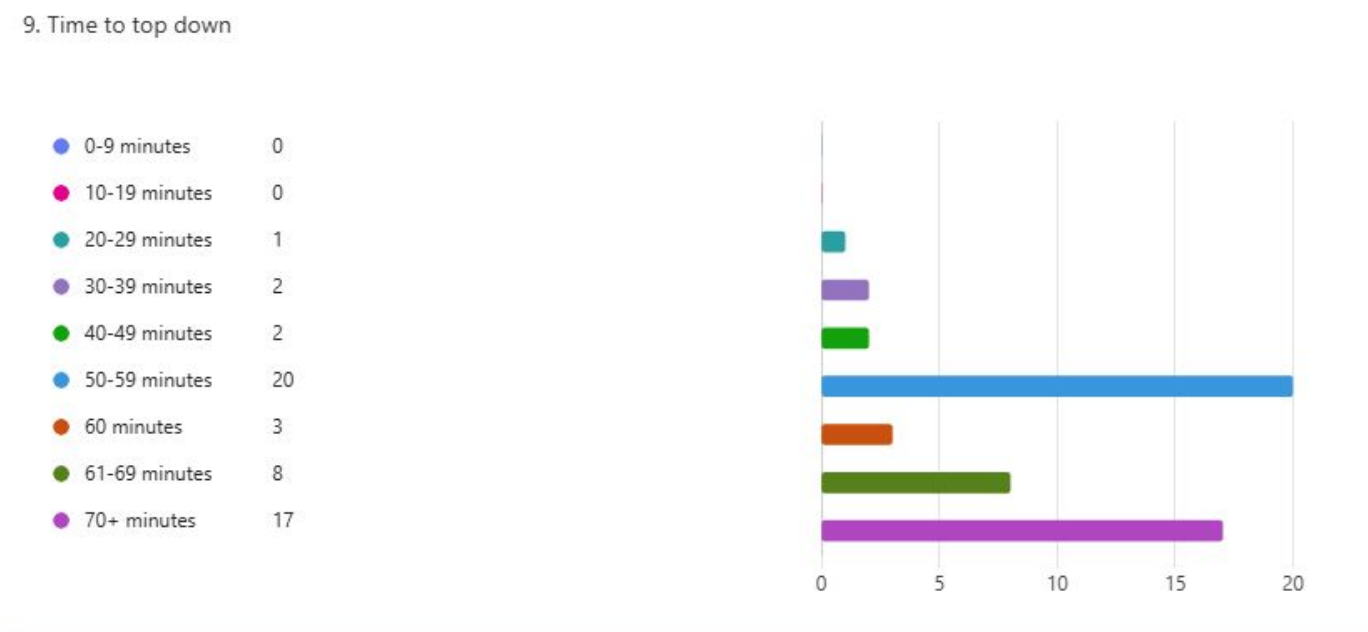




https://www.stjoesnicu.com/

Time to top down

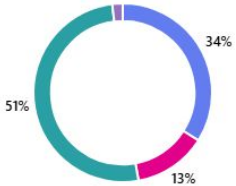
- Current average time to top down is 58 minutes



Data Tracking

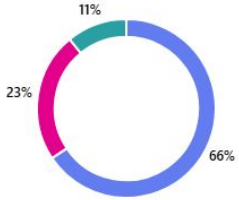
1. Was a pre huddle done?

Yes, with admitting RN	18
Yes, in the delivery room	7
No	27
Other place	1



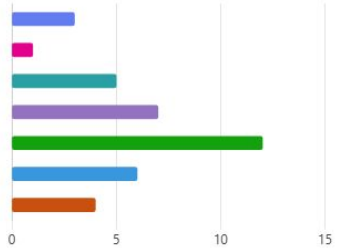
2. Was the debrief completed?

Yes	42
No	15
N/A or outborn	7



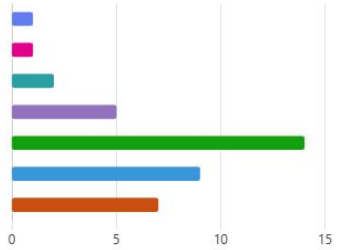
12. Time X-Ray called

0-10 minutes	3
11-20 minutes	1
21-30 minutes	5
31-40 minutes	7
41-50 minutes	12
51-60 minutes	6
61+ minutes	4



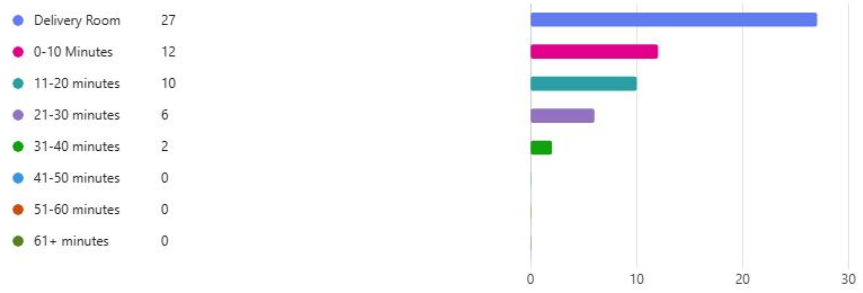
13. Time X-Ray arrived

0-10 minutes	1
11-20 minutes	1
21-30 minutes	2
31-40 minutes	5
41-50 minutes	14
51-60 minutes	9
61+ minutes	7

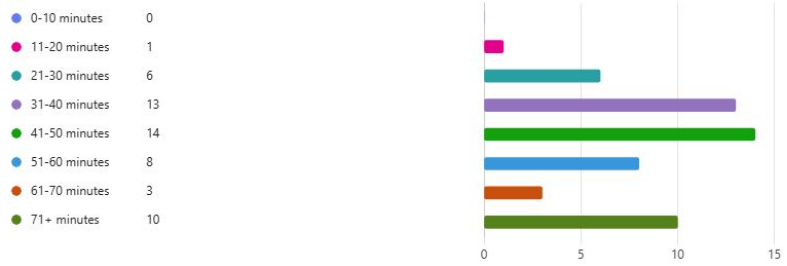


Data Tracking

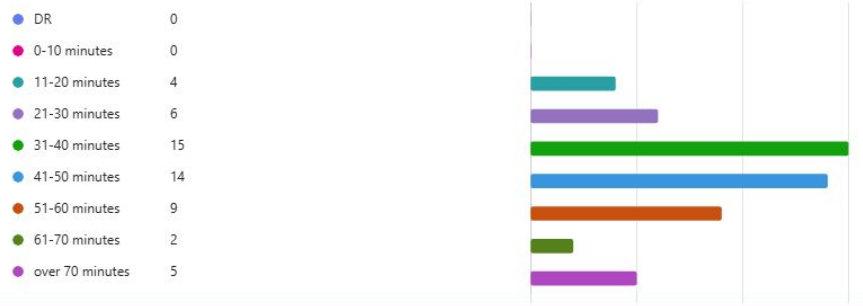
6. Time to respiratory support



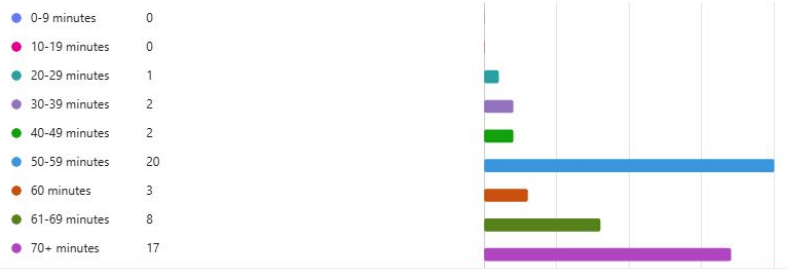
8. time to fluids started



7. Time to lines placed



9. Time to top down

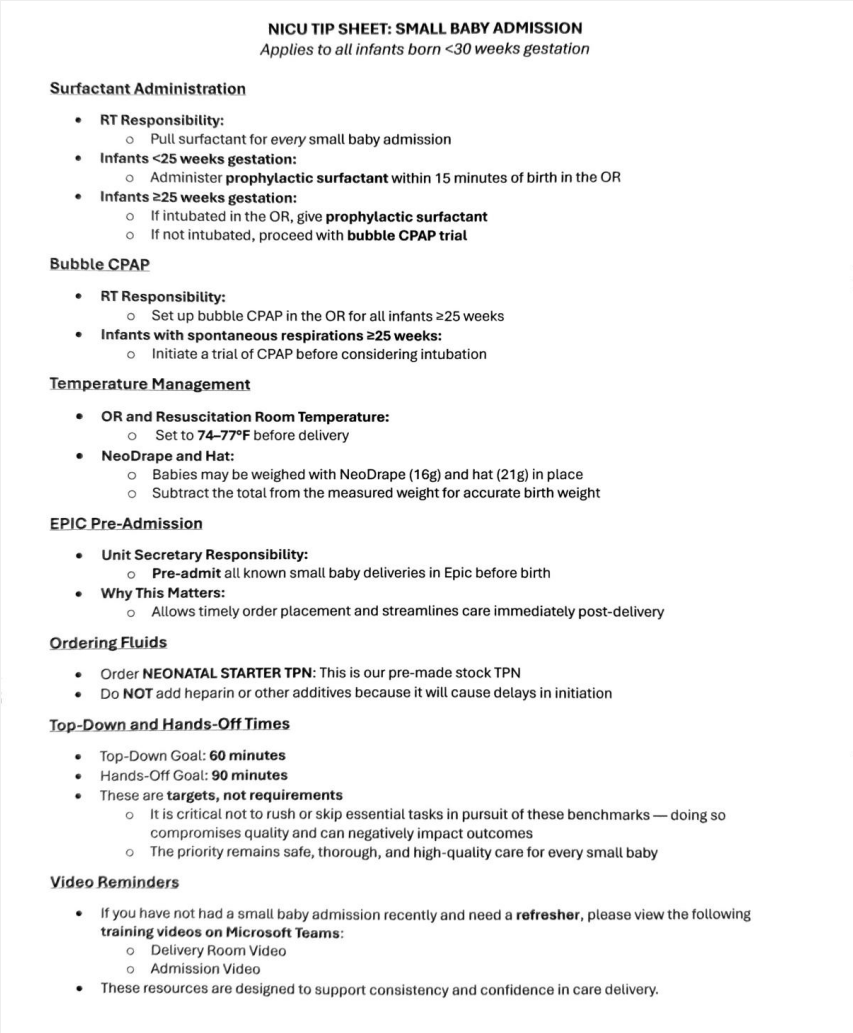


The Future of our Small Baby Team

- Everyone through our Engage Grow Thrive course
- Congruence of top down time with hands off time
  - Ideal top down time in 60 minutes with hands off at 90 minutes
- Surfactant administration
- Earlier holding of small babies
  - Currently averaging 4 days before being held
  - Striving for 3 days

Small baby Tip Sheet

- *Coming Soon*
- Roles for each discipline for SBT admission
- Placed in the OR, Secretary desk, Provider Fishbowl, and Respiratory Therapy work area



NICU TIP SHEET: SMALL BABY ADMISSION

Applies to all infants born <30 weeks gestation

Surfactant Administration

- **RT Responsibility:**
  - Pull surfactant for *every* small baby admission
- **Infants <25 weeks gestation:**
  - Administer **prophylactic surfactant** within 15 minutes of birth in the OR
- **Infants ≥25 weeks gestation:**
  - If intubated in the OR, give **prophylactic surfactant**
  - If not intubated, proceed with **bubble CPAP trial**

Bubble CPAP

- **RT Responsibility:**
  - Set up bubble CPAP in the OR for all infants ≥25 weeks
- **Infants with spontaneous respirations ≥25 weeks:**
  - Initiate a trial of CPAP before considering intubation

Temperature Management

- **OR and Resuscitation Room Temperature:**
  - Set to **74–77°F** before delivery
- **NeoDrape and Hat:**
  - Babies may be weighed with NeoDrape (16g) and hat (21g) in place
  - Subtract the total from the measured weight for accurate birth weight

EPIC Pre-Admission

- **Unit Secretary Responsibility:**
  - **Pre-admit** all known small baby deliveries in Epic before birth
- **Why This Matters:**
  - Allows timely order placement and streamlines care immediately post-delivery

Ordering Fluids

- Order **NEONATAL STARTER TPN**: This is our pre-made stock TPN
- Do **NOT** add heparin or other additives because it will cause delays in initiation

Top-Down and Hands-Off Times

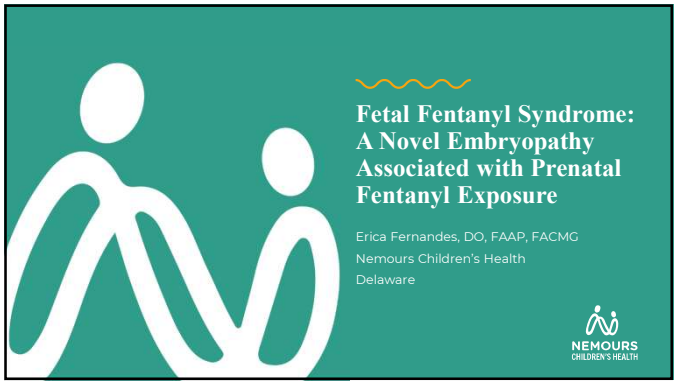
- Top-Down Goal: **60 minutes**
- Hands-Off Goal: **90 minutes**
- These are **targets, not requirements**
  - It is critical not to rush or skip essential tasks in pursuit of these benchmarks — doing so compromises quality and can negatively impact outcomes
  - The priority remains safe, thorough, and high-quality care for every small baby

Video Reminders

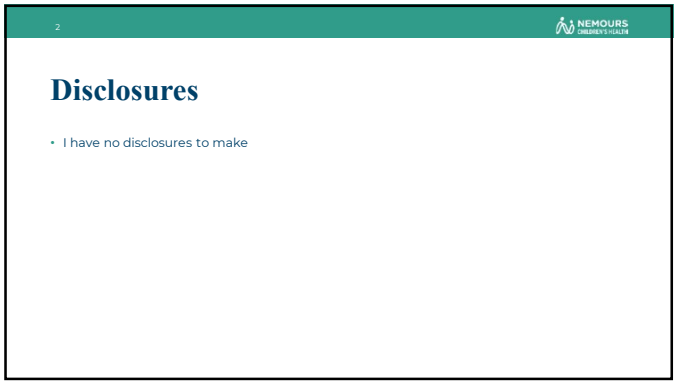
- If you have not had a small baby admission recently and need a **refresher**, please view the following **training videos on Microsoft Teams**:
  - Delivery Room Video
  - Admission Video
- These resources are designed to support consistency and confidence in care delivery.

References

- Croop, S., Thoyre, S., Aliaga, S., McCaffery, M., & Peter-Wohl, S. (2020). The golden hour: A quality improvement initiative for extremely premature infants in the neonatal intensive care unit. Journal of Perinatology, 40(3), 530-539 . doi: 10.1038/s41372-019-0545-0
- Doak, A., & Waskosky, A. (2022). Golden hour education, standardization, and team dynamics: A literature review. Neonatal Network , 41(5), 281-288. doi: 10.1891/NN-2021-0005
- Lamary, M., Bertoni, C.B., Schwabenbauer, K., & Ibrahim, J. (2023). Neonatal golden hour: A review of current best practices and available evidence. Current Opinion in Pediatrics, 35(2), 209-217. doi: 10.1097/MOP.0000000000001224


Fetal Fentanyl Syndrome: A Novel Embryopathy Associated with Prenatal Fentanyl Exposure
Erica Fernandes, DO, FAAP, FACMG
Nemours Children's Health
Delaware
NEMOURS
CHILDREN'S HEALTH

1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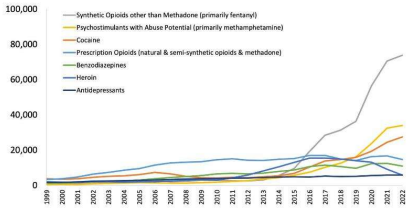
NEMOURS
Disclosures
• I have no disclosures to make

2


3
NEMOURS
Objectives
• Describe the features seen in Fetal Fentanyl Syndrome (FFS)
• Describe the proposed mechanism for prenatal fentanyl exposure that causes the physical and biochemical features in FFS
• Discuss diagnostic workup and screenings for FFS

3

Figure 2. U.S. Overdose Deaths*, Select Drugs or Drug Categories, 1999-2022



*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024.

4

Risks of prenatal opioid exposure

- In the setting of an opioid use disorder (OUD)
- Overall:
  - Preterm delivery
  - Small for gestational age
  - Increased risk of neurodevelopmental delays and behavioral issues
- What we knew previously:
  - Increased incidence of oral clefts and clubfoot with OUD and with methadone or buprenorphine (suboxone, Subutex, etc) treatment
  - These reported risks, however were still controversial with some studies showing *no* increased risk

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Nemours Cleft/Craniofacial Clinic

- Followed babies with oral clefts with various substance exposure
  - Methadone
  - Buprenorphine
  - Opioids
  - Alcohol*
    - Fetal alcohol syndrome (FAS) has known and well established associated with clefting
  - Polysubstance
- In 2022, we saw several newborns and infants with similar multiple congenital anomalies:
  - Cleft palate, club feet, microcephaly, SGA, toe syndactyly (2/3), dysmorphic facial features
  - All had prenatal drug exposure, primarily **fentanyl**
    - Positive urine and/or meconium drug screens for fentanyl

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Nemours Cleft/Craniofacial Clinic

7

Nemours Cleft/Craniofacial Clinic

- Can't be the prenatal drug use … right?
  - These anomalies never reported before in the literature with drug use including with fentanyl
- Must be something genetic
  - Features strikingly similar to Smith-Lemli-Opitz Syndrome (SLOS)
    - Caused by mutation in *DHCR7*
    - Disorder of cholesterol metabolism
    - Causes elevations of 7-dehydrocholestrol (7-DHC) and 8-dehydrocholesterol (8-DHC)

8

Genetic testing

- Several of the babies had elevations of 7- and 8-DHC, suggestive of SLOS
  - Genetic testing for SLOS negative
- Additional genetic testing – exome sequencing
  - Negative
- Levels of 7-DHC and 8-DHC were normalized on repeat testing a few weeks later

9

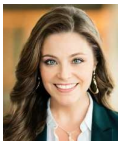
Research Study

- Suspected that the features seen in these children could be due to the prenatal fentanyl exposure
  - Only drug exposure shared across all the infants
- Found two additional infants from outside institutions with identical features and histories
- IRB study initiated in 2022

10

Discovery Team

Erin Wadman, MS, CGC
Pediatric Genetic Counselor
Nemours Children's Health



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Candace Muss, PA-C, MS, CGC
PA and Genetic Counselor
Medical Genetics
Nemours Children's Health

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November 2023

Genetics in Medicine Open (2023) ■ 100834

ELSEVIER

Genetics Medicine OPEN
An Official Journal of the ACMG
www.journals.elsevier.com/genetics-in-medicine-open

BRIEF REPORT

A novel syndrome associated with prenatal fentanyl exposure

Erin Wadman[1], Erica Fernandes[1], Candace Muss[1], Nina Powell-Hamilton[1], Monica H. Wojcik[2,3], Jill A. Madden[3], Chrystalle Katte Carreon[4], Robin D. Clark[5], Annie Stenftenagel[6], Kamal Chikalard[6], Virginia Kimonis[5], William Brucker[7], Carolina Alves[8], Karen W. Gripp[1,*]

ARTICLE INFO

Article history:

ABSTRACT

A novel syndrome was suspected in individuals sharing short stature, microcephaly, distinctive

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13 CLICK TO EDIT PRESENTATION TITLE NEMOURS CHILDREN'S HEALTH

November 2023

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Hypothesis

- Suspected that this was a novel embryopathy caused by prenatal exposure to high levels of fentanyl
- So why does FFS so strongly resemble Smith-Lemli-Opitz syndrome?

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Smith-Lemli-Opitz Syndrome (SLOS)

- Autosomal recessive disorder caused by mutations in *DHCR7*
- Clinical features are caused by a *deficiency in 7-dehydrocholesterol reductase*
  - Inability to convert 7-DHC to cholesterol in the last step of the cholesterol metabolism pathway
  - Results in elevations of 7-DHC and 8-DHC, and low total cholesterol
    - Low levels of cholesterol affect many areas of embryogenesis
    - High 7- and 8-DHC levels are neurotoxic

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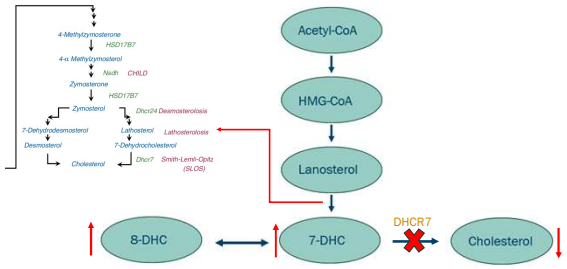
Cholesterol biosynthesis



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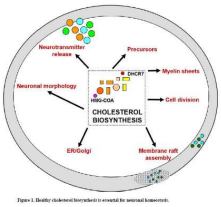
Cholesterol and embryogenesis

- Cholesterol is a critical component during embryogenesis
- Involved in *SHH* signaling
- Crucial for steroid hormone synthesis and myelination, brain cells synthesize their own cholesterol



Korade Z, Heffer M, Mirnics K. Medication effects on developmental sterol biosynthesis. Mol Psychiatry. 2022.

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Smith-Lemli-Opitz Syndrome

Features	SLOS
SGA	+
Microcephaly	+
Bitemporal narrowing	+
Short stature	+
Cleft palate	+
Micrognathia	+
Ptosis	+
Thin upper lip	+
Long philtrum	+
Anteverted nares	+
Broad, flat nasal bridge	+
GU anomalies	+
Short thumbs	+
2,3 toe syndactyly	+
Hypotonia followed by hypertonia	+

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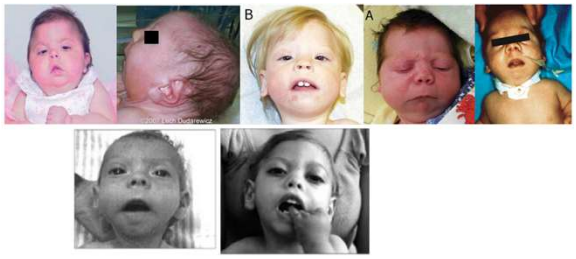
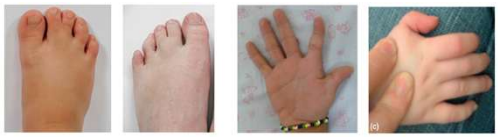
Smith-Lemli-Opitz Syndrome



Scalco, Fernanda & Otto, Paulo & Brunetti, Igyatemy & Cruaes, Vania & Moretti-Ferreira, Danilo. (2006). Smith-Lemli-Opitz syndrome: Clinical and biochemical findings in Brazilian patients. Genetics and Molecular Biology - GENET MOL BIOL. 29. 10.1590/S1415-47572006000300003.

20

Smith-Lemli-Opitz Syndrome



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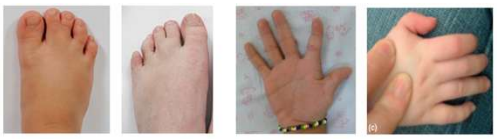
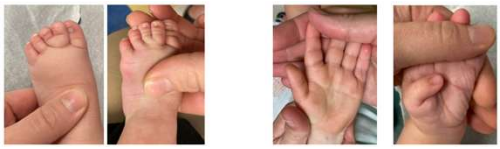
SLOS

FFS

SLOS



FFS



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SLOS versus FFS

But ...Why???
How???

Features	SLOS
SGA	+
Microcephaly	+
Bitemporal narrowing	+
Short stature	+
Cleft palate	+
Micrognathia	+
Ptosis	+
Thin upper lip	+
Long philtrum	+
Anteverted nares	+
Broad, flat nasal bridge	+
GU anomalies	+
Short thumbs	+
2,3 toe syndactyly	+
Hypotonia followed by hypertonia	+

23

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Hypothesis

- All patients appeared to have Smith-Lemli-Opitz syndrome (SLOS)
  - But they didn't
- SLOS caused by defect in cholesterol metabolism pathway
- All babies with significant and consistent prenatal exposure to fentanyl
- Hypothesis: fentanyl must be disrupting the cholesterol metabolism pathway
- Evidence (at time of publication)
  - Physical features and dysmorphisms
  - Elevated 7- and 8-DHC, which then normalizes after a few weeks since baby no longer exposed to the in-utero fentanyl

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Cholesterol pathway studies

- In 2023, reached out to the Korade lab at the University of Nebraska
  - Lab extensively studies cholesterol metabolism disorders and syndrome
  - Experts in this field
- They performed a series of experiments mouse neuronal and astrocytic cultures as well as human dermal fibroblasts with two different genotypes:
  - DHCR7 +/+ (normal, aka wild type)
  - DHCRT +/- (carriers of SLOS)

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Cholesterol pathway studies

Inhibition of post-lanosterol biosynthesis by fentanyl: potential implications for Fetal Fentanyl Syndrome (FFS)

Zelika Korade, Allison C. Anderson, Kanika Sharma, Keri A. Tallman, Hye-Young H. Kim, Ned A. Porter, Karen W. Gripp & Karoly Mirnics

Molecular Psychiatry (2024) | Cite this article

269 Accesses | 90 Altmetric | Metrics

Abstract

A recent study discovered a novel, complex developmental disability syndrome, most likely caused by maternal fentanyl use disorder. This *Fetal Fentanyl Syndrome* (FFS) is biochemically characterized by elevated *7-dehydrocholesterol* (7-DHC) levels in neonates, raising the question if fentanyl inhibition of the *dehydrocholesterol reductase 7* (DHCR7) enzyme is causal for the emergence of the pathophysiology and phenotypic features of *FFS*. To test this hypothesis, we

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Cholesterol pathway studies

- "... in vitro exposure to fentanyl disrupted sterol biosynthesis across all four in vitro models...The sterol biosynthesis disruption by fentanyl was complex, and encompassed the majority of post-lanosterol intermediates, including elevated 7-DHC and decreased desmosterol (DES) levels across all investigated models. The findings overall suggest that maternal fentanyl use in the context of an opioid use disorder leads to FFS in the developing fetus through a strong disruption of the whole post-lanosterol pathway..."

Korade et al, 2024

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Expanding cohort

- We identified several more patients at our institution
- Identified additional patients across U.S.
  - Maine, Rhode Island, California, Missouri, Kentucky, Washington, Maryland, D.C.

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Expanding cohort

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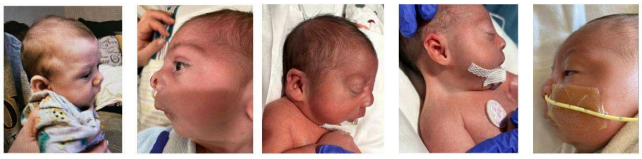
Newborn Faces

30

Newborn profile



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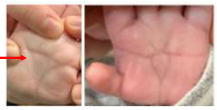
FFS – Facial phenotype

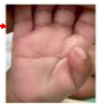
- Microcephaly (variable)
- Narrow forehead
- Short and upturned nose
- Micrognathia
- Long philtrum
- Thin upper lip
- Full cheeks

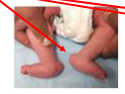
32

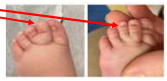
FFS – Physical features

- Single palmar crease
- Hockey stick crease
- Short, adducted thumbs
- Club feet
- Rocker bottom feet
- 2,3 toe syndactyly









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FFS work-up

- If early enough, urine and/or mec drug screen
  - ENSURE that **FENTANYL** is included on the screen (some require separate analyte order, i.e. Quest)
- If suspicion for FFS, obtain 7- and 8-DHC (sometimes called Smith-Lemli-Opitz screen)
  - ***Needs to be done within first few days of life***
    - Levels will normalize after a couple of weeks
  - Quest: test code 15992
  - Mayo: test code "SLO"

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FFS workup

- Consult Genetics!
  - Genetic testing still needs to be sent to rule out genetic disorders that can have overlapping features
    - FFS, like FAS is a diagnosis of exclusion
  - Genetic testing can be difficult if you are in a state that requires informed consent
    - Required in Colorado
    - Who can consent? Bio parents? Guardian? DFS case worker?

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FFS NICU course

- NAS treatment
  - Often prolonged course, though not always
- Feeding
  - ***Expect prolonged PO feeding difficulties***
  - Most require feeding tube support and will not PO feed well
  - Poor PO feeding goes beyond typical NAS feeding challenges
  - Many, especially those with clefts may require g-tube placement
  - Ensure good palate exam with visualization, small soft palate clefts easily missed

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Other diagnostic studies and evaluations to consider

- Echocardiogram
- MRI brain
  - Corpus callosum abnormalities
- Renal ultrasound
- Ophthalmologic evaluation
  - Can likely be outpatient
  - Optic nerve abnormalities, nystagmus, cortical vision impairment, strabismus

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Summary

- Fetal fentanyl syndrome is a newly recognized embryopathy
- Associated with prenatal fentanyl use in the context of opioid use disorder
- Fentanyl is a multi-enzyme inhibitor of cholesterol biosynthesis in developing neurons and astrocytes
  - Results in significant phenotypic overlap with other cholesterol metabolism disorders, most notably Smith-Lemli-Opitz Syndrome
- Biomarker: Elevated 7-, 8-DHC in the first 1-2 weeks only, resolved thereafter
- NICU course for babies with FFS including significant PO feeding challenges with prolonged need for NG feeds
- FFS is still a diagnosis of exclusion (similar to FAS) that requires thorough genetic work-up by Genetics team in the NICU

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Follow-Up

- Tracking long-term developmental outcomes, milestones and behaviors
- Delineating emerging spectrum of severity
  - FFS vs FFSD
  - Phenotypic differences based on timing of prenatal exposure, frequency, dosage, etc
- Enrolling additional outside cases
- Establishing diagnostic criteria

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Acknowledgements

- Erin Wadman, MS, LCGC
- Karen Gripp, MD
- Candace Muss, PA, LCGC
- Zeljika Korade, DVM, PhD
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- Miguel Del Campo, MD, PhD
- Lynne Bird, MD
- Robin Clark, MD
- William Brucker, MD
- Monica Wojcik, MD, MPH
- Virginia Kimonis, MD
- Carolina Alves, MS
- Nemours Craniofacial Clinic

NEMOURS CHILDREN'S HEALTH

University of Nebraska Medical Center
Nebraska Medicine

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Thank you to our patient families!

A **HUGE** thank you to the amazing families who have made this work possible!

"Initially, we never were on board with having a medically complex child, just because we didn't think we could handle it. We weren't really equipped," Carlisle said. "But then I said 'yes' and it was the best 'yes' I've ever said."

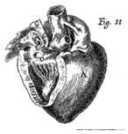
Sammy's adoptive mom,
Lindsay Carlisle
-NBC News

Sammy's first news interview!

https://www.nbcnews.com/health/health-news/fetal-fentanyl-exposure-pregnancy-birth-defects-rcna126006

41

Patent Ductus Arteriosus Where We Have Been & Where We *Might* Be Going



19 June 2025
Michael Cookson, MD
Neonatology

1

Learning Objectives

Learners will be able to:

1. Describe the evolving importance of managing the PDA in preterm neonates
2. Describe why defining "hemodynamically significance" is important
3. Understand common pitfalls of medical therapy for PDA
4. Understand the role of intervention based PDA closures

2

Educational Alignment Statement

What this talk is not:

1. Management of the ductus arteriosus in patients with congenital heart disease
2. Management of PDA in the near-term & term infant with pulmonary hypertension
3. Definitive statement on who requires PDA closure and/or how to do it
4. Comprehensive Review of the PDA literature (16 Cochranes…)

3

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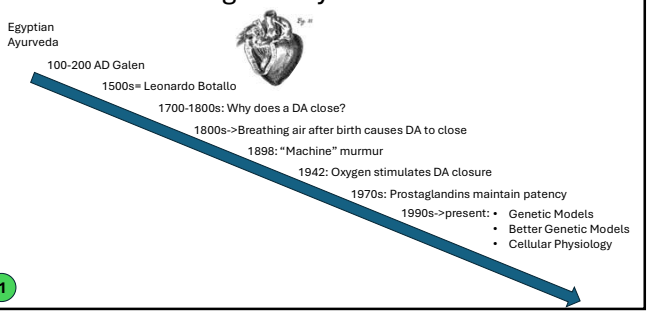
PDA: A Long History of Consideration



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Impact of PDA on Neonatal Outcomes

- Early and Late Hemodynamic Compromise
- Prolonged Intubation
- Bronchopulmonary Dysplasia (BPD)
- Necrotizing Enterocolitis (NEC)
- Intraventricular Hemorrhage (IVH)
  - Cerebral Palsy (CP) *
- Feeding Delays*

1

6

The PDA Conundrum

A. Gestation	Closed on day 4	Closed on day 7	Closed at discharge
Full term	100	100	100
≥30 weeks	90	98	98
27–28 weeks	22	36	na
25–26 weeks	20	32	na
24 weeks	8	13	na
B. Birthweight			
1000–1500 grams	35	67	94
<1000 grams	21	34	na

1

Clyman 2012

7

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Clyman 2012

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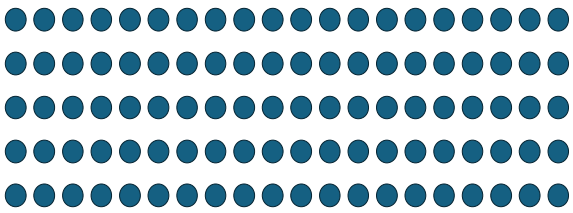
The PDA Conundrum: <28 weeks GA



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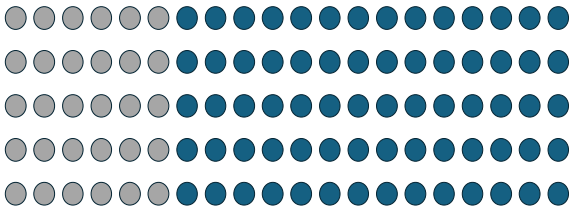
The PDA Conundrum: <28 weeks GA



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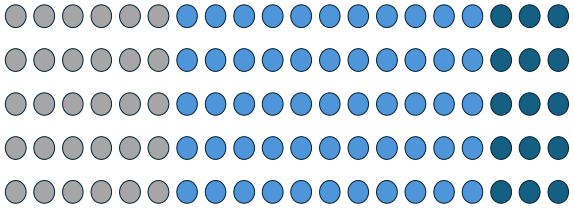
The PDA Conundrum: <28 weeks GA



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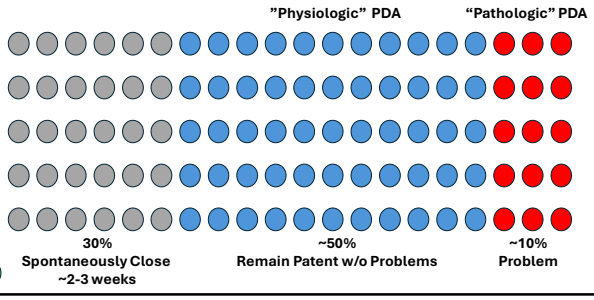
The PDA Conundrum: <28 weeks GA



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12

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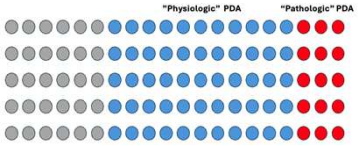
Hemodynamic Significance

Pathologic PDA=Hemodynamic Significance

- Our understanding of this will continue to evolve over time
- Simply: Too much blood is going from the Aorta to the Lungs



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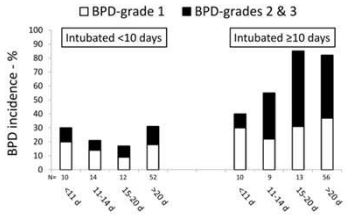
Hemodynamic Significance

Incidence of BPD in infants with prolonged "mod/large PDA Shunt"



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Clyman 2021

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Hemodynamic Significance

Physiologic Concept	What you may hear on rounds or read from ECHO study	What you know about the infant you care for
Anatomic	Size: • mm or mm/kg Flow Pattern: • Restrictive Pattern • Velocity	Murmur Pulses
Too Much Blood Flow To Lungs	Left Heart Dilation: • LA/Aorta Ratio • LV Size Pulmonary Blood Flow • "Continuous flow in branch PAs"	Difficult to Extubate Increasing/persistent FiO_2 need Prolonged Intubation Crackles on exam Edema on CXR/Pulmonary Hemorrhage
Not Enough Blood Flow to Body	Systemic Steal • "Holodiastolic flow reversal" • Retrograde Aortic flow	NEC? Rising Cr IVH

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Hemodynamic Significance

Summary: *Echocardiography should be used to confirm the presence of a left-to-right PDA shunt before considering treatment (strong recommendation).* There is insufficient evidence to suggest a set of echocardiographic criteria to define hemodynamic significance of the PDA. A PDA with a diameter of <1.5 mm is unlikely to result in a hemodynamically significant shunt, and therefore may be conservatively managed without pharmacotherapy *(conditional recommendation).*

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Mitra 2022

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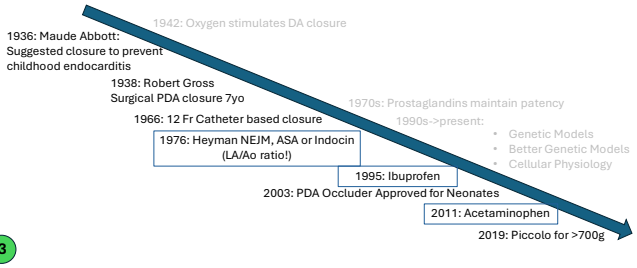
PDA: A Long History of Therapy



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Management

	The How	The Downsides
Conservative	Nutrition Fluid Restriction Diuretics PEEP	None proven to work Inadequate nutrition
Pharmacologic	Indocin Ibuprofen Acetaminophen	AKI Electrolyte abnormalities Thrombocytopenia Theoretical liver injury
Catheter Based	Femoral Vein Access to PDA	Failed Procedure Embolization (PA/Ao) Bleeding
Surgical Ligation	Clippy clippy through lateral thoracotomy	Failed procedure Bronchus ligation Bleeding Post-Ligation Syndrome

3

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Pharmacotherapy Effectiveness…

In a sample of 107 neonates with GA of ~26w, Pharmacotherapy was "successful" in 61%.

- Second course (n=41): Closure rate of 37%
- Third course (n=25): Closure rate of 33%

Impact of GA:

- >26w: 70% Closure rate w/ 1st treatment
- 22-26w: ~40% Closure rate w/ 1st treatment

3

Dani 2025; Weems 2025

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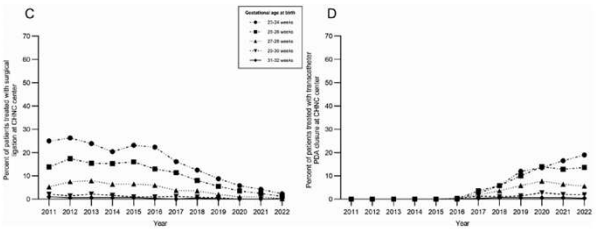
Transcatheter Closure is Increasing



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Weems 2025

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Transcatheter Closure: When? Who? Why?

When?

- Evolving, but before it becomes a problem…
- Single Study: <4 weeks of chronological age w/ improved outcomes (Philip 2021)

Who?

- Consider for infants who have failed x2 medical closures and continue to have a "hemodynamic significant" PDA (Mitra 2022)
- >700g, but largely institutional specific

Why?

- Improved outcomes compared to surgical ligation (Melchior 2024)

4

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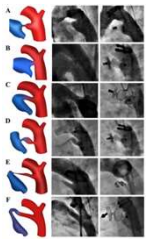
Surgical Ligation: When? Who? Why?

When?
- Evolving, but before it becomes a problem…
- Too unstable for transcatheter

Who?
- Unfavorable anatomy, too wide

Why?
- Limited experience with occluders
- Any of the above



Philip 2016

4

25

The Future???

Trial of Selective Early Treatment of Patent Ductus Arteriosus with Ibuprofen

Authors: Samir Gupta, M.D., Nimish V. Subhedar, M.D., Jennifer L. Bell, M.Sc., David Field, M.D., Ursula Bowler, Elizabeth Hutchison, M.A., Sam Johnson, Ph.D., [+4], for the Baby-OSCAR Collaborative Group* Author Info & Affiliations

Published January 24, 2024 | N Engl J Med 2024;390:314-325

Expectant Management or Early Ibuprofen for Patent Ductus Arteriosus

Authors: Tim Hundscheid, M.D. [redacted], for the BeNeDuctus Trial Investigators* Author Info & Affiliations

Published December 6, 2022 | N Engl J Med 2023;388:980-990

TREOCAPA: prophylactic treatment of the ductus arteriosus in preterm infants by acetaminophen—statistical analysis plan for the randomized phase III group sequential trial

Moreno Ursino, Corinne Alberti, Gilles Cambonie, Ruth Kemps, Aure Vanhecke, Lea Levoyer, Alpha Diallo, Mikko Hallman & Jean-Christophe Rozé for the TREOCAPA study group

Selective early medical treatment of the patent ductus arteriosus in extremely low gestational age infants: a pilot randomised controlled trial protocol (SMART-PDA)

4

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Learning Objectives-Recap

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Learning Objectives-Recap

Learners will be able to:

1. Describe the evolving importance of managing the PDA in preterm neonates
- It is changing rapidly and will likely continue to do so…tricky job we have
- Most PDAs are not bad

28

Learning Objectives-Recap

Learners will be able to:

1. Describe the evolving importance of managing the PDA in preterm neonates
2. Describe why defining "hemodynamic significance" is important
- Hemodynamic Significance=Pathologic
- Hard to Define. Hard to know which PDAs are going to cause a problem

29

Learning Objectives-Recap

Learners will be able to:

1. Describe the evolving importance of managing the PDA in preterm neonates
2. Describe why defining "hemodynamic significance" is important
3. Understand common pitfalls of medical therapy for PDA
- Pharmacologic PDA treatment closes PDAs ~50-70% of the time
- Not without side effects, which we do not yet fully understand

30

Learning Objectives-Recap

Learners will be able to:

1. Describe the evolving importance of managing the PDA in preterm neonates
2. Describe why defining "hemodynamic significance" is important
3. Understand common pitfalls of medical therapy for PDA
4. Understand the role of intervention based PDA closures

- Becoming common place and being done in tiny infants
- Not without significant side effects

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AAP Recommendations-2025

Key recommendations

Following are among the recommendations in the report for clinical practice and further research:

- Prophylactic medical treatment is not recommended at any gestational age or birth weight.
- Early closure (less than 14 days of life), whether pharmacologic, surgical or transcatheter, has not been shown to improve outcomes and is not recommended. A conservative approach awaiting spontaneous closure may reduce unnecessary exposure to medical or procedural interventions.
- Beyond two weeks of life, data guiding management of hemodynamically significant PDAs remain limited. The risks and benefits of conservative management, pharmacologic therapy, transcatheter closure and surgical ligation require further study.
- Many clinicians attempt medical closure with one or two courses of ibuprofen, with acetaminophen or indomethacin as acceptable alternatives. Transcatheter closure may be considered for infants with a persistent hemodynamically significant PDA beyond two weeks of life.

PDA management in preterm infants continues to evolve. While pharmacologic and procedural interventions can close the PDA, current evidence on major neonatal outcomes is limited. Ongoing clinical trials may provide critical data to refine best practices in PDA management.

April 28th, 2025 AAP, *Ambalavanan*

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Thank You

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References

Can send PDFs and full reference list to anyone who wants one
Michael.Cookson@cuanschutz.edu

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MJO

Ventilation for Evolving Lung Disease of Prematurity

Sadie Houin, MD CHCO
Medical Director SPROUT Team
Jen Miller, NNP CHCO
SPROUT APP Subject Matter Expert

1

Introduction to Supporting Preemie Respiratory OUTcomes

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Supporting Preemie Respiratory OUTcomes

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2

SPROUT Team: Supporting Preemie Respiratory OUTcomes

Mission: To provide a unified approach to respiratory care in infants with/at risk for sBPD to improve respiratory and neuro-developmental outcomes.

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3

SPROUT Team: Supporting Preemie Respiratory OUTcomes

Mission: To provide a unified approach to respiratory care in infants with/at risk for sBPD to improve respiratory and neuro-developmental outcomes.

Population
Preemies born <29 weeks with significant positive pressure needs at >4-6 weeks of age

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Team
Physicians opt in to the team

Dedicated NNPs and PNPs.

Pharmacists, therapists, social workers, RTs, RNs.

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Weekly Meetings
Discuss long term plans and acute issues.

Multidisciplinary

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Multidisciplinary

Education
Educational rotation for NICU fellows to focus on chronic ventilation strategies.

Regional resource

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Development of the Team and Goals

Team launched July 2021, has since cared for 118 infants

Referrals from 17 birth hospitals across 8 states

Average LOS at CHCD - 163 days

Goals

- More standardized and consistent care
- Better outcomes
- Contingency plans for nights/weekends
- Improved provider, nursing, and family satisfaction with care

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Evolution of Becoming a BPD Infant

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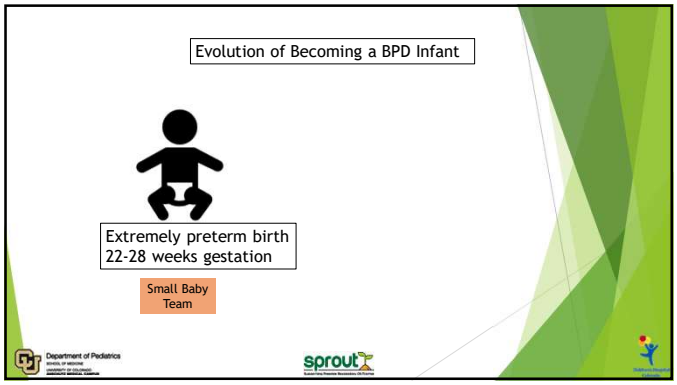
Evolution of Becoming a BPD Infant
Extremely preterm birth
22-28 weeks gestation
Small Baby Team
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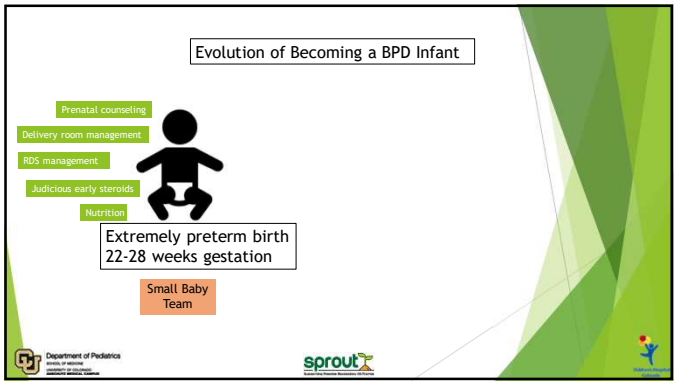
Evolution of Becoming a BPD Infant
Prenatal counseling
Delivery room management
RDS management
Judicious early steroids
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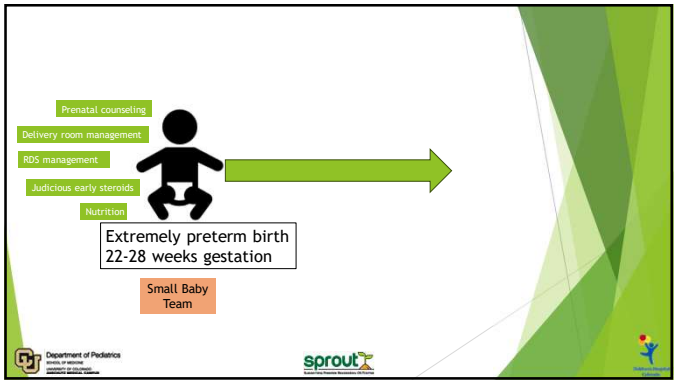
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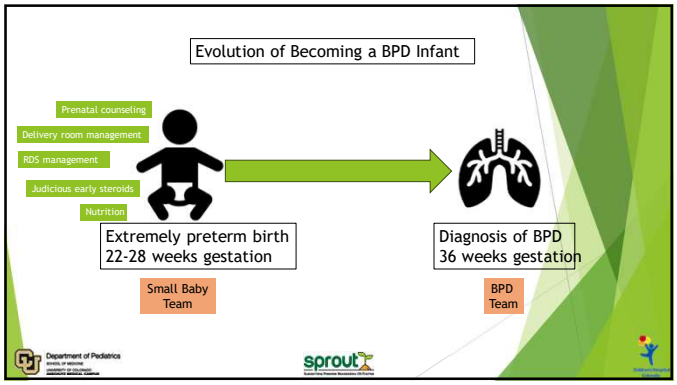
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36 weeks gestation
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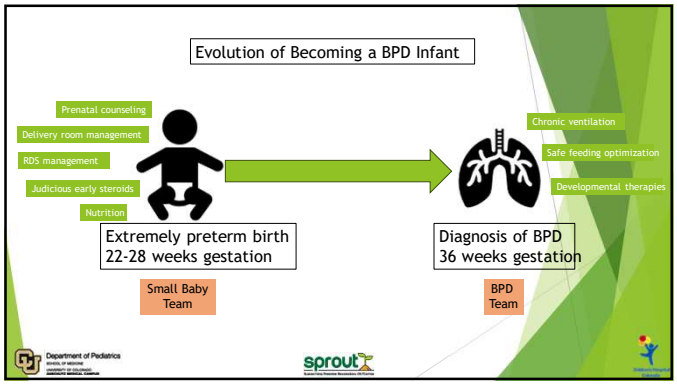
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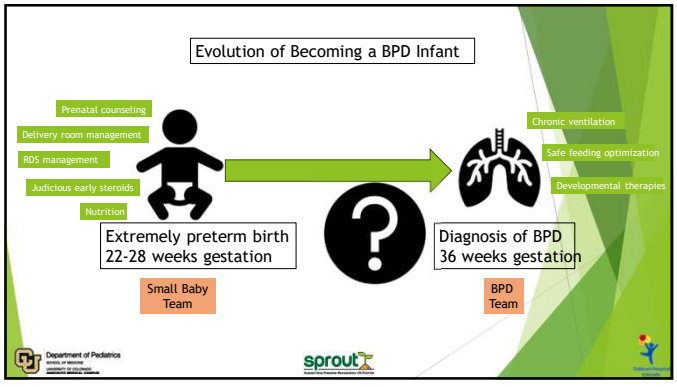
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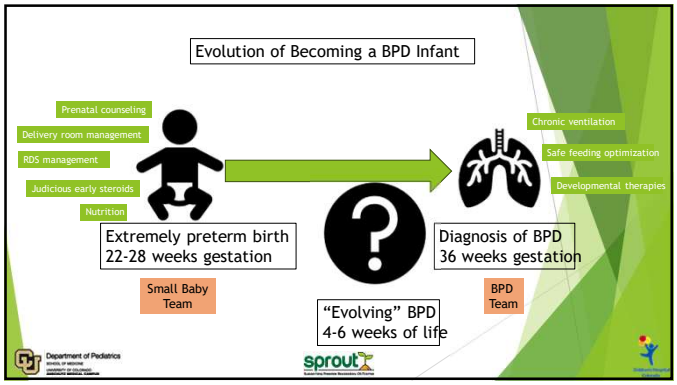
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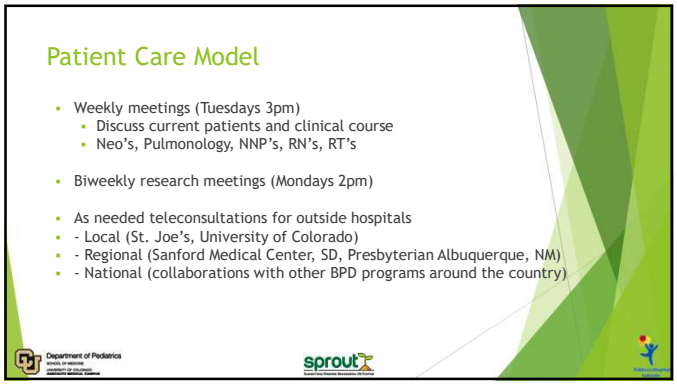
Patient Care Model
Weekly meetings (Tuesdays 3pm)
Discuss current patients and clinical course
Neo's, Pulmonology, NNP's, RN's, RT's
Biweekly research meetings (Mondays 2pm)
As needed teleconsultations for outside hospitals
- Local (St. Joe's, University of Colorado)
- Regional (Sanford Medical Center, SD, Presbyterian Albuquerque, NM)
- National (collaborations with other BPD programs around the country)
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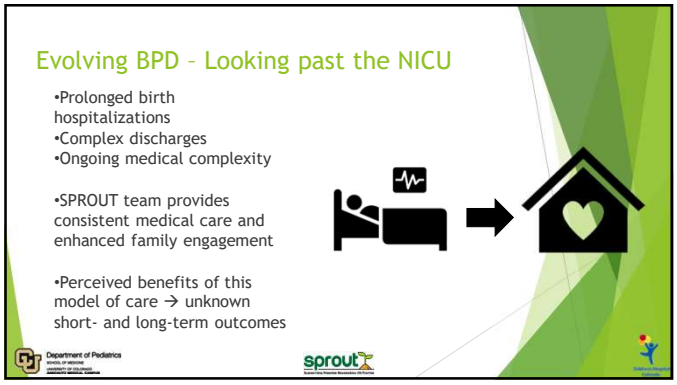
Evolving BPD – Looking past the NICU
•Prolonged birth hospitalizations
•Complex discharges
•Ongoing medical complexity
•SPROUT team provides consistent medical care and enhanced family engagement
•Perceived benefits of this model of care → unknown short- and long-term outcomes
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Numbers by year

Year	#SPROUTlings
2021	8
2022	30
2023	34
2024	42

total of 17011 patient days – average of 160 days in the NICU per patient

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Pathophysiology of Severe BPD

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Severe Bronchopulmonary Dysplasia (sBPD)

- Incidence of sBPD is around 16% of all babies born < 32 weeks
  - 91% survived to discharge
  - 66% discharged on supplemental oxygen
  - 5% received a tracheostomy
  - 4% were discharged on mechanical ventilation
- Marked variability in care within and between NICUs throughout the country
  - 11-58% prevalence of sBPD across US centers
- Many common struggles
  - Babies have complex and prolonged clinical courses
  - There can be poor commination between providers and amongst the clinical team
  - high staff turnover increases the need for standardization

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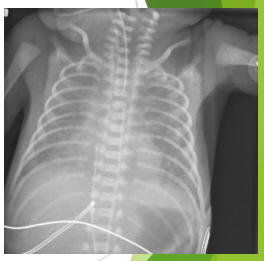
Acute Ventilation is Ideal for Respiratory Distress Syndrome

- **Homogeneous** lung disease
  - CXR with low lung volumes and ground glass appearance
- Lung compliance is **LOW**
  - Stiff lung that is hard to inflate and maintain inflation
- Airway resistance is **NORMAL**
  - Tidal volume will empty very quickly on expiration, short time constants
- **Ventilation strategy: Low tidal volume, low PEEP and higher rate**



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Goal of acute ventilation is to minimize damage and remove ETT as early as possible.

Mechanical ventilation (MV) is both essential and detrimental for extremely preterm infants.

Severe bronchopulmonary dysplasia (sBPD) occurs 16% of preemies <32 weeks.[2]

Longer duration of MV associated with increased risk of BPD.[1]

Each additional week of MV associated with increased risk of neurodevelopmental impairment (NDI).[3-4]

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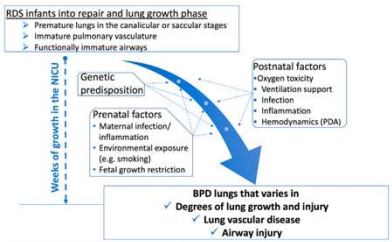
1. Jensen EA et al, 2015
2. Padula MA et al., 2013
3. Walsh MC et al., 2005
4. Vilegonthart RJS, et al, 2019

23



Many interactions that occur both pre- and postnatally result in variations in BPD pathophysiology

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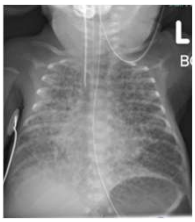
Evolution of Severe BPD from RDS

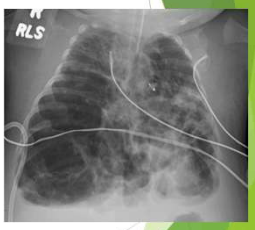
First weeks of life (RDS)



-**Low** compliance
-**Homogeneous** aeration
-**Normal** airway resistance

Same patient 5 months later

Evolving chronic lung disease



-**Increased** compliance
-**Heterogenous** aeration
-**High** airway resistance

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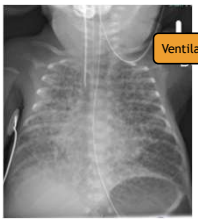
Evolution of Severe BPD from RDS

First weeks of life (RDS)

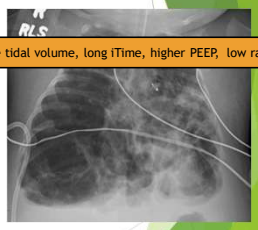


-**Low** compliance
-**Homogeneous** aeration
-**Normal** airway resistance

Ventilation Strategy: Large tidal volume, long iTime, higher PEEP, low rate

Same patient 5 months later

Evolving chronic lung disease



-**Increased** compliance
-**Heterogenous** aeration
-**High** airway resistance

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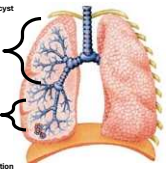
Respiratory Phenotypes in BPD: Airway

- Increased Airway resistance puts babies at risk for to over-inflation/air-trapping
  - CO2 retention
  - Inefficient respiratory effort
- Ventilation strategy:
  - **Low rate** to allow exhalation
  - **Higher PEEP** to stent open floppy airways

Central Airways:
Tracheomalacia
Subglottic stenosis, cyst
Granulomas
Bronchomalacia
Bronchial stenosis



Small Airways:
Structural remodeling
- Mucus gland hyperplasia
- Epithelial injury, edema
- Smooth muscle proliferation
Bronchoconstriction
Hyperreactivity

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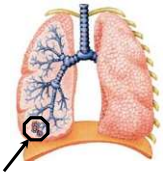
Respiratory Phenotypes in BPD: Parenchyma and Vasculature

- Alveolar simplification – less surface area for gas exchange
  - Stiff fibrotic scarred lung
  - Injured emphysematous lung
- Reduced / abnormal pulmonary vascular bed
  - Increased risk for pulmonary hypertension
- Ventilation strategy:
  - **Big tidal volume** due to airway and alveolar dead space
  - **Long inspiratory time** to fill the stiff lung compartments

Other:
- Control of breathing
- Sleep disordered breathing (OSA)
- Chest wall stability
- Diaphragmatic function



Distal Airspace and Vasculature:
- Decreased alveolarization, vascular growth
- Abnormal vascular remodeling, tone and reactivity
- Impaired lymphatic function, structure

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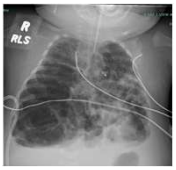
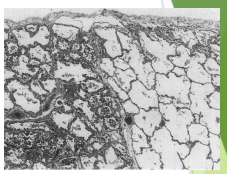
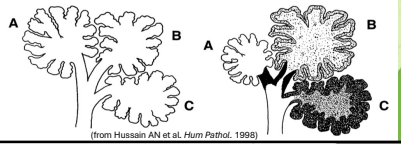
Regional Heterogeneity of Lung Disease in Severe BPD







(from Hussain AN et al. *Hum Pathol.* 1998)

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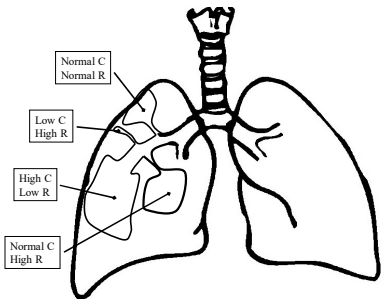
Respiratory Phenotypes in BPD: Airway

- R= resistance
  - High resistance results in increased difficulty moving air through the airways
- C= compliance
  - A floppy alveoli is difficult to empty and has high compliance
  - A stiff alveoli is difficult to fill and has low compliance
- Time constant = resistance x compliance
  - Indicates the time needed to fill or empty the alveoli



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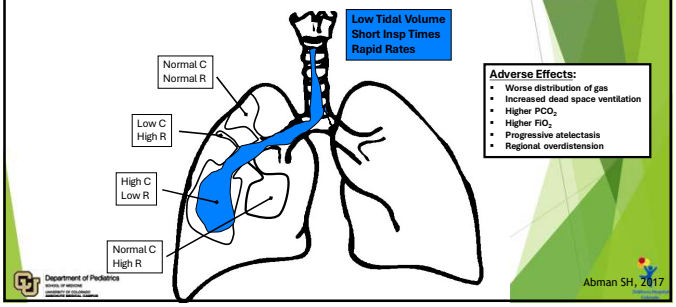
Effect of using acute ventilation in a baby with BPD



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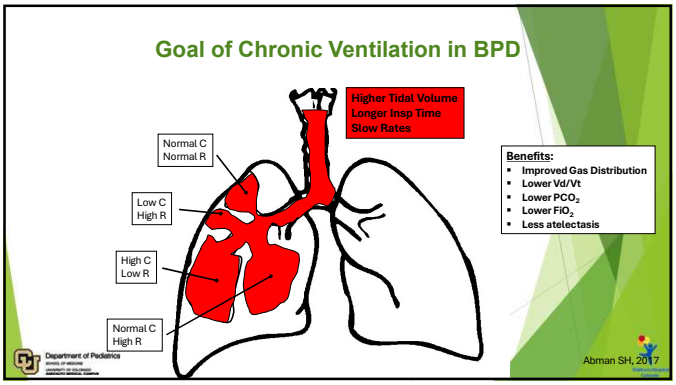
Goal of Chronic Ventilation in BPD



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Management of Ventilator-Dependent Infants with evolving and severe BPD

- Ventilation must be optimized to address the pulmonary function present in the damaged part of the lung.
- If only ventilating the little remaining healthy tissue- must compensate by absorbing the entire ventilatory load
- Slow ventilator adjustments over time as infant's lung injury develops and acute ventilator support settings become non physiologic.

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Goals of Transitional/Chronic Ventilation

Open Lung
Distribute the tidal ventilation evenly throughout the lungs

PEEP to maintain alveolar recruitment during exhalation.

Gradual Change

Ventilator adjustments over time that respond to the baby's current lung disease to deliver the support needed.

Stability and Growth

Must have patience

Minimize Injury

Volutrauma

Oxygen Toxicity

Atelectotrauma

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When should the transition occur?

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Poll Question #1

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When should the transition occur?

- Atelectasis
- Derecruitment
- Hyperexpansion
- Rising oxygen needs
- Rising CO_2
- Lability

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Risks of not fully supporting a baby with severe lung disease

Growth failure due to increased energy expenditure
- Growth correlates with lung growth

Intermittent hypoxemia: due to lability
- Risk factor for PH, ROP, neurodevelopmental impairment

Atelectotrauma: sheer trauma leads to inflammation and edema

Hypercapnia: due to ventilating only part of the lung
- Severe hypercapnia associated with PH, NEC, altered brain activity

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Risks of inadequate support: Steroid Use

- Steroids are one of the few postnatal medications that have been shown to decrease BPD[1,2,3] and aid in weaning from mechanical ventilation. [1,2,3,5]
- They are widely used in preemies
- "Late" steroid studies include use mostly in the first several weeks of life
- Systemic steroids are often used in patients with established BPD despite a paucity of data

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Risk of inadequate support: Steroid Use

Steroids impair lung development

Alveolar septation is inhibited and lung growth is diminished.[1] (Neonatal rat model).

Longer term use of steroids impairs linear growth

No improvement seen past 7 days in prolonged prednisolone course, only side effects.[2]

Steroids should be used judiciously for a brief period, with a short term goal in mind

Multiple courses or very prolonged use to avoid more supportive ventilation strategies has not been proven safe.

1. Tschanz et al 2002.
2. Linafelter et al 2019.

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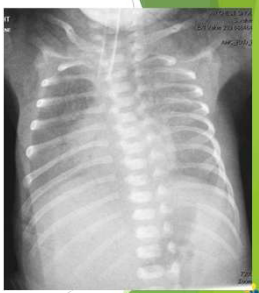
Clinical Case

41

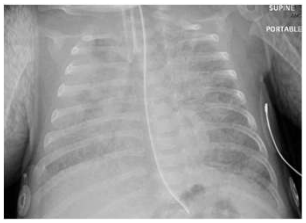
Twin boy B, early clinical course

- Twin boy born at 24 weeks, delivery due to placental abruption.
- NICU Course
  - Evolving chronic lung disease
  - Serratia and Stenotrophamonas tracheitis.
  - DART treatment course (started day 31)
  - Transitional ventilation at 8 weeks of age.
  - He remains on high FiO2 and is labile and “doesn’t like to be touched”.
  - transfer to Children’s Hospital Colorado.



42

Day of Transfer to SPROUT Team



- Day 56 (32+2 weeks)
- Hamilton Ventilator
- Tidal Volume 6.7ml/kg
- iTime 0.45
- Rate 20
- PEEP 10
- PS 10
- FiO2 82%
- CBG: 7.34/60

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Poll Question #2

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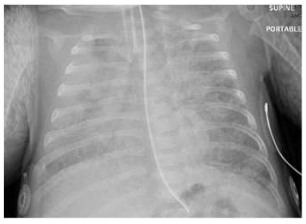
Day of Transfer to SPROUT Team



- Day 56 (32+2 weeks)
- Hamilton Ventilator
- Tidal Volume 6.7ml/kg→ 8ml/kg
- iTime 0.45 →0.5
- Rate 20
- PEEP 10 →8
- PS 10
- FiO2 82%
- CBG: 7.34/60

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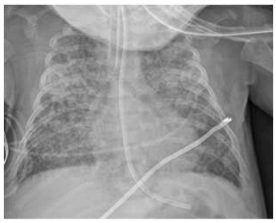
The next day on the SPROUT Team



- Day 57 (32+3 weeks)
- Servo Ventilator
- Tidal Volume 8 ml/kg
- iT 0.5
- Rate 20
- PEEP 8
- PS 10
- FiO2 68%
- CBG: 7.33/61

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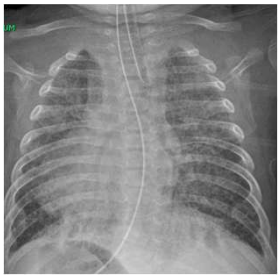
Now he is 39 weeks corrected

- Vt 8.5 ml/kg,
- rate 12
- PEEP 8
- PS 10
- FiO_2 25%
- Extubation goals?



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Poll Question #3

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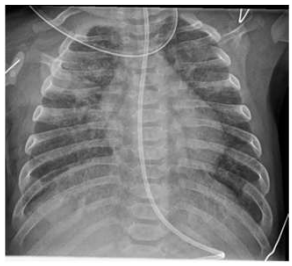
Final Course

- Transitioned to invasive NAVA to extubate
  - Started on NAVA level 1.5, PEEP 8, 26%
  - Weaned to NAVA level 1
- Extubated to NI-NAVA then weaned off positive pressure.
- Discharged at 5 months old, 48 weeks corrected
- Discharged on 0.1 lpm nasal cannula oxygen



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Family Engagement

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NICU SPROUT Welcome Meetings

- Pilot started in July of 2023
- How do we know when a patient is coming?
- Goal is to meet with the family within 24 hours of admission
- Currently being done with social work and charge nurse
- Documentation for the team

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Goals of Welcome Meeting
To help families adjust to a new NICU and hospital setting
Allow the family to share about their baby
To discuss and review communication preferences for the family
To establish expectations to support a collaborative relationship between the family and the NICU care providers
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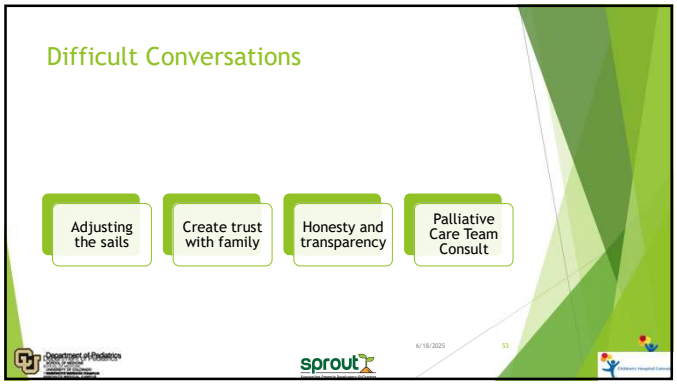
Difficult Conversations
Adjusting the sails
Create trust with family
Honesty and transparency
Palliative Care Team Consult
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6/18/2025
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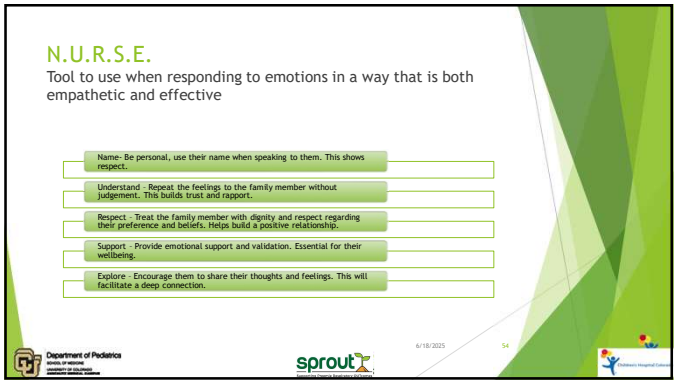
N.U.R.S.E.
Tool to use when responding to emotions in a way that is both empathetic and effective
Name- Be personal, use their name when speaking to them. This shows respect.
Understand – Repeat the feelings to the family member without judgement. This builds trust and rapport.
Respect – Treat the family member with dignity and respect regarding their preference and beliefs. Helps build a positive relationship.
Support – Provide emotional support and validation. Essential for their wellbeing.
Explore – Encourage them to share their thoughts and feelings. This will facilitate a deep connection.
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	Example	Notes
Naming	"It sounds like you are frustrated"	In general, turn down the intensity a notch when you name the emotion
Understanding	"This helps me understand what you are thinking"	Think of this as another kind of acknowledgment but stop short of suggesting you understand everything (you don't)
Respecting	"I can see you have really been trying to follow our instructions"	Remember that praise also fits in here eg "I think you have done a great job with this"
Supporting	"I will do my best to make sure you have what you need"	Making this kind of commitment is a powerful statement
Exploring	"Could you say more about what you mean when you say that…"	Asking a focused question prevents this from seeming too obvious

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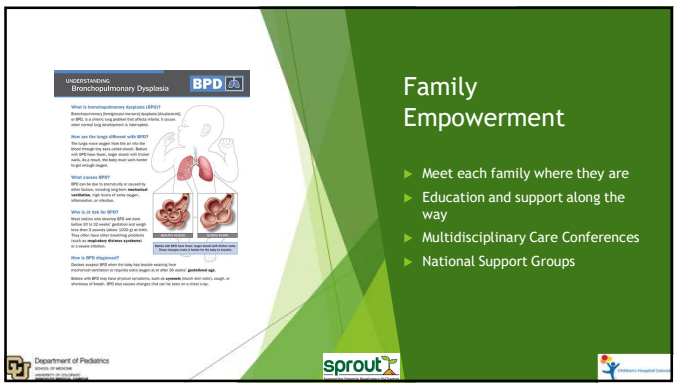

Family Empowerment

- Meet each family where they are
- Education and support along the way
- Multidisciplinary Care Conferences
- National Support Groups

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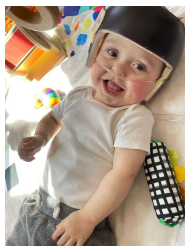
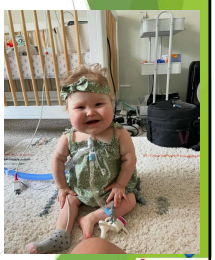
Discharge/Transfer Respiratory Support



Nasal Cannula 24/7	34%
Daytime nasal cannula, nighttime CPAP/BiPap	18%
Trach/Vent	39%



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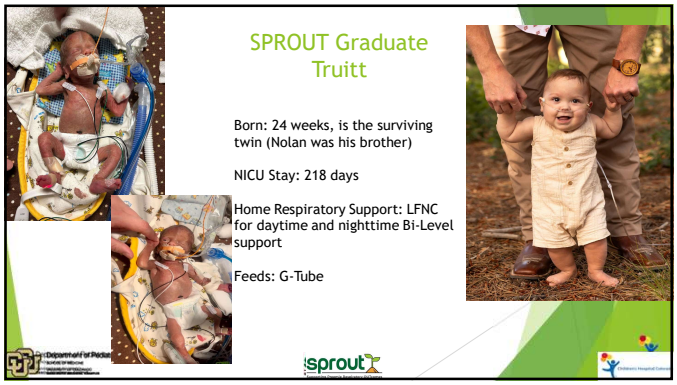
SPROUT Graduate
Truitt
Born: 24 weeks, is the surviving twin (Nolan was his brother)
NICU Stay: 218 days
Home Respiratory Support: LFNC for daytime and nighttime Bi-Level support
Feeds: G-Tube
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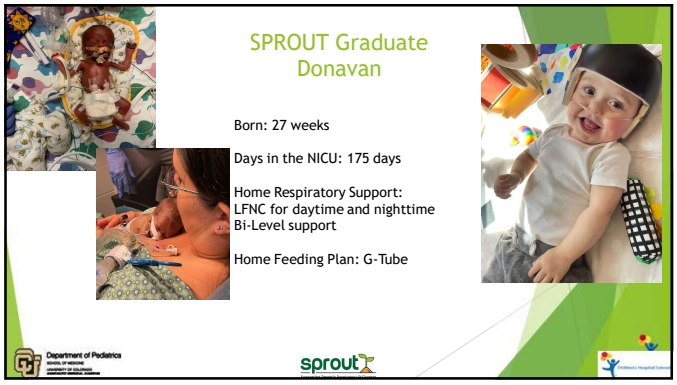
SPROUT Graduate
Donavan
Born: 27 weeks
Days in the NICU: 175 days
Home Respiratory Support:
LFNC for daytime and nighttime
Bi-Level support
Home Feeding Plan: G-Tube
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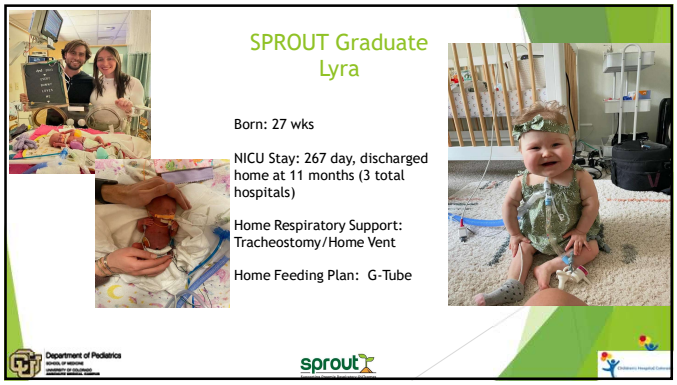
60


SPROUT Graduate
Lyra
Born: 27 wks
NICU Stay: 267 day, discharged home at 11 months (3 total hospitals)
Home Respiratory Support: Tracheostomy/Home Vent
Home Feeding Plan: G-Tube
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It takes a village to support the babies and families!
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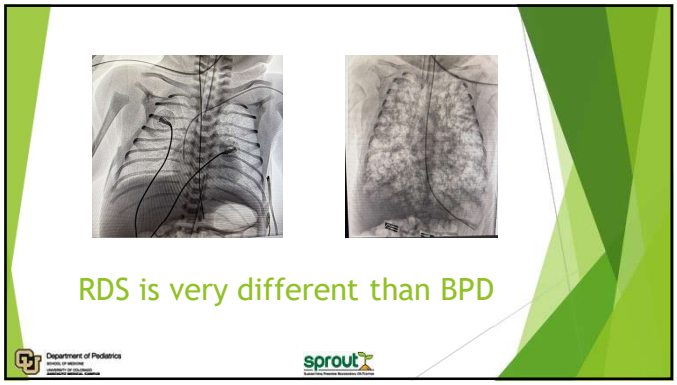
RDS is very different than BPD
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NEONATAL TELEMEDICINE

VALERIE BEASCOCHEA, APRN, NNPC-BC

1

NEONATAL TLEMEDICINE

2

3

KEY OBJECTIVES

Telemedicine history and advancements

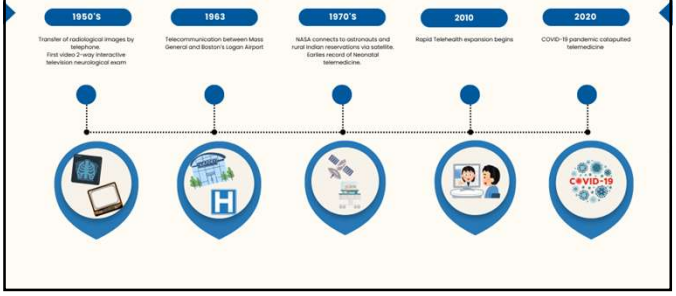
Telemedicine barriers

APP role in telemedicine

Is the telemedicine APP role right for you

4

TELEMEDICINE TIMELINE



5

CURRENT TELEMEDICINE

- Change in video Teleconferencing for critically ill infants
- Increased collaboration between rural communities and tertiary centers
- Telemedicine helps address the problem of decreased neonatal providers to rural communities
- Rural providers must have a multitude of skills

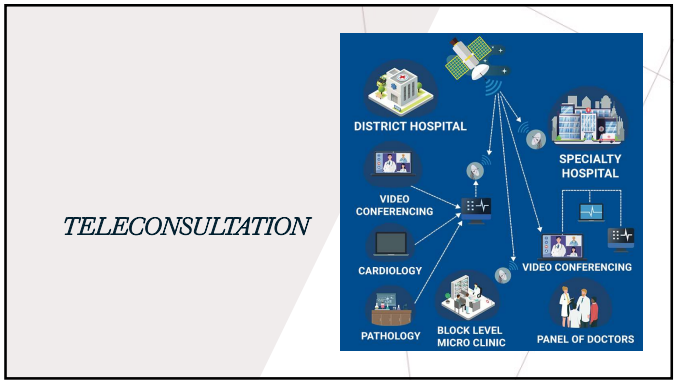
6


TELEPRACTICE
TELECONSULTATIONS
NEONATAL TELE-RESUSCITATION PROGRAMS
TELERESEARCH
TYPES OF NEONATAL TELEMEDICINE

7


TELEPRACTICE

8


TELECONSULTATION
DISTRICT HOSPITAL
SPECIALTY HOSPITAL
VIDEO CONFERENCING
CARDIOLOGY
VIDEO CONFERENCING
PATHOLOGY
BLOCK LEVEL MICRO CLINIC
PANEL OF DOCTORS

9

TELECARDIOLOGY IN THE NICU

10

TELENEUROLOGY IN THE NICU

11

TELERESEARCH

12

NEONATAL TELE-RESUSCITATION

(a) (b)

13

TeleROP SCREENING IN NICU

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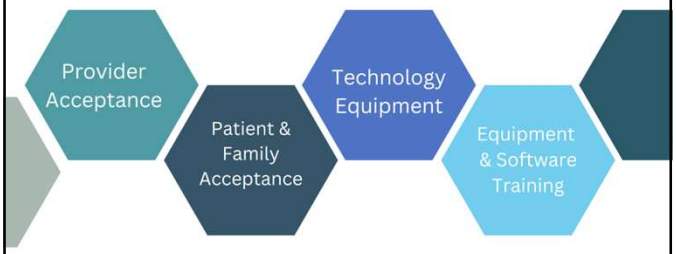
Telemedicine Barriers



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TELEMEDICINE REIMBURSEMENT
The 2 Types of Payers

Public Payer	Private Payer
Medicare Medicaid	Private insurance

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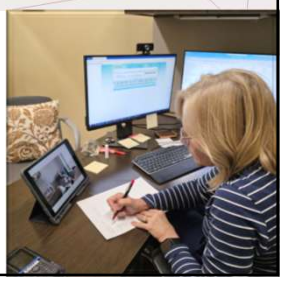
NEONATAL TELEMEDICINE FACTS

- Lack of specialized neonatal care in rural America
- Provider shortage
- Tele-NICU



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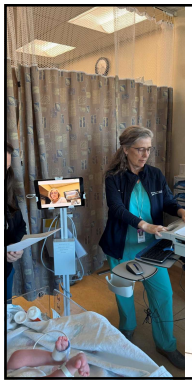

APP ROLE IN TELE-NICU

- Tele-NICU care
- Tele-NICU levels and patient population
- Different model types
- APP responsibilities in NICU and throughout hospital
- Educating nursing staff
- Experience

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TRANSPORT
CHALLENGES
IN RURAL
NICUS

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CONCLUSION

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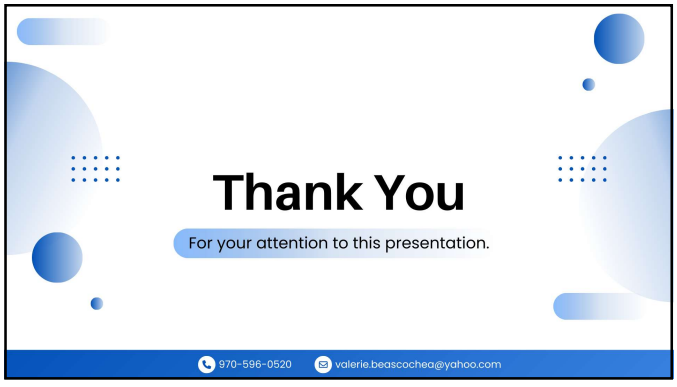
Thank You
For your attention to this presentation.
970-596-0520
valerie.beascochea@yahoo.com

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DISCUSSION AND QUESTIONS

22

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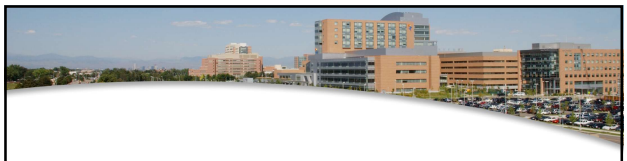

Neonatal Surgical Emergencies

Children's Hospital Colorado
Affiliated with University of Colorado Anschutz Medical Campus

Caroline Credille, MSN PNP-AC
Instructor, Division of Pediatric Surgery
Department of Surgery
University of Colorado School of Medicine
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1

I have no affiliations or disclosures to report

2

2

Goals

Increase comfort and confidence in recognizing and diagnosing surgical emergencies in the neonatal patient

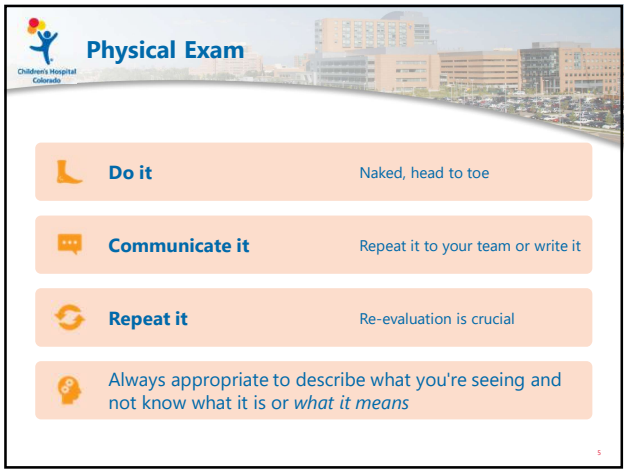
Improve initial management of surgical emergencies during the diagnostic period

3

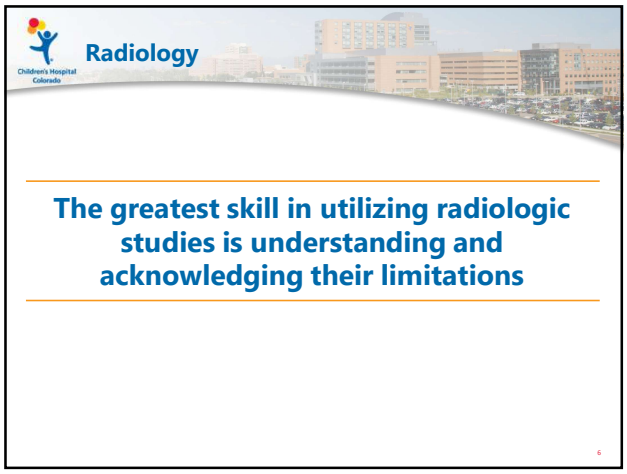
3


Priorities
HISTORY
EXAM
COMMUNICATION
RADIOLOGY
4

4


Physical Exam
Do it
Naked, head to toe
Communicate it
Repeat it to your team or write it
Repeat it
Re-evaluation is crucial
Always appropriate to describe what you're seeing and not know what it is or what it means
5

5


Radiology
The greatest skill in utilizing radiologic studies is understanding and acknowledging their limitations
6

6

Surgical Pathology

- **Obstruction**
  - Volvulus
  - Atresia
  - Web
  - Meconium
  - Mass
  - Hernia
  - Anorectal Malformations
- **Infection**
  - Initial
  - Sequalae
- **Perforation**
  - Air and stool

7

7

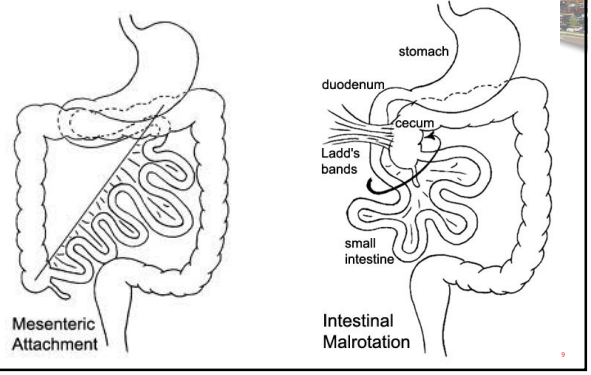
Obstruction – Malrotation/Volvulus

Presentation:	Bilious emesis
	Irritability or lethargy
	Abdominal distention
	Abdominal tenderness
Goals of care:	Proximal decompression for prevention of perforation
	Emergent imaging (XR, US, UGI)
	Transfer/Surgical detorsion

8

8

Obstruction – Malrotation/Volvulus



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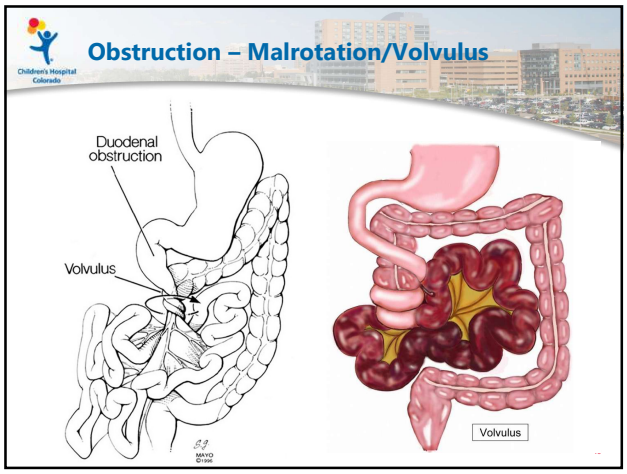
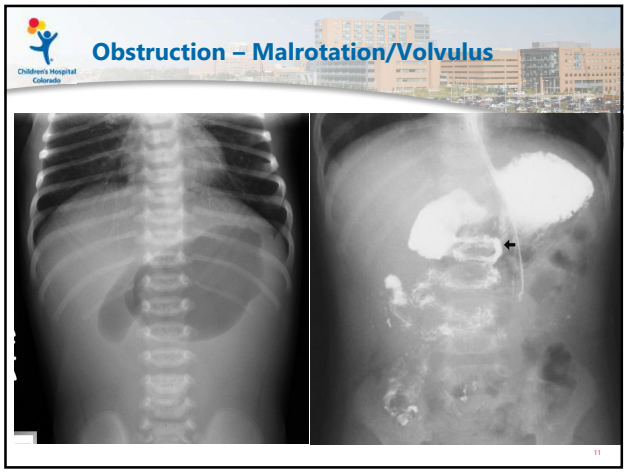
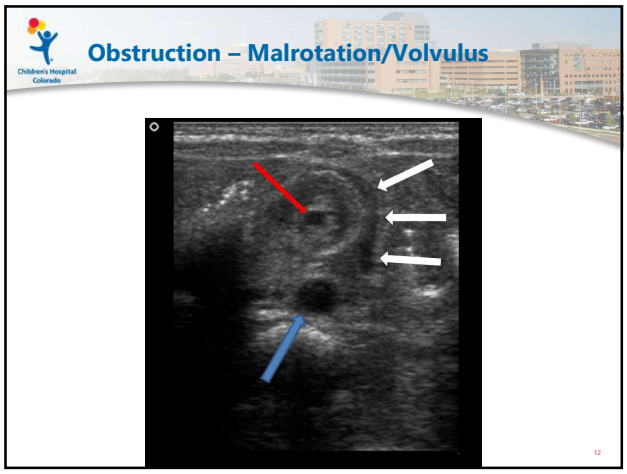

Obstruction – Malrotation/Volvulus
Duodenal obstruction
Volvulus
Volvulus

10


Obstruction – Malrotation/Volvulus

11


Obstruction – Malrotation/Volvulus

12

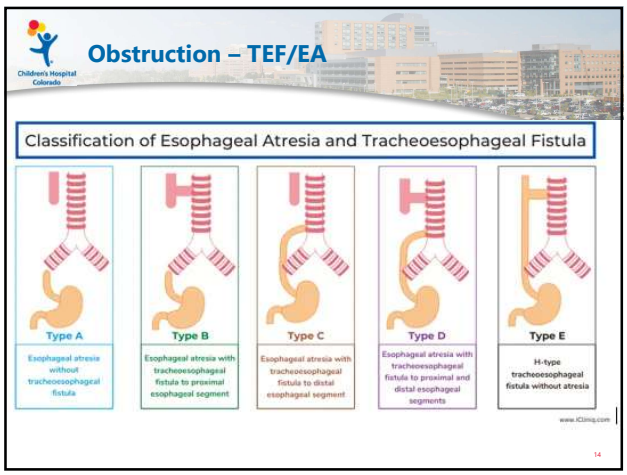
Obstruction – TEF/EA

Presentation:	Respiratory distress or failure
	Intolerance of secretions or hypersecretory
	Coughing, gagging and retching of saliva
	Early intolerance of PO feeds
	Inability to pass OG
	Dilated gastric lumen
Goals of care:	Protection of proximal pouch
	Protection of airway
	Monitor abdominal distention
	Eval for additional GI obstructions

13

13

Obstruction – TEF/EA



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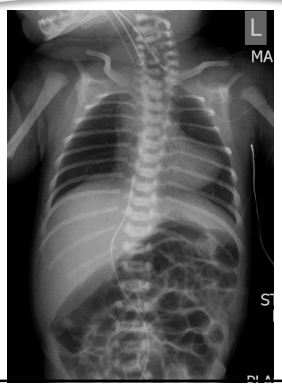
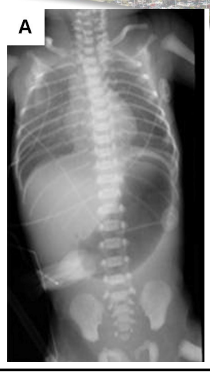
Obstruction – TEF/EA





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Obstruction - Duodenal Atresia

Presentation:	Bilious emesis
	Abdominal distention
	Intolerance of feedings
	Double bubble without distal air
Goals of Care:	Decompression of proximal GI tract
	Prevention of perforation

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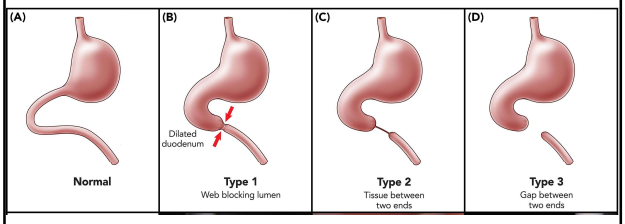
Obstruction - Duodenal Atresia



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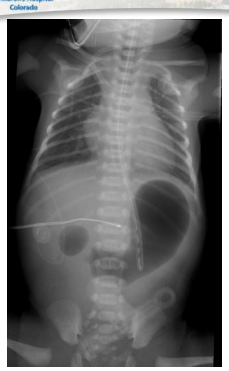
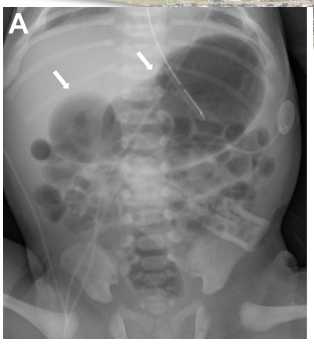
Obstruction – Duodenal Atresia/Web





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18

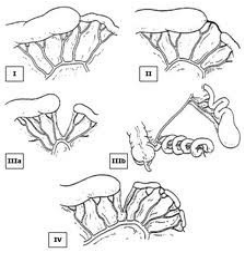
Obstruction– Jejunal/Ileal Atresia

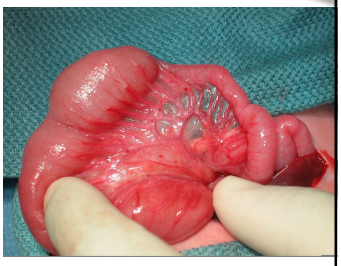
Presentation:	Emesis, bile or partially digested feed
	Feeding intolerance
	Abdominal distention
	Delayed passage of meconium
Goals of Care:	Proximal bowel decompression
	Prevention of perforation
	NPO to prevent infection

19

19

Obstruction– Jejunal/Ileal Atresia





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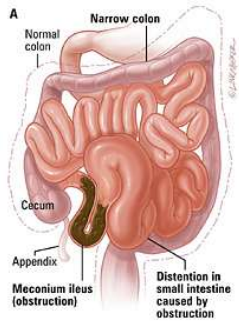
Obstruction – Meconium Ileus

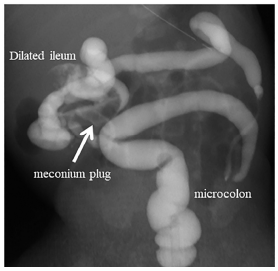
Presentation:	Failure to pass stool in the first 24-72 HOL
	Vomiting
	Abdominal distention
	Diagnosis of cystic fibrosis on prenatal screens
Goals of Care:	Removal of inspissated meconium
	Prevention of proximal bowel dilation and perforation

21

21

Obstruction – Meconium Ileus





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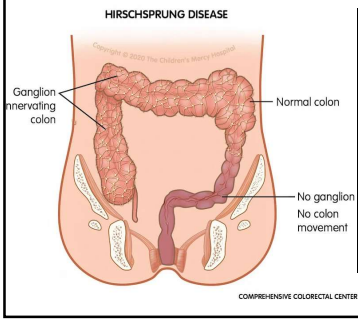
Obstruction - Hirschsprung Disease

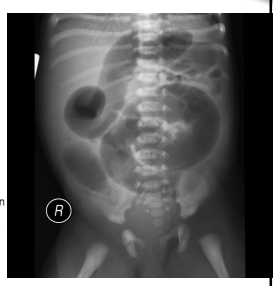
Presentation:	Failure to pass meconium in the first 48 HOL
	Abdominal distention
	Vomiting
	Explosive stool
	Sepsis/enterocolitis
Goals of Care:	Evacuation of stool
	Prevention of infection/perforation
	Enteral feeding

23

23

Obstruction - Hirschsprung Disease





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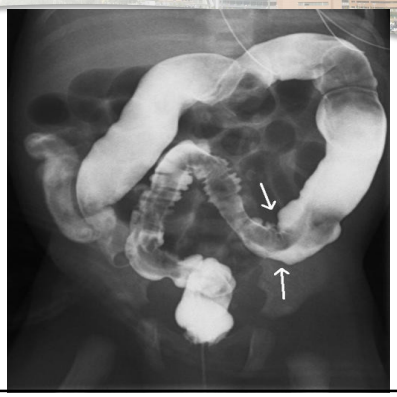
Obstruction - Hirschsprung Disease



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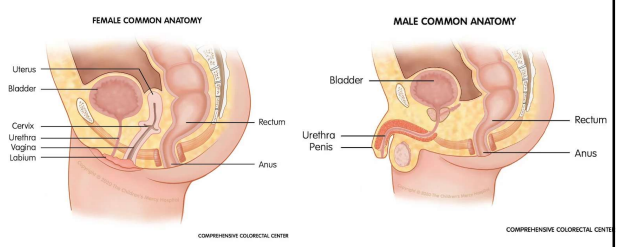
Obstruction – Anorectal Malformation

Presentation:	Failure to pass meconium in the first 48 HOL
	Abdominal distention
	Abnormal GU and rectal exam
Goals of Care:	Decompression of proximal bowel
	NPO if not passing stool
	Prevention of infection and perforation

26

26

Obstruction – Anorectal Malformation



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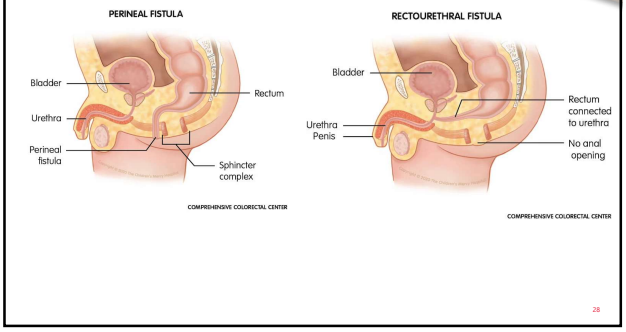
Obstruction – Anorectal Malformation



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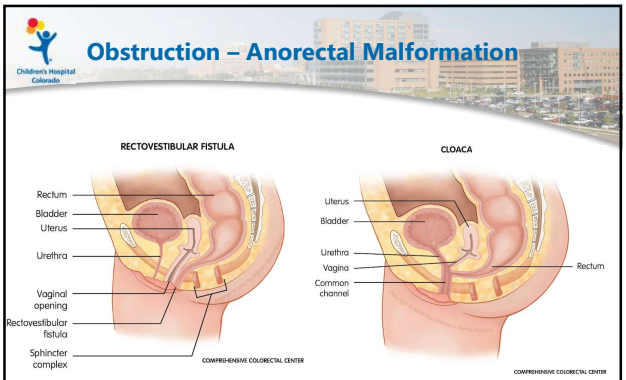
Obstruction – Anorectal Malformation



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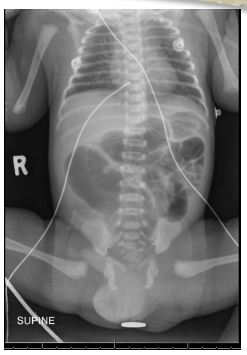
Obstruction – Anorectal Malformation



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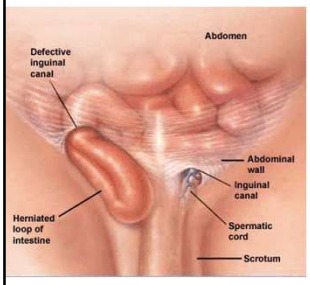
Obstruction – Hernia (Inguinal)

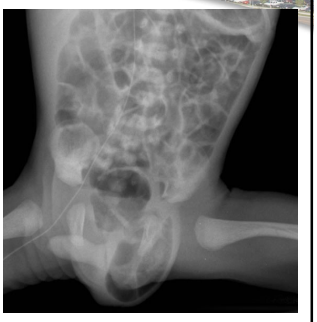
Presentation:	Enlarged groin area
	Difficulty stooling, straining
	Incarcerated:
	Abdominal distention
	Vomiting
	Systemic illness
	Evidence of necrosis or perforation
Goals of Care	Bowel decompression
	Restoration of perfusion
	Reduction of herniated bowel

31

31

Obstruction – Hernia (Inguinal)





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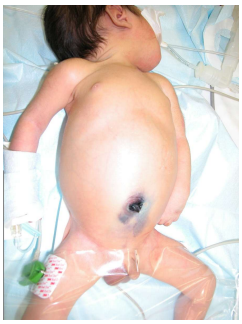
Infection - NEC

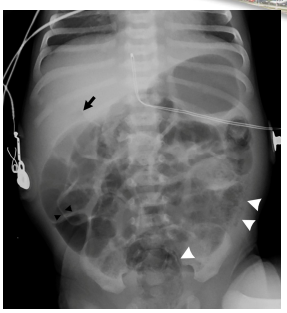
Presentation:	Bloody stools
	Emesis
	Abdominal distention
	Systemic illness
Goals of Care:	NPO
	Antibiotics
	Prevention of perforation

33

33

Infection – NEC





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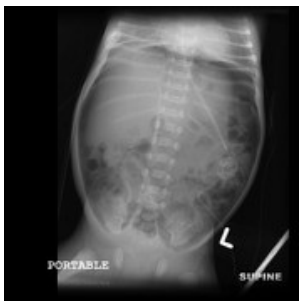
Perforation

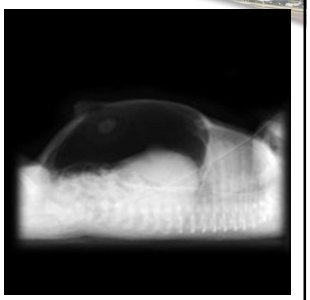
Presentation:	Current NEC infection?
	Abdominal distention
	Abdominal tenderness
	Abdominal wall discoloration
	Irritability
Goals of Care:	NPO
	Bowel decompression
	Gram negative antibiotic coverage

35

35

Perforation





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36

A very special thank you to Dr. Kristine Corkum and Dr. Tom Rauth for their guidance and support around the development of this presentation

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QUESTIONS?

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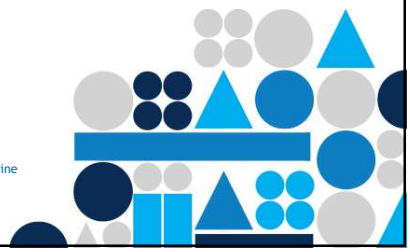
38

JUNE 19, 2025

Neonatal Seizures

Andra Dingman MD
Associate professor of Child Neurology
University of Colorado School of Medicine
Children's Hospital Colorado



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Disclosures

I have no disclosures

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Learning Objectives

- Identify the most common causes of neonatal seizures
- Describe importance and different modes of seizure monitoring
- Understand the importance of treating seizures
- Identify most commonly used anti-seizure medications in neonates and emerging therapies.
- Understand the importance of minimizing medication use and appropriate timing of stopping medication.

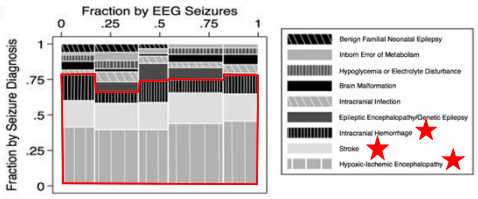
3

Neonatal Seizure Incidence and Causes

Neonatal seizures are common and estimated to occur in 1-3.5/1000 live births[1,2]

Most common etiologies include:

- **HIE (hypoxic ischemic encephalopathy) – 38%**
- **Arterial or venous ischemic stroke – 18%**
- **Intracranial hemorrhage - 12%**
- Neonatal epilepsy – 13%
- Infection - <5%
- Brain malformation - <5%
- Transient metabolic disturbance - <5%



Glass HC, Shellhaas RA, Wusthoff CJ; Neonatal Seizure Registry Study Group. Contemporary Profile of Seizures in Neonates: A Prospective Cohort Study. J Pediatr. 2016 Jul;174:98-103.e1. doi: 10.1016/j.jpeds.2016.03.035. Epub 2016 Apr 19. PMID: 27106855; PMCID: PMC4925241.

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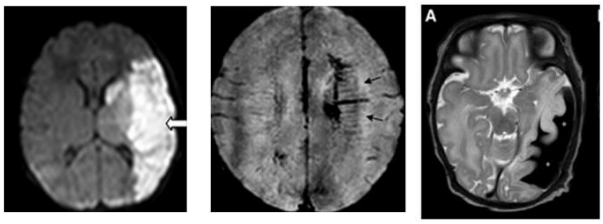
Arterial ischemic stroke | Hemorrhagic venous infarction | Subpial hemorrhage



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Intracranial Hemorrhage and Neonatal Seizures

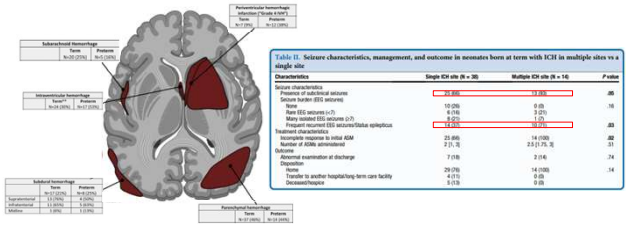


Table II. Seizure characteristics, management, and outcome in neonates born at term with ICH in multiple sites vs a single site

Characteristics	Single ICH site (N = 38)	Multiple ICH site (N = 14)	*P* value
Seizure characteristics			
Presence of subclinical seizures	34 (89)	13 (93)	.95
Seizure burden (EEG seizures)			
None	10 (26)	0 (0)	.16
Rare EEG seizures (<7)	6 (16)	3 (21)	
Many isolated EEG seizures (≥7)	8 (21)	1 (7)	
Frequent recurrent EEG seizures/Status epilepticus	14 (37)	10 (71)	.03
Treatment characteristics			
Complete response to initial ASM	25 (66)	14 (100)	.02
Number of ASMs administered	2 [1, 3]	2.5 [1.75, 3]	.33
Outcome			
Abnormal examination at discharge	7 (18)	3 (14)	.74
Disposition			
Home	29 (78)	14 (100)	.14
Transfer to another hospital/long-term care facility	4 (11)	0 (0)	
Deceased/hospice	5 (13)	0 (0)	

Herzberg EM, Machie M, Glass HC, et al. Seizure Severity and Treatment Response in Newborn Infants with Seizures Attributed to Intracranial Hemorrhage. J Pediatr. 2022 Mar;242:121-128.e1. doi: 10.1016/j.jpeds.2021.11.012. Epub 2021 Nov 13. PMID: 34780777.

6

Signs of Neonatal Seizures

- Encephalopathy
- Focal clonic movements*
- Unexplained Apnea
- Bicycling or swimming movements
- Forced gaze deviation
- Repetitive myoclonus

7

How Reliable are Clinical Signs for Diagnosing Seizures?

8

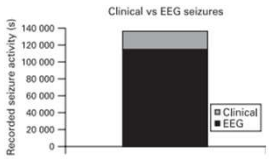
Defining the gap between electrographic seizure burden, clinical expression and staff recognition of neonatal seizures

D M Murray,[1] G B Boylan,[1] I Ali,[1] C A Ryan,[1] B P Murphy,[1] S Connolly[2]

- cEEG monitoring of 52 infants at risk for seizures (most had HIE)
- Clinical staff marked suspected seizures on a bedside chart.
- Compared cEEG to video and clinical seizure log.

9

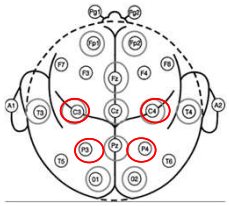
- 526 electrographic seizures
- 34% had any clinical sign when analyzing the cEEG video
- Only 9% were recognized by staff.
- Only 48% of clinically suspected seizures were actually electrographic seizures.

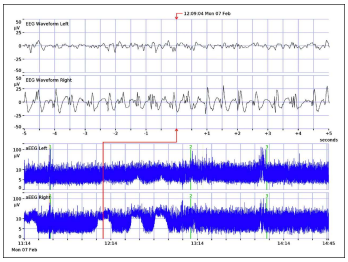


Murray, D. et al. 2008. *Archives of Disease in Childhood - Fetal and Neonatal Edition*. 93, 3 (2008), F187–F191.

10

What about aEEG?





11

What about aEEG?

- 35 neonates monitored with both cEEG and aEEG.
- 169 seizures captured by cEEG
- aEEG had a sensitivity of 33.7% for seizures.
- 50% of patients identified by aEEG as having seizures did not have any electrographic seizures.
- aEEG has limited sensitivity and specificity for seizures.

Rakshasbhuvankar, Abhijeet et al. *Journal of child neurology* vol. 32,9 (2017): 815-822.

12

American Clinical Neurophysiology Society (ACNS) Recommendations

- Neonates at **high risk for seizures** should be monitored with conventional EEG for **24 hours** to screen for seizures
  - A 1-hour EEG is considered inadequate to screen for seizure
- If seizures are detected, EEG monitoring should continue until the patient has been found to be **seizure-free for at least 24-hours** (unless in consultation with a neurologist a decision is made to discontinue monitoring earlier)
- EEG monitoring for the differential diagnosis of suspicious clinical events should continue until multiple typical events are captured

Shellhaas RA, Chang T, Tsuchida T, Scher MS, Riviello JJ, Abend NS, Nguyen S, Wusthoff CJ, Clancy RR. The American Clinical Neurophysiology Society's Guideline on Continuous Electroencephalography Monitoring in Neonates. J Clin Neurophysiol. 2011 Dec;28(6):611-7. doi: 10.1097/WNP.0b013e31823e96d7. PMID: 22146359.

13

Newborn Brain Society Recommendations

- Neonates at high risk for seizures, including those with encephalopathy should undergo cEEG monitoring for at least 24 hours.
- In neonates undergoing therapeutic hypothermia cEEG monitoring during cooling and rewarming should be considered.

El-Dib M, Abend NS, Austin T, et al. Neuromonitoring in neonatal critical care part I: neonatal encephalopathy and neonates with possible seizures. *Pediatr Res*. 2023;94(1):64-73. doi:10.1038/s41390-022-02393-1

14

cEEG Background Information

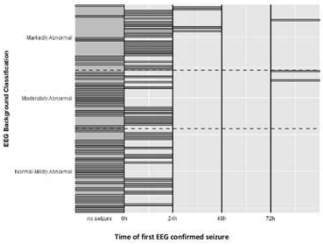
- EEG background features can be classified as “normal”, or as “mild”, “moderate” or “severe” encephalopathy.
- Infants with normal EEG tracings within the first 24 hours have generally good outcomes, while those with severely abnormal or inactive EEGs in the first 24 hours have generally poor outcomes
- In addition, early EEG may also provide information about which neonates are at highest risk for seizures

Murray DM, O'Connor CM, Ryan CA, Korotchikova I, Boylan GB. Early EEG Grade and Outcome at 5 Years After Mild Neonatal Hypoxic Ischemic Encephalopathy. Pediatrics. 2016 Oct;138(4):e20160659. doi: 10.1542/peds.2016-0659. Epub 2016 Sep 20. PMID: 27650049.

15

Can EEG background predict seizures?

- EEGs performed on 114 term or near-term infants undergoing therapeutic hypothermia for HIE: majority of seizures (88%) occurred during the first 24 hours of recording



Benedetti GM, Vartanian RJ, McCaffery H, Shellhaas RA. Early Electroencephalogram Background Could Guide Tailored Duration of Monitoring for Neonatal Encephalopathy Treated with Therapeutic Hypothermia. J Pediatr. 2020 Jun;221:81-87.e1. doi: 10.1016/j.jpeds.2020.01.066. Epub 2020 Mar 25. PMID: 32222256.

16

Can early EEG background predict seizures?

- Infants with a **normal or mildly abnormal** EEG background either had seizure onset within the first 24 hours or never developed seizures
- 4 patients had seizure onset between 24 and 48 hours
  - All had **markedly abnormal initial** EEG backgrounds
- 3 patients had seizure onset beyond 72 hours
  - All had **moderate or severely abnormal** early continuous video EEG backgrounds and ultimately found to have clinical characteristics **atypical for HIE**

Benedetti GM, Vartanian RJ, McCaffery H, Shellhaas RA. Early Electroencephalogram Background Could Guide Tailored Duration of Monitoring for Neonatal Encephalopathy Treated with Therapeutic Hypothermia. J Pediatr. 2020 Jun;221:81-87.e1. doi: 10.1016/j.jpeds.2020.01.066. Epub 2020 Mar 25. PMID: 32222256.

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Practice Recommendations

- Based on these results, the authors recommended that infants with a **normal** or **mildly abnormal** EEG background in the first 24 hours of recording be only monitored **for 24 hours**
- Additional recommendation that infants with a **moderately or severely abnormal** early EEG background should be monitored **throughout cooling and rewarming** due to the higher risk of seizure onset beyond 24 hours

Benedetti GM, Vartanian RJ, McCaffery H, Shellhaas RA. Early Electroencephalogram Background Could Guide Tailored Duration of Monitoring for Neonatal Encephalopathy Treated with Therapeutic Hypothermia. J Pediatr. 2020 Jun;221:81-87.e1. doi: 10.1016/j.jpeds.2020.01.066. Epub 2020 Mar 25. PMID: 32222256.

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Background classificatin

Figure 1: Neonatal EEG Grading Scale, adapted from Benedetti, et al 2020.

EEG characteristics	Normal or mildly abnormal background	Moderately abnormal background	Markedly abnormal background
Continuity	Wakefulness and active sleep: continuous Quiet sleep: IBI < 7 s	Quiet Sleep: IBI 7-15 s	Discontinuous with IBI > 15 s
Amplitude	Wakefulness and active sleep: 25-50 μV Quiet sleep: some < 25 μV but often ≥ 25 μV	Wakefulness and active sleep: 5-15 μV Quiet sleep: 10-25 μV, some IBIs < 10 μV	< 10 μV
Symmetry	Symmetric	May be asymmetric	May be asymmetric
Synchrony	Synchronous with no more than rare asynchronous bursts in quite sleep	Persistent asynchrony during discontinuous segments	Persistent asynchrony
State cycling	Spontaneous state cycling	Poor state modulation	No state cycling
Reactivity	Reactive to external stimulation	Inconsistent response to external stimuli	Nonreactive
Normal graphoelements	Contains an age-appropriate admixture of frequencies and normal graphoelements	Paucity of normal features	No normal graphoelements
Epileptiform abnormalities	None or mildly excessive negative sharps	Excessive negative sharps and/or BRDs	Excessive negative sharps and/or BRDs

19

To treat or not to treat??

Do neonatal seizures cause additive injury to the brain??

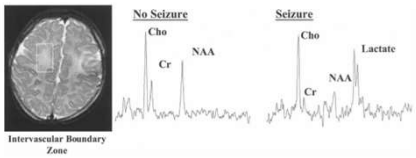
Do neonatal seizures contribute to poor developmental outcomes??

Do antiseizure medications contribute to poor outcome??

20

Seizures may exacerbate acquired brain injury

- Increased Lactate and decreased NAA in watershed zones in babies with more severe seizures.



Miller et al. 2002. *Neurology*. 58, 4 (2002), 542–54

21

Neurodevelopmental Outcome and Neonatal Seizures

- Studies demonstrate reduced neurodevelopmental outcomes associated with seizures even after controlling for severity of injury
- Neonates with severe neonatal seizures had an average 29.7-point lower adjusted FSIQ score (95% CI = -45.2 to -14.2) and those with mild/moderate seizures had a 14.2-point lower FSIQ (95% CI = -26.5 to -1.9)
- Children with neonatal seizures also more likely to have an abnormal neurological exam at 4 years after controlling for severity of injury

Table III. WPPSI-R FSIQ score at age 4 years by seizure severity in 77 children at risk for perinatal hypoxic-ischemic brain injury

FSIQ score, mean (95% CI)	Severe seizures (n = 11)	Mild/moderate seizures (n = 14)	No seizures (n = 52)	P*
Unadjusted	64.7 (52.6 to 76.9)	83.1 (72.4 to 93.9)	100.2 (94.6 to 105.8)	< .0001
Adjusted†	67.2 (54.8 to 79.8)	82.7 (72.7 to 92.7)	96.9 (90.7 to 103.1)	.001

*F-test.
†Scores were adjusted for the severity of brain injury as determined by basal nuclei and watershed injury measurements on MRI.

Glass HC, Glidden D, Jeremy RJ. Clinical Neonatal Seizures are Independently Associated with Outcome in Infants at Risk for Hypoxic-Ischemic Brain Injury. J Pediatr. 2009 Sep;155(3):318-23. doi: 10.1016/j.jpeds.2009.03.040. Epub 2009 Jun 21. PMID: 19540512; PMCID: PMC3014109.

22

Question: Does cEEG improve outcome?

Treating EEG Seizures in Hypoxic Ischemic Encephalopathy: A Randomized Controlled Trial

Preethi Srinivasakumar, MD*, John Zempel, MD, PhD*, Shumik Trivedi, MD*, Michael Wallendorf, PhD*, Rakesh Rao, MD*, Barbara Smith, R.EEG T*, Terrie Inder, MD*, Amit M. Mathur, MD*

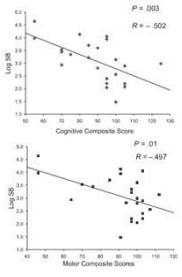
- 69 infants with HIE
- cEEG in all infants through rewarming
- Randomized to treating electrographic seizures (ESG), or only treating clinical seizures (CSG).
- Infants who developed status epilepticus in either group were unblinded and treated.
- Study powered to detect a difference in seizure burden.

Srinivasakumar et al. 2015. *PEDIATRICS*. 136, 5 (2015), e1302–e1309.

23

Question: Does cEEG improve outcome?

- 65% of infants developed electrographic seizure
- Seizure burden was much lower in ESG group.
- Time to seizure treatment was significantly lower in ESG group.
- 18-24 month outcomes were not different between groups.
- When all patients were combined, lower motor and cognitive scores were all correlated with higher seizure burden.



Srinivasakumar et al. 2015. *PEDIATRICS*. 136, 5 (2015), e1302–e1309.

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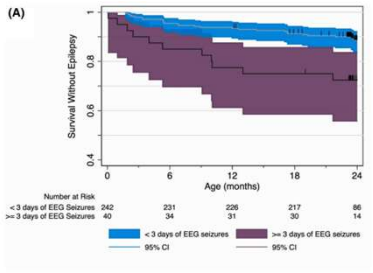
Neonatal Seizures and Future Epilepsy



Shellhaas RA, Wusthoff CJ, Numis AL, et al. Early-life epilepsy after acute symptomatic neonatal seizures: A prospective multicenter study. Epilepsia. 2021 Aug;62(8):1871-1882. doi: 10.1111/epi.16978. Epub 2021 Jul 2. PMID: 34212365.

25

ILAE Consensus guidelines

4.5 | Recommendation 5: Associations between seizure burden and outcome

Consensus-based recommendations

Treating neonatal seizures (including electrographic-only seizures) to achieve a lower seizure burden may be associated with improved outcomes (neurodevelopment, reduction of subsequent epilepsy).

Level of agreement: **Moderate.**

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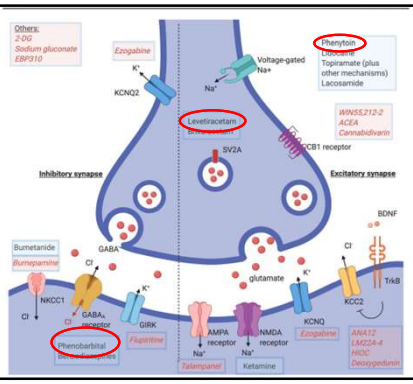
How Should Neonatal Seizures be Treated?

27

Neonatal Seizure – Sites of Action



Ziobro JM, Eschbach K, Shellhaas RA. Novel Therapeutics for Neonatal Seizures. Neurotherapeutics. 2021 Jul;18(3):1564-1581. doi: 10.1007/s13311-021-01085-8. Epub 2021 Aug 12. PMID: 34386906; PMCID: PMC8608938.

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Levetiracetam Versus Phenobarbital for Neonatal Seizures: A Randomized Controlled Trial

Cynthia Sharpe, MBChB,[a] Gail E. Reiner, DNP,[b] Suzanne L. Davis, MBChB, PhD,[c] Mark Nespeca, MD,[a] Jeffrey J. Gold, MD, PhD,[a] Maynard Rasmussen, MD,[c] Rachel Kuperman, MD,[a] Mary Jo Harbert, MD,[a] David Michelson, MD,[a] Priscilla Joe, MD,[a] Sonya Wang, MD,[a] Naggy Rismanchi, MD, PhD,[a] Ngoc Minh Le, MD,[a] Andrew Mower, MD,[a] Jae Kim, MD,[a] Malcolm R. Battin, MBChB,[d] Brian Lane, MD,[e] Jose Honold, MD,[f] Ellen Knodel, RCP,[g] Kathy Annell, RN,[a] Renee Bridge, BSN, RN,[f] Lilly Lee, BA,[a] Karin Ernstrom, MS,[a] Rema Raman, PhD,[a] Richard H. Haas, MB, BChir,[a] FOR THE NEOLEV2 INVESTIGATORS

Pediatrics, June 2020

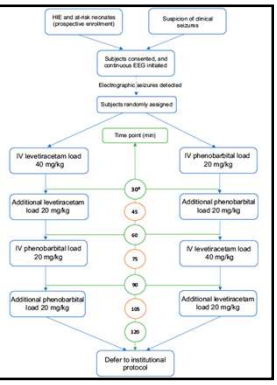

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TABLE 2 Prespecified Primary and Secondary Outcome Measures (Modified Intention-To-Treat Population)

	Phenobarbital (20–40 mg/kg), *n* (Cessation %)	Levetiracetam (40–60 mg/kg), *n* (Cessation %)	Fisher's Exact *P*	Relative Risk (95% CI)
Primary outcome measure				
24-h seizure cessation rate (*N* = 83)	24 of 30 (80)	15 of 53 (28)	<0.001	0.35 (0.22–0.56)
Secondary outcome measures				
48-h Seizure cessation rate (*N* = 75)	18 of 28 (64)	8 of 47 (17)	<0.001	0.26 (0.13–0.53)
1-h Seizure cessation rate (*N* = 83)	28 of 30 (93)	26 of 53 (49)	<0.001	0.53 (0.39–0.7)
Subanalysis of patients with HIE treated with hypothermia				
24-h seizure cessation rate (*N* = 27)	9 of 10 (90)	6 of 17 (35)	0.014	0.39 (0.2–0.77)

Sharpe et al, Pediatrics, June 2020

30

Care guidelines for neonatal seizures improve outcomes

- In one study implementing a protocol to treat neonatal seizures resulted in*:
  - Decreased maximum phenobarbital serum concentration
  - Decreased % of patients that progressed to status epilepticus.
  - Decreased length of hospital stay by 9.7 days.
- Decrease discrepancies in practice.
- Standardized, evidence based care.

*Harris, M. et al. 2016. *Journal of Child Neurology*. 31, 14 (2016), 1546–1554.

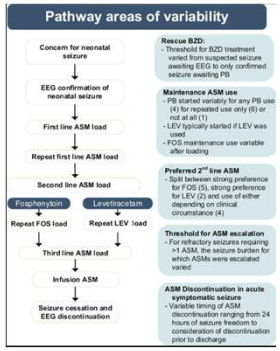
31

Comparison of 11 Neonatal Seizure Guidelines

- 9/11 started with a rescue benzodiazepine (midazolam or lorazepam)
- 11/11 used phenobarbital as the first line agent.
- 11/11 repeated phenobarbital for any seizures (9) or for a certain seizure threshold (2).
- 2nd line agent: 5/11 used fosphenytoin, 2/11 used levetiracetam.
- 3rd line agent: 8/11. Three recommended proceeding directly to midazolam drip.
- Drip: 11/11 recommended midazolam drip if 2nd/3rd line agents failed. Three included Lidocaine drip as an alternative.
- 9/11 recommended discontinuing anti-convulsants.
  - 3 within 48 hours
  - 1 within 5 days of injury
  - 4 prior to discharge
  - 1 within 2-4 weeks.

Keene JC, Morgan LA, Abend NS, et al. Treatment of Neonatal Seizures: Comparison of Treatment Pathways From 11 Neonatal Intensive Care Units. *Pediatr Neurol*. 2022;128:67-74.

32



Keene JC, Morgan LA, Abend NS, et al. Treatment of Neonatal Seizures: Comparison of Treatment Pathways From 11 Neonatal Intensive Care Units. *Pediatr Neurol*. 2022;128:67-74.

33

Can we minimize anti-seizure medication (ASM) usage?

Stopping ASMs does not increase risk of remote seizures.

- Retrospective study of 59 neonates with HIE who had follow up data available.
- 36% had electrographic seizures.
- 49% of those with seizures went home on ASMs.
- 11% with acute seizures had remote seizures.
- None of the patients discharged *without* ASMs had remote seizures.

Fitzgerald MP, Kessler SK, Abend NS. Early discontinuation of antiseizure medications in neonates with hypoxic-ischemic encephalopathy. *Epilepsia*. 2017;58(6):1047-1053. doi:10.1111/epi.13745

34

Why minimize anti-convulsant usage?

- In young rodents phenobarbital, phenytoin, vigabatrin, benzos and valproate all cause apoptosis (programmed cell death).
  - Bittigau, P. et al. 2002. *Proceedings of the National Academy of Sciences*. 99, 23 (2002), 15089–15094.
- Children treated for up to 2 years with Phenobarbital for febrile seizures had late cognitive impairment.
  - Sulzbacher, S. et al. 1999. *Clinical Pediatrics*. 38, 7 (1999), 387–394.
  - Farwell, J. et al. 1990. *The New England Journal of Medicine*. 322, 6 (1990), 364–369.
- Rodent studies suggest that phenobarbital may augment neuroprotective effect of hypothermia after HIE.
  - Barks, J. et al. 2010. *Pediatric Research*. 67, 5 (2010), 532–537.

35

Stopping Antiseizure Medications

- Recommend that maintenance antiseizure medications, if started, are discontinued 48 hours after seizure freedom.
- A longer course of anticonvulsant therapy can be used at the discretion of providers if the patient is considered high risk of recurrent seizures (eg CNS infection).

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Alternative Treatment Options

1. Lacosamide
2. Ketamine
3. Lidocaine

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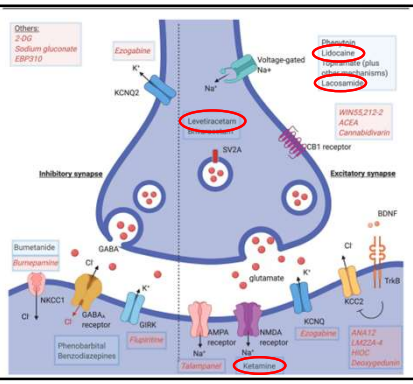
Neonatal Seizure – Sites of Action



Ziobro JM, Eschbach K, Shellhaas RA. Novel Therapeutics for Neonatal Seizures. Neurotherapeutics. 2021 Jul;18(3):1564-1581. doi: 10.1007/s13311-021-01085-8. Epub 2021 Aug 12. PMID: 34386906; PMCID: PMC8608938.

38

Lacosamide

- Lacosamide is a sodium-channel blocking agent with a novel mechanism through slow inactivation of voltage-gated sodium channels
- Rare reports of PR interval prolongation with IV administration in pediatrics
- Case reports regarding use in neonates but limited data
- Recently FDA approved for infants as young as 1 month
- Current phase 2/3 randomized clinical trial as second line therapy for the treatment of neonatal seizure (NCT04519645)
- Sodium-channel blocking medications can be helpful for certain genetic epilepsy syndromes

Ziobro JM, Eschbach K, Shellhaas RA. Novel Therapeutics for Neonatal Seizures. Neurotherapeutics. 2021 Jul;18(3):1564-1581. doi: 10.1007/s13311-021-01085-8. Epub 2021 Aug 12. PMID: 34386906; PMCID: PMC8608938.

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Lidocaine

- Often used second or third line – more commonly used in other countries
- Narrow dosing range with risk of cardiac arrythmia
- Metabolized by the liver cytochrome p450 system
- Seizure response reported to be approximately 50-70% - sustained seizure freedom in 20%

TABLE 1 Proposed lidocaine dosing regimen[33,34]

	Bolus		Loading phase		Maintenance phase I		Maintenance phase II	
Weight	Dose	Duration	Dose	Duration	Dose	Duration	Dose	Duration
Normothermia								
< 1.6 kg	2 mg/kg	10 min	5 mg/kg	4 h	2.5 mg/kg	12 h	1.25 mg/kg	12 h
1.6–2.6 kg	2 mg/kg	10 min	6 mg/kg	4 h	3 mg/kg	12 h	1.5 mg/kg	12 h
> 2.6 kg	2 mg/kg	10 min	7 mg/kg	4 h	3.5 mg/kg	12 h	1.75 mg/kg	12 h
Hypothermia								
< 2.5 kg	2 mg/kg	10 min	6 mg/kg	3.5 h	3 mg/kg	12 h	1.5 mg/kg	12 h
≥ 2.5 kg	2 mg/kg	10 min	7 mg/kg	3.5 h	3.5 mg/kg	12 h	1.75 mg/kg	12 h

Favié LMA, Huitema ADR, van den Broek MPH; Lidocaine as treatment for neonatal seizures: Evaluation of previously developed population pharmacokinetic models and dosing regimen. Br J Clin Pharmacol. 2020 Jan;86(1):75-84. doi: 10.1111/bcp.14136. Epub 2020 Jan 3.

40

Ketamine

- Non-competitive N-methyl-D-aspartate (NMDA) glutamate receptor antagonist
- During refractory status epilepticus:
  - Decrease in GABA receptor inhibition as GABA receptors internalize
  - Concentration of NMDA receptors increase
  - Further propagates seizure activity
- In animal models of status epilepticus ketamine may decrease neuroinflammation
- Recent retrospective study in pediatric patients including neonates with refractory status epilepticus
  - Seizure termination in 6/13 (46%)
  - Seizure reduction in 1/13 (8%)
  - No change in 6/13 (46%)

Jacobwitz M, Mulvihill C, Kaufman MC. Ketamine for Management of Neonatal and Pediatric Refractory Status Epilepticus. Neurology. 2022 Sep 20;99(12):e1227-e1238. doi: 10.1212/WNL.0000000000200889. Epub 2022 Jul 11. PMID: 35817569.

Ziobro JM, Eschbach K, Shellhaas RA. Novel Therapeutics for Neonatal Seizures. Neurotherapeutics. 2021 Jul;18(3):1564-1581. doi: 10.1007/s13311-021-01085-8. Epub 2021 Aug 12. PMID: 34386906; PMCID: PMC8608938.

41

What should you think about when there is not an acquired brain injury?

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Genetic Epilepsies Presenting in Neonates

- Benign Familial Neonatal Seizures
  - Seizures start in the first week of life (usually focal clonic seizures)
  - Inter-ictal EEG background is fairly normal
  - Autosomal dominant disorder, typically KCNQ2 mutation
  - Seizures stop by 4 months of age
  - Low risk of Later epilepsy.
- Early Infantile Epileptic Encephalopathy
  - Severely abnormal EEG background
  - Can also be due to KCNQ2 mutations, among others
  - Multiple seizure types
  - Incomplete response to ASMs.
  - Poor neurodevelopmental outcome

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Neonatal seizures due to metabolic disorders

- Early Infantile myoclonic epilepsy
  - Can be due to mitochondrial disorders, non-ketotic hyperglycinemia (NKH)
- Acute seizures due to hyperammonemia
  - Always check an ammonia when there is no identifiable cause of seizures!
- Pyridoxine dependent seizures
  - EEG background between seizures is very abnormal and improves significantly with a high dose pyridoxine (B6) challenge*.
  - Early initiation of oral pyridoxine is the treatment.
- Pyridoxal 5'—phosphate dependent epilepsy
  - Similar to Pyridoxine dependent epilepsy, but responds to PLP, a metabolite of B6.

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Conclusions

- Neonatal seizures are common and often provoked by acute brain injury
- Continuous EEG monitoring is the gold standard for evaluation of neonatal seizures
  - Recommended for neonates with clinical concern for seizures AND for neonates at high risk of seizures
- Neonatal seizures are associated with reduced neurodevelopmental outcomes even when controlling for extent of injury
- Phenobarbital is still the most effective first line therapy for neonatal seizures.
- Clinical pathway for neonates with acquired brain injury (provoked seizures) to improve timeliness of treatment and treatment with first-line therapy
- There are emerging treatment options currently being studied given incomplete efficacy of current antiseizure medication options

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