NECROTIZING ENTEROCOLITIS SYMPOSIUM

A Transdisciplinary Approach to Improved Outcomes

Conference Summary

April 5 - 7, 2017
On the UC Davis Campus

NEC SOCIETY

UCDAVIS CHILDREN'S HOSPITAL

Made possible by a Patient-Centered Outcomes Research Institute Engagement Award

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Introduction

The Necrotizing Enterocolitis Symposium was made possible by the NEC Society and was partially funded through a Patient-Centered Outcomes Research Institute (PCORI) Engagement Award Initiative (1517-NEC). The content does not necessarily represent the views of the Patient-Centered Outcomes Research Institute (PCORI), its Board of Governors, or Methodology Committee. The Symposium was also made possible by the UC Davis Department of Pediatrics and the NEC Society's incredible community of supporters. The 2017 NEC Symposium was the first meeting in North America to focus specifically on improved outcomes of necrotizing enterocolitis.

The NEC Society, a non-profit organization dedicated to reducing the incidence of necrotizing enterocolitis, is led by two mothers, Jennifer Canvasser and Erin Umberger, who each lost a child to necrotizing enterocolitis. The organization, established in 2014, prides itself on being transdisciplinary, as it strives towards improved NEC outcomes.

The NEC Society includes over 400 patient-family advocates from around the world, representing nearly all 50 U.S. states and 24 countries. These patient-family advocates were the driving force behind the 2017 NEC Symposium. Some of these families lost their child to NEC, while others have survivors, yet they all share one common experience: they had no idea what NEC was until their baby was dying, or nearly dying, from the disease. They were blindsided by the NEC diagnosis. Oftentimes, their baby was stable, even strong and healthy, and then within a matter of hours their baby was dead or critically ill. The NEC Society seeks to change this devastating experience.

The 2017 NEC Symposium was one of the NEC Society's first steps towards improved outcomes. The Symposium sought to drive change by sparking new collaborations, leading to impactful, measurable improved outcomes, through these four overarching goals:

1. **Review the current understanding of the pathogenesis, prevention and treatment of NEC.**
2. **Establish a transdisciplinary collaboration of stakeholders to accelerate the implementation and standardization of established evidence based practices that can help to reduce the incidence and morbidity of NEC.**
3. **Explore methods for empowering parents/families and supporting their engagement as part of their baby's care team.**
4. **Serve as a venue for researchers to create new collaborations and lines of investigation, including shared clinical databases and tissue banking.**

The NEC Symposium attracted a multidisciplinary audience of approximately 225 participants, including diverse clinicians, investigators, patient-family advocates, industry, nonprofits, and regulatory agencies from 30 U.S. states as well as Canada, Brazil, the United Kingdom and Sweden. The NEC Society would like to thank the following individuals and groups for their support:

- Dr. Mark Underwood and the UC Davis Department of Pediatrics for hosting the 2017 NEC Symposium.
- The NEC Symposium's Leadership Committee, who also serve on the NEC Society's Advisory Council: Dr. Jae Kim, Dr. Samir Gadepalli, Dr. Sheila Gephart, Dr. Steve McElroy, and Dr. Mickey Caplan.
- The NEC Society's Advisory Council members: Dr. Gail Besner, Dr. Ravi Patel, Dr. Troy Markel, Dr. Alex Penn and Dr. Amy Hair.
- The 2017 NEC Symposium faculty who so generously donated their time and expertise resulting in the meeting's success.
- The Patient-Family Advocates who provided their insight and whose precious babies were the inspiration behind the conference.

Appreciation

NICUniversity: The NEC Society is grateful for support from NICUniversity, a web-based medical education center for physicians, nurse practitioners, nurses, respiratory therapists, and pharmacists, dedicated to delivering the highest quality information designed to stimulate critical thinking and analysis of the current issues and trends in neonatology.

MEDNAX: The NEC Society is grateful for support from MEDNAX, a national health solutions partner specializing in neonatal, maternal-fetal, pediatric subspecialties, anesthesia and teleradiology. MEDNAX began as a single neonatology group in 1979, and while their company's focus has expanded, its commitment to preventing and improving the outcomes of necrotizing enterocolitis has remained a priority.

KicKee Pants: The NEC Society is grateful for support from KicKee Pants, a clothing company committed to creating the most buttery soft, whimsical clothing for babies, children and women. The company is well known for its philanthropic, generous nature, especially when it comes to the health of babies.

International Neonatal Consortium, NEC Workgroup

International Neonatal Consortium, NEC Workgroup
Facilitated by Michael Caplan, MD; Jennifer Canvasser, MSW

The International Neonatal Consortium (INC) was formed to accelerate the development of safe and effective therapies for neonates, and is organized by the Critical Path Institute (C-Path). C-Path is an independent, non-profit organization dedicated to bringing scientists from the FDA, industry and academia all together to collaborate and improve the drug development and regulatory process for medical products.

The INC NEC Workgroup was recently launched and held its first face-to-face meeting in conjunction with the NEC Symposium.

The INC NEC Workgroup has prioritized the following projects:

- Develop biomarkers for early diagnosis
- Clarify NEC definition and diagnosis

The INC NEC Workgroup is an on-going project of approximately 25 international NEC stakeholders. To learn more, please visit: www.c-path.org/programs/inc/

"After this conference, I will reduce anemia through fewer lab draws, encourage the use of human milk, and institute a NEC prevention checklist."
- Symposium attendee

"One of the best conferences I've been to. The ability to convene scientific researchers, families and health care providers is astounding and much appreciated."
- Symposium attendee

Session Dedication

The 2017 NEC Symposium integrated the patient-family experience in all aspects of the conference, including dedicated sessions, which served two purposes:

- Dedicated sessions provided families with a meaningful way to honor and celebrate their children.
- Dedicated sessions humanized and personalized the meeting by reminding participants about the critical importance and urgency of their work.

At the beginning of each dedicated session, faculty took a moment to show the child's photo, read the child's name, birthday and short quote from her/his family. These dedications were incredibly moving for both the families in attendance as well as the professional participants.

Dedicated sessions:

Micah Canvasser
Human Milk and NEC

Hope Marie Luchsinger
Innate Immunity and NEC

Antonio Rosito Robyn
Treatment Options for NEC

Brooks Hamilton Cossey
NEC and Stem Cell Therapy

Noah Michael Propst
Probiotics and NEC

Emily Specht
Animal Models of NEC

Grayson Kapferer
NEC Clincial Trials

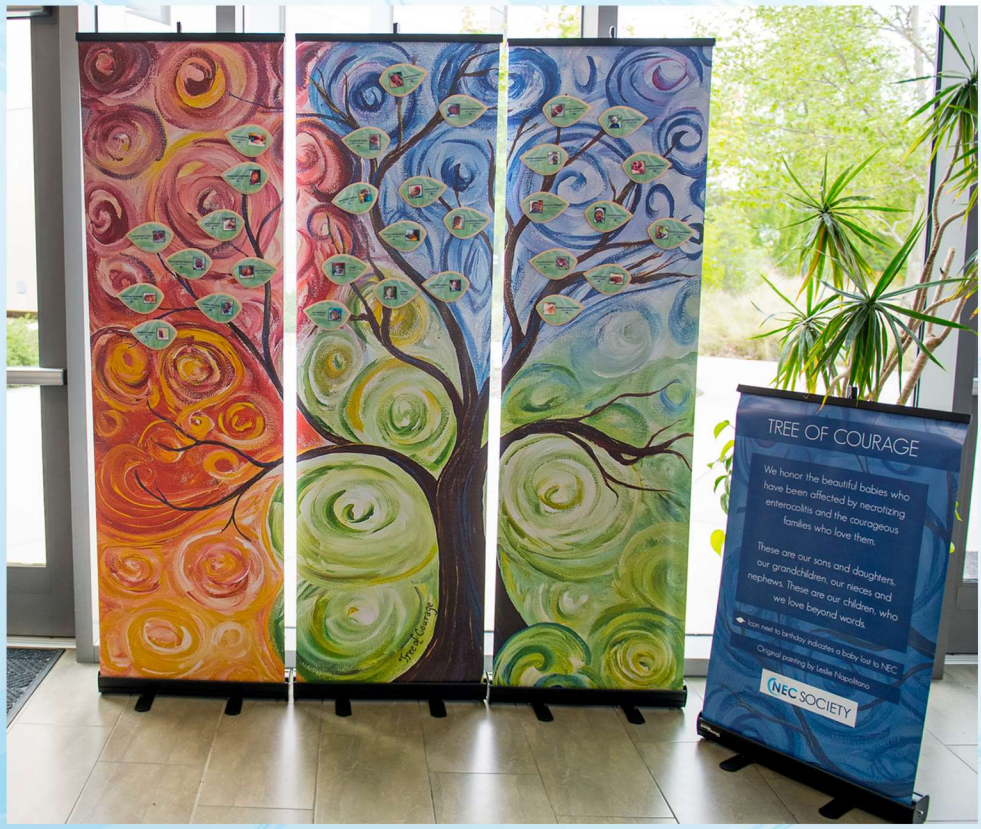
Sarah Rose Raab
Biomarkers and Biology of NEC

Carol & Lydia
Parent Engagement

Tree of Courage

The Tree of Courage displayed at the 2017 NEC Symposium included the names, birthdays and photos of dozens of babies impacted by NEC from around the world. Like the dedicated sessions, the vision for the Tree of Courage was to provide families with a way to honor their children, while simultaneously providing professional participants with a humanized, personalized, inspiring visual highlighting the importance of their work.

The original Tree of Courage canvas painting by artist Leslie Napolitano, hangs in the Pediatric Intensive Care Unit in C.S. Mott Children's Hospital in Ann Arbor, Michigan. Leslie Napolitano painted the Tree of Courage to celebrate her grandson Micah Canvasser, and then donated the artwork to Mott Children's Hospital when Micah passed away from complications of necrotizing enterocolitis. For more information on the Tree of Courage, visit www.NECsociety.org/donate-2/



Strategies to Foster NEC Advocacy

Dedicated to Lydia J.R. Fortin
Facilitated by Jennifer Canvasser, MSW; Michael Staley, Health Lobbyist

The founder of the NEC Society, Jennifer Canvasser, provided an overview of strategies to address the inadequate awareness, funding and prioritization of necrotizing enterocolitis. Michael Staley, a health lobbyist, contributed his perspective and joined the panel discussion of NEC experts, featuring Dr. Jae Kim, Dr. Gail Besner, Dr. Michael Caplan and Dr. Sheila Gephart, to explore core advocacy strategies focused on the following key areas:

Establish Standards of Care: Focus on standardizing the use of human milk, feeding protocols, decreased use of inappropriate antibiotics

Increase Awareness: Empower families with information, build a transdisciplinary team that values the protective benefits of human milk for fragile infants

Secure Funding: Protect NIH funding, focus on prevention, engage legislators

Effective Policies: Insurance coverage of donor milk and hospital grade breast pumps

The NEC Society will publish a full review of *Strategies to Foster NEC Advocacy* in a White Paper, with a release date of Fall of 2017.

Evidence-Based Techniques to Enhance Quality of Life for Premature Infants & Their Families

Facilitated by Erin Umberger, Associate Director of the NEC Society, Registered Architect; Brianna Negrete, MA; Sandee Wishon, RN, MSN; Catherine Rottkamp, MD, PhD

Premature infants are often hospitalized for long periods of time. NICU parents report feeling overwhelmed, disempowered, and in a state of shock. How do we nurture infants who are often isolated for hours, days, weeks or even months, when developmentally, they are still supposed to be engulfed in their mother's warmth? What are the best ways to promote infant-parent bonding? This session explored evidence-based techniques that enhance the quality of life for premature infants and their families, with an emphasis on the built physical environment, music therapy, pediatric palliative care, and kangaroo care.

Evidence-based NICU design: Through the use of evidence-based design, family stress can be reduced, staff satisfaction increased, and patient outcomes improved.

Noise: Most NICUs are too loud. Strategies to control noise include reducing alarms, installing noise sensors, using sound absorbing ceiling tiles, and posting signage about the need for quiet.

Light: NICUs need fully-controllable light and natural light wherever possible. Provide dimmers on all artificial light and automatic window shades that close when a maximum light level is reached. Teach families how to control the lighting.

Nature and Art: Real or simulated views of nature decrease stress levels for parents and staff. Include nature photography throughout the unit. To decrease family stress, remove non-essential equipment in patient spaces.

Open Bays vs Single Family Rooms (SFRs): SFRs mean lower parent stress, increased family presence, improved outcomes for babies, better staff satisfaction, and decreased nosocomial infections. If SFRs are not possible, approximate them by providing as much privacy and family control of the bedside space as possible.

Music Therapy: Goals of NICU music therapy include reducing stress, enhancing respiration, reinforcing non-nutrient sucking, providing parent education, and promotion of developmental skills. Music therapy is much more than simply playing music in the NICU. NICUs should utilize staff that are trained in the unique needs of neonates to be most effective and recognize signs of overstimulation.

Teaching parents music therapy procedures empowers them and leads to improved parent visitations. Pacifier activated lullaby increases oral tolerance. Heartbeat recordings with added music can be created as a part of comfort care.

Palliative Care: Palliative care includes advanced communication (being open and present), optimizing quality of life, and family support. Palliative care may or may not include hospice care. Palliative care provides tools for decision-making, pain management, and expressive therapies. Early involvement is important, as palliative care can benefit families at all different points in their experience. Respect for the family and their decision-making process is crucial. Palliative care requires participation from a fully integrated team of caregivers, not just one individual.

Kangaroo Care: A 2016 Cochrane review showed improvement in several short term outcomes with kangaroo care, and a 2017 long term follow-up of the original cohort showed improvement in several long term outcomes.

Kangaroo holding increases breast milk intake, improves sleep, improves Bayley scales, and decreases pain during blood draws. Intermittent Skin-to-Skin Care, alternative types of contact, can be utilized for infants who are less stable. In addition to improved patient outcomes, these techniques have been shown to improve breastfeeding, increase parental involvement, and decrease parental stress.

The Evolution of Lactation as a Guide to Understanding Nourishment and Prevention in the 21st Century

Facilitated by Bruce German, PhD

Darwinian forces have ensured that human milk contains ingredients that will improve the survival of the infant. Milk oligosaccharides, the third most abundant component of human milk, are undigestable by humans. We now understand that they enrich particular bacteria in the infant gut. In the gut ecosystem, whoever eats wins. So, milk feeds the intestinal microbiota and guides its products.

Unfortunately, modern medical practices have changed the infant microbiome. Therefore we must establish, restore and maintain a healthy gut microbiome. Good digestion leads to proper cell signaling, resulting in intestinal immunity and neurological development in the gut. Digestion releases bioactive peptides, which may be antimicrobial. The next generation of food ingredients may be enzymes. With more research, we may be able to replace the enzymes lost during human milk pasteurization to better approximate mother's own milk.

Learn more about Dr. Bruce German's work:
www.ffhi.UCdavis.edu or www.EvolveBiosystems.com

Keynote: NEC Historical Perspectives and Future Directions

Michael Caplan, MD

Human milk reduces NEC incidence. Small studies have shown an exclusive human milk diet (no bovine fortifier) to be beneficial; however, typical mother's milk contains 10% bovine based proteins, thus more study is needed.

Unpasteurized human milk may be beneficial in NEC reduction, although it may also increase risk of CMV, which could lead to neurodevelopmental issues. Research still needed includes: impact of donor milk on NEC, safety and efficacy of fresh/frozen/pasteurized HM, impact of an exclusive HM diet, whether delayed feedings/increasing volumes affect NEC, and the safety and efficacy of oral mother's milk for preterm infants.

Inflammation appears to play a role in NEC. Platelet-activating factor (PAF) is a lipid mediator that causes inflammation. Blocking PAF reduces NEC. Also, permeability of the epithelial cells of the gut depends on toll-like receptor TLR-4. Mice without TLR-4 are resistant to NEC. SIGGR is part of the TLR-4 signalling pathway, and there is a higher incidence of SIGGR mutations in patients with NEC. Can pharmacologic intervention modulate this signalling and reduce NEC?

There is a paucity of bacteria in the ELBW gut. Human milk increases bacterial diversity. Gram negative bacteria are associated with NEC, and providing probiotics can reduce NEC, presumably by forcing out the bad bacteria. We must identify quality controlled probiotics to use on preterm infants. Also, we must develop biomarkers that herald the onset of NEC. Finally, we should consider what we can learn from fecal transplants to correct intestinal dysbiosis and how similar approaches might safely be considered in premature infants.

"It was so helpful to learn what NICUs across the country are doing, so that I can improve the practice in my own unit. "
-Symposium attendee

Innate Immunity and NEC

Dedicated to Hope Marie Luchsinger
Facilitated by Steven McElroy, MD; Ravi Patel MD, MSc

Current thoughts on pathophysiology were discussed, including epithelial and cellular components of NEC, the role of the immune system, and host-microbe interactions.

The human intestinal tract is a massive, extremely complex organ. The surface area of the small intestine is roughly ½ the size of a standard tennis court and represents the largest surface of our body that interacts with the external environment. Thus, the lumen of our intestines should be thought of as "outside" of our bodies. The intestine is lined by a single protective layer of epithelial cells, which are held together by tight junctions. This layer is folded on itself into finger-like projections (vili) that extend into the intestinal lumen. Tight junctions are "leaky" in premature infants and likely play a role in NEC.

Intestinal stem cells, which are located at the base of the intestinal vili are constantly producing new epithelial cells to replace the intestinal lining. These epithelial cells are comprised of several subtypes of cells, some of which absorb nutrients, and some of which secrete protective substances. Goblet cells produce the protective mucus that coats the intestinal layer, forming part of its protective barrier. Premature infants have fewer functional goblet cells, leading to less protective mucus. Paneth cells produce antimicrobial peptides to shape the intestinal microbiota and maintain stem cell health. Paneth cells are first seen around 13 weeks of gestation and gradually increase in number until term. NEC is associated with Paneth cell loss which may be related to Paneth cell dysfunction leading to an altered gut microbiota and systemic inflammation. The current hypothesis of NEC is that injury occurs when intestinal bacteria gain entry to the baby's intestinal cells through or between disrupted or abnormal epithelial cells, causing subsequent inflammation and injury.

Toll-like receptors manage the inflammatory response and permeability of the intestine. Harmful bacteria bind to these receptors to open the "gates," leading to injury and inflammation. By contrast, beneficial commensal bacteria helps to maintain intestinal health and decrease inflammation. As the intestine matures, the inflammatory response becomes better regulated. The presence of good bacteria can help accelerate the maturation process and reduce inflammation. Supplementing prebiotics and probiotics to the preterm infant can supply good bacteria that may help reduce the risk of NEC.

Regulatory Considerations in Development of NEC Therapeutics

Facilitated by Gerri R. Baer, MD, FAAP

Dr. Gerri Baer is a Medical Officer and Team Leader for Neonatology in the Office of Pediatric Therapeutics at the Food and Drug Administration. At FDA, she has established the Neonatal-Perinatal Medicine consultation service and is involved with development of neonatal products across the Centers. She is a member of the coordinating committee of the International Neonatal Consortium (INC) and represents the FDA on INC working groups. Dr. Baer conveyed the benefits of FDA approval for pediatric and neonatal therapeutics, including established effectiveness, pre- and post-marketing safety assessments, and defined clinically-meaningful endpoints. In the case of NEC, prevention of disease is a clinically-meaningful outcome.

Dr. Baer also provided information on drug development tools that are relevant to NEC research, including clinical outcome assessments, biomarkers (e.g. for prediction of a patient's risk), and animal models.

Finally, potential clinical questions were considered for the next phase of NEC research:

- What non-pharmacologic strategies for NEC prevention are most effective?
- Is there a clinical prediction strategy that can help define at-risk babies, either for non-pharmacologic prevention or pharmacologic prevention?
- What are the most effective treatment strategies for promoting long-term health?

Learn more about Dr. Gerri Baer's work at the FDA: http://bit.ly/FDA_NEC2017

"The information gleaned from this amazing symposium has motivated me to share information with other local providers and colleagues to improve outcomes."
-Symposium attendee

"My take-home message from the conference is the importance of family engagement in the care of the patient and understanding their role as observers and caregivers."
-Symposium attendee

Probiotics and NEC

Dedicated to Noah Michael Propst
Facilitated by Mark Underwood, MD; David A. Mills, PhD

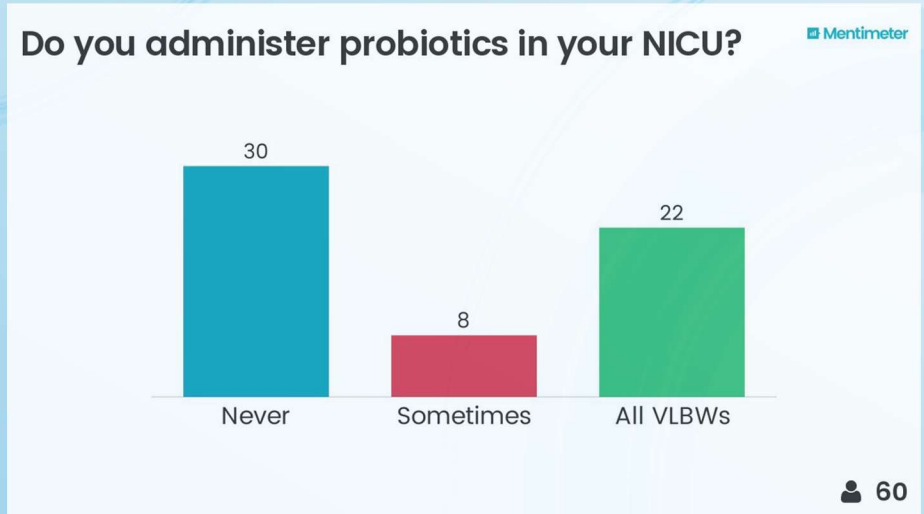
The gut microbiota of the premature infant is different and much more likely to be dominated by pro-inflammatory proteobacteria than that of the term infant. Each day of antibiotic treatment of a preterm infant increases the risk for later development of NEC. Acid suppression (H2 blockers) also alters the gut microbiota and increases the risk of NEC. These observations support the hypothesis that intestinal dysbiosis is common in preterm infants and precedes NEC.

Probiotics have been found to be protective against NEC in animal studies. Animal models are useful for elucidating mechanisms. Species specific effects of probiotic treatment include attenuation of altered apoptosis (cell death) and mucin production, increased expression of TOLLIP/SIGIRR, blunting of TLR4 activation resulting in decreased expression of pro-inflammatory cytokines and chemokines, increased expression of tight junction proteins, and improved intestinal motility. In published clinical trials and cohort studies including more than 20,000 premature infants, probiotics decrease the incidence of NEC and death. Cross contamination (detection of a probiotic in the feces of infants receiving the placebo) is common and limits the value of further randomized clinical trials. Cluster randomization of NICUs to compare probiotic products may be a more effective strategy for future trials.

Risks of using probiotics in preterm infants include sepsis from the administered organism, sepsis from a contaminant, and uncertainty of purity and viability. These risks appear to be small and can be reduced through the use of well-studied products with demonstrated purity, viability, and efficacy. Promising products include FloraBaby by RenewLife (Health Canada), Infloran, ProTectis, Natren Life Start, and Evolve (not yet commercially available).

Human milk shapes the developing gut microbiota. Human milk oligosaccharides are highly abundant but not digestible by the infant intestinal tract. Only some species of bifidobacteria and Bacteroidetes are capable of using intact human milk oligosaccharides as a food source. Pairing the probiotic with the carbohydrate it consumes improves colonization (e.g. B. infantis + HMOs). If the gut microbes are only able to partially consume human milk oligosaccharides, the residual monosaccharides may then cross-feed intestinal pathogens. Probiotics are currently not approved by the FDA or recommended by the AAP.

The content of *Probiotics and NEC* will be presented in the February 2018 issue of *Seminars in Pediatric Surgery.*



Live polling results from the audience during Dr. Underwood's talk.

Human Milk and NEC

Dedicated to Micah Canvasser
Facilitated by Jae Kim, MD, PhD; Amy Hair, MD

A growing body of data supports the protective qualities of human milk in the preterm gut. How does human milk decrease the risk of NEC? Should an exclusive human milk diet be the standard of care? How can human milk standards be established and what efforts are being made around the globe?

Human milk is a liquid tissue. It reduces NEC risk in numerous ways: allows for faster digestion and improves gut motility, secretory IgA enhances gut immunity, lactoferrin reduces bad microbes, probiotics provide good bacteria to compete against bad bacteria, and prebiotics (human milk oligosaccharides or HMOs) promote probiotic growth. Infant formula cannot recreate the complex makeup of human milk.

Human milk oligosaccharides (HMOs) resist human digestion and instead feed good bacteria. Bacterial components in human milk are not destroyed by freezing, but many human components related to immunity are, such as white blood cells and neutrophils. Many other bioactive proteins may be destroyed through freezing. This includes: IgA, which supports immune development and is present in high concentrations in colostrum; and anti inflammatory factors and cytokines, essential to the immune and anti inflammatory responses.

Preterm infants have gut dysbiosis (an unbalanced microbiome) due to frequent C-section delivery, use of broad-spectrum antibiotics, delay in enteral feedings, sterilization of formula and colonization by hospital-acquired “bad” bacteria.

We must work toward full support of a human milk diet (not formula). This includes supporting maternal lactation and use of donor milk. This may also include human milk-based fortifier and added human milk derivatives to increase proteins and bioactive components.

The AAP currently supports a human milk diet for all preterm infants. Mother’s own milk should be the primary diet if possible. If not possible, donor human milk (DHM) should be provided. Pasteurized DHM has been demonstrated to significantly reduce NEC over formula. DHM is lower in calories and fat than formula. To avoid growth failure, fortification is standard in North America. Some studies have found the use of an exclusive human milk diet (human milk-based fortifier) to reduce the risk of NEC over bovine-based formula.

Consider a “bundled” human milk quality improvement (QI) project in your NICU. This could include the use of mother’s own milk, availability of DHM, a standardized feeding protocol, and a human milk-based fortifier.

The content of *Human Milk and NEC* will be presented in the February 2018 issue of *Seminars in Pediatric Surgery.*

“I now have so much more knowledge about possible future outcomes of NEC. I feel so much positivity!”
-Symposium attendee

NEC and Stem Cell Therapy

Dedicated to Brooks Hamilton Cossey
Facilitated by Gail Besner, MD; Agostino Pierro, MD; Troy Markel, MD

Future innovative therapies for NEC are on the horizon. This session investigated the potential of stem cell therapy for NEC. The benefits of different types of stem cells and the mechanisms by which stem cells exert their effects were discussed.

Stems cells are primitive cells with the ability to differentiate into multiple kinds of cells. They can reduce inflammation, fight apoptosis (cell death), and self replicate. The human body produces different kinds of stem cells as it matures, from embryonic germ cells (EG) to fetal tissue stem cells to cord blood and placental stem cells, to adult stem cells. Stem cell therapy could be potential therapy for NEC.

The enteric nervous system (ENS) is located in the wall of the intestine. It controls intestinal motility, absorption and secretion. Enteric nervous system abnormalities are present in human NEC, causing long term dysfunction of neural cells and glial cells. In animal models, transplantation of neural stem cells has been shown to protect the intestines from NEC, but when administered by IV, many stem cells are trapped in the lungs. Stem cells have also been implicated in tumor formation.

Exosomes (cell-derived particles found in many fluids of the body) may mediate the ability of stem cells to protect the intestines and ENS from NEC. In animal models, stem cell derived exosomes grafted into injured intestines appears to prevent NEC, reversing injury and preserving gut barrier function. This may lead to a novel future therapy for NEC.

Injection of mesenchymal stem cells in a rat model improves survival from hypoxic gut injury model (similar to NEC). They appear to improve intestinal perfusion (circulation). They also affect paracrine (cell to cell communication) effects. Injury to intestinal cells causes them to signal stem cells to activate, releasing paracrine factors. This leads to less cell death and more cell recovery. One such paracrine factor released by stem cells is hydrogen sulfide. In animal models, hydrogen sulfide improves outcomes in NEC. It appears to work through nitric oxide pathways. Stem cell therapy and nitric oxide therapy are potential therapies to improve survival and outcomes in neonates.

The content of *NEC and Stem Cell Therapy* will be presented in the February 2018 issue of *Seminars in Pediatric Surgery.*

Development of a Necrotizing Enterocolitis Prevention Checklist (Workgroup)

Facilitated by Sheila Gephart, PhD, RN; Rebecca Vartanian, MD

While NEC pathogenesis remains a topic of research, some NICUs are "getting to zero" rates of NEC by adopting evidence based practices to prevent the disease. To do so, delivery of care has to be consistent for every baby. Using a checklist has helped to reduce other infections in the NICU but has not yet been applied to NEC. This workgroup leveraged lessons learned from low rate NICUs, evidence on NEC prevention, and clinical successes to create a checklist for NEC prevention. The multi-disciplinary group reviewed two primary checklists: one for practices that the organization needs to address and one that focuses on an individual baby's NICU stay.

The state of the science and practice for NEC prevention was first reviewed that addressed:

- Actions to prioritize human milk beginning with mom's own milk. Access to donor milk is recommended if mom's milk is unavailable. An organization may need to make a plan for payment of donor milk.
- Standardized feeding guideline adoption that includes "what if" decision making for signs of feeding intolerance and details on when to start, stop, advance and fortify feeding.
- Donor human milk-derived fortifier compared to bovine-derived
- Transfusion management (i.e. increased awareness of risk within 48 hours of a transfusion, adopting strategies such as delayed cord clamping and minimizing blood draws to prevent anemia)
- Strategies and tools for early recognition that include a strategy for team communication and consistent risk assessment (e.g. through using GutCheckNEC or eNEC to assess and communicate risk across transitions)
- Limited (<5 days but some units 24-48 hours) empiric antibiotics in the first days of life
- Avoidance of histamine-2 antagonists (e.g. ranitidine).

In the audience were representatives from a handful of NICUs who have reduced their rates to "zero" and several more with very low rates. Participants recommended adding these items to the checklists:

- Establish a multidisciplinary team
- Address milk preparation
- Address indwelling time and handling of enteral feeding tubes
- Consider probiotics
- Work with obstetricians and L & D staff to give antenatal steroids, plan for delayed umbilical cord clamping, and try to avoid fluid overload of mom that delays milk production
- Using a family-centered approach to empower parents to watch for warning signs (use brochures and initiate conversations around feeding changes or abdominal assessments). Use the words "necrotizing enterocolitis" vs. other less specific terms.
- Plan to measure processes, monitor compliance and unit's progress toward zero NEC. This will involve communicating with all NICU staff about progress (i.e. post your NEC rate).

A full review, including the checklists, of *Development of a Necrotizing Enterocolitis Prevention Checklist* will be published in a white paper, with a release date in Fall of 2017.

> As a result of attending this conference, will do a better job advocating for the use of human milk or donor milk for our babies. I will limit the use of antibiotics to reduce the risk of NEC, and I will be better equipped to differentiate between NEC and SIP.
>
> -Symposium attendee

Developing a Necrotizing Enterocolitis Registry and Biorepository (Workgroup)

Facilitated by Misty Good, MD; Steven McElroy, MD; Troy Markel, MD; David Hackam, MD, PhD

To better understand the development and progression of NEC in patients, researchers must reach beyond traditional animal models of NEC. Access to a large array of human intestinal tissue and other biological specimens would allow for better understanding of progression of disease and for the identification of predictive markers that could aid in risk stratification. This working group discussed how to best prepare and fund a biological repository that also links patient demographic and clinical data to each specimen. Topics of discussion included central versus virtual repositories, funding considerations, utilization of multicenter IRB networks, and database management. Virtual biorepository with central Redcap database was discussed. Consistency in collection, storage, shipping of samples will be critical.

The development of a necrotizing enterocolitis registry and biorepository will promote, facilitate, and accelerate basic and clinical-translational observational studies of NEC in vulnerable infants.

The content of *Developing a Necrotizing Enterocolitis Registry and Biorepository* will be presented in the February 2018 issue of *Seminars in Pediatric Surgery*.

"I met colleagues at this meeting that will stimulate collaborative projects related to NEC research. I was especially pleased and informed by having a multidisciplinary perspective on this disease, it increased my awareness of the obstacles and challenges we face in preventing this disease."
-Symposium attendee

Defining NEC (Workgroup)

Facilitated by Alexander Penn, PhD; Phillip Gordon, MD, PhD; Robert Christensen, MD

Necrotizing enterocolitis has long been "defined" clinically through the use of Bell's staging system. This was originally designed to help determine which infants with NEC were most likely to require surgery but rapidly became the dominant paradigm. There is consensus that the Bell's criteria are not meeting our needs.

The development of a new definition of NEC that better describes the broad range of mechanisms of pathogenesis underlying NEC would improve the quality of the data we collect and our capacity to measure improvement in outcomes.

Also, we must be consistent in exclusion of spontaneous intestinal perforation (SIP). Term and preterm NEC are not the same. We should consider the value of pneumatosis, ultrasound and biomarkers.

The content of *Defining NEC* will be presented in the February 2018 issue of *Seminars in Pediatric Surgery.*

Enhancing Parent Engagement and Empowerment (Workgroup)

Dedicated to Lydia and Carol Nell
Facilitated by Erin Umberger, Associate Director, NEC Society;
Sue Hall, MD

Many NICU parents report feeling disempowered regarding the care and decisions involving their fragile infants. These NICU parents seek increased collaboration with their infants' providers to foster their knowledge and engagement. Practitioners must value and prioritize the empowerment of parents and deliberately increase parental involvement in the NICU. Barriers to fully engaging parents were explored in this session, with solutions suggested to surmount these barriers.

Communication about NEC and human milk in the NICU is poor. In 2014, the NEC Society surveyed families impacted by NEC. Only 32% of parents felt satisfied/very satisfied with the NEC information provided prior to diagnosis. Only 56% were aware of potential benefits of breast milk in prevention of NEC. Nearly 20% felt their NICU perceived formula to be equivalent to breast milk. Finally, 56% of parents suspected something was wrong prior to diagnosis, but of those who notified medical staff, over 50% felt that nothing was done.

Some families experience financial, cultural, or other barriers that make it difficult for them to be fully involved in their baby's care. Also, different families need different levels of support. Evaluate families to determine the level of support they need: from family-centered care to targeted support, to clinical mental health treatment, as needed.

Strategies to improve family communication and support:

- Discuss NEC as early as possible. Use the establishment of pumping as an opportunity to discuss the protective benefits of human milk.
- Staff should visit ante-natal families who are likely to have preterm births. Follow up a visit by a neonatologist with a visit from NICU nurses, who can provide similar information in a different way.
- Provide staff training to better educate families.
- Use peer-to-peer mentors.
- Encourage families to ask questions and attend rounds.
- Provide information in multiple formats (verbal, written, and videos, from multiple types of staff).
- Provide access to medical records.
- Develop a unit policy on human milk and share it with families.
- Display educational posters within the unit.
- Provide continuity of care (use primary nursing as much as possible).
- When speaking with parents, take time to sit down and use their baby's name during conversations.
- Provide periodic family conferences to review baby's course and begin discharge/transition planning.
- Consider implementing The National Perinatal Association's "Psychosocial Support Recommendations", which include tools to improve family support.

Listening to parents, validating and normalizing their emotional distress is important. Family empowerment requires a cultural shift to view families as care partners with the medical team. To learn more visit, www.Support4NICUparents.org. The content of *Enhancing Parent Engagement and Empowerment* will be presented in the February 2018 issue of *Seminars in Pediatric Surgery*.

"As a result of this conference, I will advocate for human breast milk and HBM fortifiers, support lactating mothers, improve family education and advocate for families to be part of their baby's care team."

-Symposium attendee

Low-cost, No-sponsor Multi-center NEC Clinical Trials (Workgroup)

Dedicated to Grayson Edward Kapferer
Facilitated by Samir Gadepalli, MD; Mark Underwood, MD

As promising novel approaches to the prevention and treatment of NEC become available, it is essential to develop feasible models for conducting multi-center clinical trials. Currently, many centers report single hospital clinical trials and cohort studies of NEC that are limited by small sample size and population homogeneity. Traditional multi-center trials are costly and take years to complete. In this workshop we addressed alternate models to complete larger trials for lower cost, including linkage of electronic records, standardized quality improvement projects, and web-based strategies for participation in cluster- randomized clinical trials.

Prevention trials need 2000 infants per arm. Treatment trials need 200 infants per arm. Costs are prohibitive. A central website with consent forms, IRB forms, data collection forms, randomization is needed. Core site for data collection, cleaning and analysis would make it feasible. Each site would provide its own CRC/IRB.

Quality Improvement Approach to Reducing NEC (Workgroup)

Facilitated by Aloka Patel, MD; Patoula G. Panagos, MD

This session described quality improvement methods to reduce necrotizing enterocolitis in very low birth weight infants using examples from an actual quality improvement initiative. Recommendations include:

- Form an interdisciplinary team with frontline representation. Understand that not all staff are innovators or early adopters.
- Form a concise aim statement.
- Understand the NEC incidence in your particular NICU:
  - Use the QI tools like a fishbone diagram and process maps when talking with frontline staff.
  - Examine characteristics (i.e. feeding advancement, antibiotics, transfusions, sepsis) in previous NEC cases
- Develop a key driver diagram showing the interventions as a road map to a multi-modal NEC reduction bundle.
- Use Plan-Do-Study-Act (PDSA) cycles as a vehicle for implementation to test and learn from change.
- Communicate with the staff that a PDSA cycle is a test of change that may lead to revisions of the bundle.
- Celebrate small scale success.

Using actual examples, common implementation problems and solutions were explored for the following key drivers.

- Feeding guidelines
- NG tube maintenance
- Antibiotics stewardship
- pRBC transfusion practices
- Donor Milk Program

The NEC Society will publish a full review of *A Quality Improvement Approach to Reduce NEC* in VLBW Infants in a White Paper, with a release date of Fall 2017.

Keynote: Bugs, Germs and Genes in the Pathogenesis of NEC

David Hackam, MD, PhD

David Hackam, the chief of pediatric surgery at the Johns Hopkins University in Baltimore, provided an overview of the multiple ways in which host genes along with microbial factors converge to initiate the development of necrotizing enterocolitis in premature infants, and also described several experimental strategies that could be used the develop novel prevention or treatment strategies for this devastating disease.

Specifically, Hackam showed that the receptor for gram negative bacteria, namely toll like receptor 4 (TLR4), serves as a switch within the newborn intestine, which becomes activated by strains of colonizing bacteria within the lumen of the premature gut. When TLR4 is turned into the "on" position, an inflammatory cascade develops, resulting in the loss if the mucosal lining of the gut, as well as an impairment in blood flow to the newborn bowel due to a loss of local production of nitric oxide. Accordingly, experimental strategies to block TLR4, or to reverse nitric oxide inhibition, can reverse these effects and prevent NEC in mice and piglets.

In additional studies, Hackam showed that premature infants are at particularly higher risk for NEC development as they express significantly higher TLR4 levels as compared to full term babies, which is an unintended consequence of the recently described role that TLR4 plays in normal gut development in utero. As a result, the premature infant, whose intestine is still developing, is born with high TLR4 levels, which then become activated by gram negative bacteria, leading to NEC.

In more recent studies, Hackam showed how breast milk protects against NEC developing in infants, by showing that this precious fluid is rich in natural TLR4 inhibitory compounds which serve to limit signaling by the elevated TLR4 levels within the premature infant intestine.

Dr. Hackam closed his talk with the hope that by continuing to bring scientists, physicians, nurses and families together in meetings such as the 2017 NEC Symposium, we will one day live in a world in which no family ever again has to face the devastation caused by this awful illness.

Learn more about Dr. David Hackam's work: http://bit.ly/HackamLab_NEC2017

The content of *Bugs, Germs and Genes in the Pathogenesis of NEC* will be presented in the February 2018 issue of *Seminars in Pediatric Surgery*.

Biomarkers and Biology of NEC: Insights to Cause and Prevention

Dedicated to Sarah Rose Raab

Facilitated by Sheila Gephart, PhD, RN; Katherine Gregory, PhD, RN; Karl G. Sylvester, MD; Akhil Maheshwari, MD

Potential biomarkers are emerging that may be predictive of impending NEC. Which are most promising and how can these markers be made widely available for use in early detection efforts? A number of clinical tools to support NEC risk are also being developed and were discussed.

A biomarker is a defined characteristic that can be measured to indicate normal or abnormal biological processes. When discussing potential NEC biomarkers, we must ask ourselves the following: How plausible is early detection of NEC? If we can detect it early, would it change outcomes? What are accurate, available and ready to use as biomarkers for NEC today?

Clinical Predictors: We currently lack objective diagnostic and prognostic parameters for NEC. Clinical signs of NEC are inconsistent and have been shown to appear in a subtle fashion over days as well as all at once. Currently used treatments may not be tailored to the unique characteristics of the infant or disease severity. So, we must find objective molecular indicators. Current biomarkers have not translated into clinical practice, study sample sizes have been small, diagnostic accuracy has been only modest, and reproducibility has been limited.

Metabolic biomarkers: No single organism has been closely associated with NEC, although there is an established pattern of bacterial colonization and dysbiosis (microbial imbalance.) The disease onset typically occurs at 27-34 weeks gestation and highest incidence occurs in neonates under 1,000 grams. There is an inverse relationship between age at onset and the severity of the symptoms.

Premature newborns have metabolic dysfunction that can lead to them acquiring NEC. Screening to determine extent of metabolic dysfunction and stool assays to determine the metabolic products of dysbiosis could identify patients at higher risk for NEC.

Molecular biomarkers: Intestinal fatty acid binding protein (iFABP, found in urine) may be an important biomarker of NEC. Within a week of diagnosis, iFABP predicts NEC with 60% sensitivity (how likely it is to detect the presence of the disease in one who has it) and 78% specificity (how likely someone with a positive test is to have the disease). The ability to measure iFABP in urine is an advantage, as it avoids additional blood draws to an already hemodynamically compromised infant.

Microbial biomarkers: We know that intestinal dysbiosis is associated with NEC. Microbiome biomarkers could hold promise.

Clinical predictors, metabolic markers, molecular signals, and microbial patterns all have promise as early predictors of NEC, and may be most useful if combined. Challenges include low prevalence of NEC and overlap between feeding intolerance and the various sub-types of NEC. The importance of reporting positive predictive values in all studies of NEC was stressed. The content of *Biomarkers and Biology of NEC: Insights to Cause and Prevention* will be presented in the February 2018 issue of *Seminars in Pediatric Surgery.*

"This was an extremely informative symposium, exposing me to the latest medical innovations and treatments for NEC. An aspect that I think made this conference standout was the parent involvement. It is rare at any conference to be reminded of the parent experience and hear them share their feelings, concerns and questions."

-Symposium attendee

Animal Models of NEC

Dedicated to Emily Specht
Facilitated by Steven McElroy, MD; Doug Burrin, PhD; Catherine Hunter, MD

Advantages and disadvantages of current animal models were discussed, along with promising new models.

Rat model: The rat model was the first used to study NEC in animals. Laboratories have similar but not identical methods for using a rat model. Limitations include lack of readily available transgenic (genetically modified) strains and a higher tolerance for bacterial contamination and endotoxin vs. humans. Benefits include low cost and high litter size. A rat model has been used successfully to investigate numerous aspects of NEC.

Mouse model: Mice are smaller and more difficult to handle than rats but our ability to modify their DNA makes them a powerful tool to understand the mechanisms of NEC. In order to simulate NEC in mice, the following procedures are used: hypoxia (low oxygen)/hypothermia (cold)/formula, induced microbial dysbiosis (imbalance), chemically-induced inflammation, and paneth cell disruption (paneth cells are important for bacterial regulation and stem cell maintenance). All mouse models produce injury that is similar to human NEC and are powerful tools to understand this disease. As with all animal models, there are pros and cons to each method and the method used should be reflective of the question being asked.

Piglet model: The larger body size of piglets provides advantages. Their diet and digestive tract is comparable to humans. Their metabolism, organ system and body composition is also more similar to humans than other models. Piglets are a very promising preclinical model to show safety and efficacy of novel strategies prior to consideration for clinical trials in humans.

The content of *Animal Models of NEC* will be presented in the February 2018 issue of *Seminars in Pediatric Surgery.*

"Because of this meeting, I plan to implement more family-centered care and encourage the use of mom's own breastmilk as much as possible."
-Symposium attendee

Strategies to Support Equitable Access to Human Milk for Premature Infants

Panelists: Jennifer Canvasser, MSW; Jae Kim, MD, PhD; Pauline Sakamoto, MS, RN, PHN; Aloka Patel, MD; Steve Gwiazdowski, MD

This panel discussion, led by Dr. Jae Kim, brought together diverse perspectives to explore how to best ensure all fragile infants at risk of developing necrotizing enterocolitis receive human milk. The panel explored access to lactation support, and mothers own milk, as well as donor milk, while considering how to engage communities and families that are not culturally primed to breastfeed. Panelists proposed the following strategies to overcome some of the barriers that prevent equitable access to human milk for premature infants:

Accessibility:
Engage peer-to-peer mentors, partners and grandmothers

Costs/Funding:
Insurance companies mandated to cover the costs of a hospital grade breast pump/pasteurized human milk

Education:
Integrate formal instruction on human milk in medical/nursing school curriculum

Public Awareness:
Engage midwives/OB/GYNs in informing their patients, during the antenatal period, about the lifesaving power of human milk for fragile infants and the opportunity for mothers to donate their excess milk to a milk bank

Policy:
Comprehensive family support and maternity leave

To learn more, please visit: www.MothersMilk.org

The NEC Society will publish a full review of *Strategies to Support Equitable Access to Human Milk for Premature Infants* in a White Paper, with a release date of Fall 2017.

Treatment Options for NEC

Dedicated to Antonio Rosito Robyn
Facilitated by Samir Gadepalli, MD; Shinjiro Hirose, MD

Medical management of NEC: Includes bowel rest and decompression, IV fluids and nutrition, antibiotics, serial X-rays and exams, and monitoring for clinical deterioration.

Variation in antibiotic use: There is great variation in antibiotic choice and duration for the treatment of NEC, and there is a lack of evidence for the best practice.

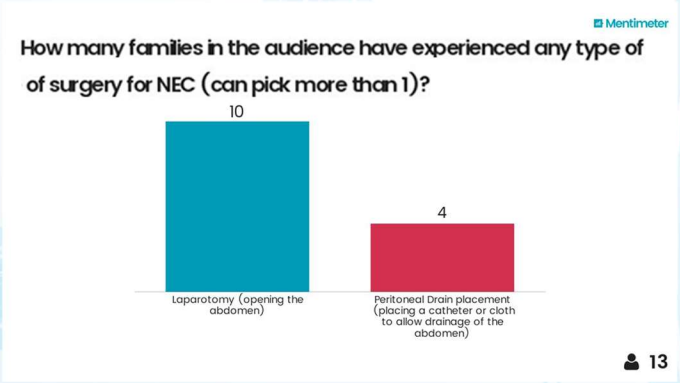
Surgical management: There is only one absolute indication for surgery: pneumoperitoneum (air within the peritoneal cavity). All others are relative indications and are subjective. Peritoneal drain and laparotomy (open surgery) have about similar outcomes, although drains seem to have fallen out of favor in older/larger children due to possible worse neurodevelopmental outcomes (NEST study results pending for those under 1 kg).

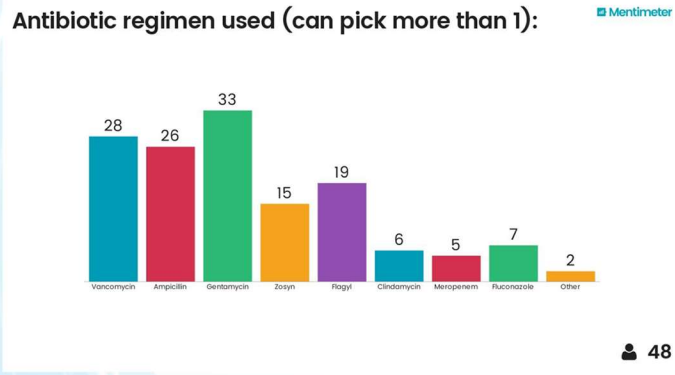
Management of complications: Surgical complications include wound related hernia, fistula (abnormal connection between organs), and fluid loss due to drainage; ostomy (creation of an opening in the body for discharge of waste) complications; stricture, short gut syndrome, and problems due to TPN (IV nutrition). Long-term gastrointestinal and neurodevelopmental issues remain common problems.

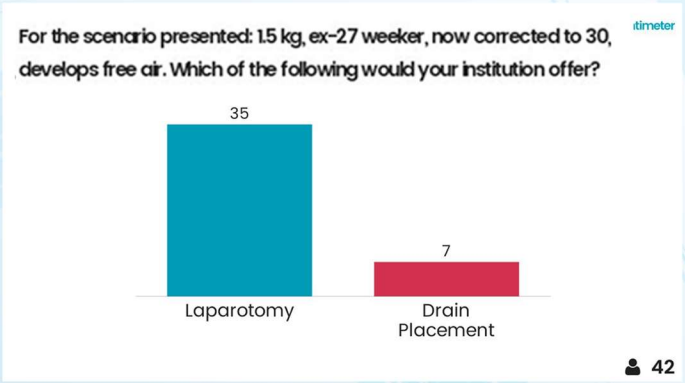
Alternative therapies: Future research on non-surgical interventions is needed. This may include stem cell therapy, altering the microbiome, and investigating mucosal integrity and growth factors.

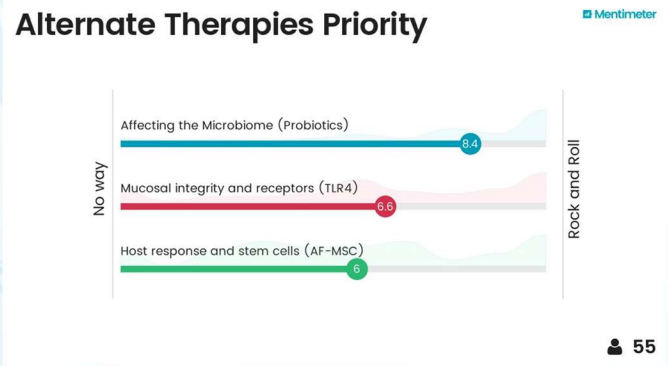
"This was an exceptional conference! I will be able to share this information with others on my unit and I will be able to initiate a more parent-inclusive plan of care for our families."
-Symposium attendee

Live polling data collected during the Treatment Options for NEC presentation:









NEC and Neurodevelopment

Facilitated by Camilia Martin, MD; Jing Lu, PhD

What is known about the impact of NEC on the developing brain? Nutritional impact, anesthesia impact, and the role of the gut-brain connections were discussed.

There is a significant risk of neurodevelopmental and cognitive impairment in infants with surgical NEC. Neurodevelopmental outcomes are worse for surgical NEC than medical NEC. Intestinal perforations also increase the risk of neurodevelopmental delays. Neurodevelopmental issues include white matter injury; global deficits in motor skills, cognitive ability, attention and visual perception; and delayed neural conduction in the brainstem.

Potential etiologies (causes):

Anesthesia and prolonged sedation in the NICU may cause cell death, inflammatory responses and disruption of gene transcription. Drain placement may be considered instead of laparotomy if it would reduce anesthesia exposure.

Surgical NEC and spontaneous intestinal perforation are associated with cytokinemia (protein imbalance), which is linked to neurodevelopmental issues.

IUGR (intrauterine growth restriction) and NEC can lead to poor postnatal growth, which can lead to poor development. Also, nutrient deprivation/ frequent NPO (withholding of feeds) could lead to improper nutrition, poor growth, and an altered gut/brain axis due to an imbalanced microbiome and gut hormone signalling.

Gut health equals systemic health. Impaired gut health leads to local and systemic morbidities. The gut-brain axis means that abnormal brain/nervous system function, which can affect circulation, hormonal and immune response, can lead to gut disease and intestinal dysbiosis. Meanwhile, gut function can affect neurotransmitters and metabolism, which can lead to impaired nervous system function.

NEC is associated with microbiome imbalance. C-section, formula feeding, antibiotic exposure and prenatal stress all affect the microbiome. Microbiota can affect the nervous system by impacting immune activation, neural pathways and metabolism. Additionally, the microbiome affects growth factors like IGF1 (insulin like growth factor 1). Finally, the microbiome affects cognitive function and social behaviors.

The content of *NEC and Neurodevelopment* will be presented in the February 2018 issue of *Seminars in Pediatric Surgery.*

Transfusion Associated NEC

Facilitated by Robert Christensen, MD;
Akhil Maheshwari, MD

The state of the science about transfusion associated NEC was discussed. Is there any relationship between transfusion and NEC? This is a somewhat contentious issue. We know that not every case of NEC is preceded by a transfusion. Not every transfusion is followed by NEC. Most cases of NEC have no obvious relationship with a transfusion. If there is a causal relationship between transfusion and subsequent NEC, it is a weak relationship or obscured by other variables. A number of peer-reviewed publications suggest a relationship, but more recent studies conclude otherwise. So how do we decide if transfusion is a risk factor for NEC?

Should NICU practice change on the basis of a possible weak association between risk of anemia/transfusion and NEC risk? Yes, we should try to avoid anemia (e.g. using delayed umbilical cord clamping, limiting blood draws, and using cord blood for admission labs), adopt other "anemia prevention" programs that keep the hematocrit from falling into "transfusion" ranges, and be more vigilant for NEC within 48 hours of a RBC transfusion.

Should we withhold feedings before, during, and after transfusion? Since the association between transfusion and NEC is "somewhere between real and fake," but the consequences of withholding feeding are known, perhaps we should consider not withholding feedings- especially for infants receiving human milk until better information is available.

Facilitated by Mark Underwood, MD; Jennifer Canvasser, MSW

The 2017 NEC Symposium brought together diverse stakeholders from around the world to foster connections, collaborations and progress in a way that the world's best technology cannot. The human-to-human relationships made at the 2017 NEC Symposium will help to propel this community's work forward.

Participants were given the following five steps which they personally can work to address immediately:

- Provide thoughtful feedback, share ideas and suggestions for improvement.
- Encourage the families in your Unit to visit the NEC Society and Preemie Parent Alliance www.NECsociety.org and www.PreemieParentAlliance.org
- Create a culture that values patient-family centered care and views parents as a critical component of the baby's care team.
- Engage a transdisciplinary team so that everyone has the same message, on the prioritization and protective factors of human milk, for example.
- Advocate. Speak up and contact your legislators. Vote. Ensure that science, prevention efforts, and support for families are of highest priority.

With the 2017 NEC Symposium complete, the NEC Society has launched a series of next steps, including:

- Feedback and evaluation data will be analyzed
- NICUniversity will publish video recordings from select sessions
- The February 2018 issue of Seminars in Pediatric Surgery will be dedicated to the review of the 2017 NEC Symposium
- Select sessions that are not included in the February 2018 issue of Seminars in Pediatric Surgery will publish White Papers to ensure the content is disseminated
- The NEC Society Research Collaborative has prioritized the following projects:
  Benchmarking standards of care in NEC prevention and treatment
  Human sample biorepository
  Quality Improvement projects related to NEC

The NEC Society will hold a 2019 NEC Symposium and efforts are now underway to secure funding. The date and location of the 2019 meeting will be announced in Fall 2017.

In the closing session, participants were asked to use one word to describe the NEC Symposium, and here were their responses:

The 2017 NEC Symposium featured 36 research abstracts, as well as four posters from families impacted by NEC and one summary poster that highlighted the experiences of dozens of families impacted by NEC.

Characterization of the Th17 Cytokine Profile in Infants with Necrotizing Enterocolitis
Alexa Bolock , Zerina Hodzic, Olivia Parks, Congrong Ma, Misty Good

Acute Kidney Injury in Necrotizing Enterocolitis Predicts Mortality
Cory N. Criss, Bipin Sunkara, Joshua S. Gish, Lily Hsieh, Jennifer McLeod, Jason O. Robertson, Niki Matusko, David T. Selewski, Samir K. Gadepalli

Role of Parents in NEC: International Survey of Parental Perspectives of NEC Communication in the NICU
Jennifer Canvasser, Samir K. Gadepalli, Sheila M. Gephart, Jae H. Kim, MD

Evidence-based prevention of necrotizing enterocolitis using live bacteria
Eamonn Connolly

Necrotizing Enterocolitis (NEC) and NEC totalis: A 2 year quality improvement at St. Francis Medical Center (SFMC) :2015-2016
Kamakshi Devarajan, Amy Manantan, Phallee Wooldridge, Kelle Falbo, Ofelia Stoianoivici, Andy Moosa

Significant reduction of Necrotizing enterocolitis associated with higher oxygen saturations
Kiran Dwarakanath, Mari Goldade

Extended-Release Hydrogen Sulfide Donor is Protective in Mouse Model of Necrotizing Enterocolitis
Natalie A. Drucker, Amanda Jensen, Sina Khaneki, Troy Markel

Probiotics for the prevention of necrotizing enterocolitis: meta-analysis of surgical outcomes
Simon Eaton, Clare M. Rees, Nigel J. Hall, Paul Fleming

The gut symbiont Bifidobacterium longum subsp. infantis restores ecosystem function in breastfed infants
Steve Frese, Andra A. Hutton, Lindsey N. Contreras, Claire A. Shaw, Michelle N. Palumbo, Gege Xu, Jasmine Davis, Carlito Lebrilla, Bethany M. Henrick, Samara Freeman, Daniela Barile, J. Bruce German, David A. Mills, Jennifer T. Smilowitz, and Mark Underwood

What is a NIPU? Essential Care for Every NICU Parent
Hall S, Hynan MT, Goyer E, Phillips R, Craig J, Hatfield B, Lassen S, Cohen H

Narratives of NEC: Impact of Infant Feeding Practices on Parent Decision-Making
Sarah Holdren, Aunchalee Palmquist

Reducing Risk of Bowel Perforation in Very Preterm Infants
Angela Huang, Priya Jegatheesan

Pulmonary Epithelial Toll-like Receptor 4 Activation leads to Lung Injury in Neonatal Necrotizing Enterocolitis
Hongpeng Jia*, Chhinder P. Sodhi*, Yukihiro Yamaguchi*, Peng Lu*, Laura Y. Martin*, Misty Good†, Qinjie Zhou*, Jungeun Sung*, William B. Fulton*, Diego F. Nino*, Thomas Prindle Jr*, John A. Ozolek‡, David J. Hackam*

IL10 Expression and RORγ+ Regulatory T-cells are Specifically Reduced in Surgical Necrotizing Enterocolitis
Liza Konnikova, Rajsavi Anand, Joern-Hendrik Weitkamp, Jeffrey Goldsmith and Scott Snapper

The Collaboration: Our NICU's Journey to Improve NEC Rates by the Formation of an Interdisciplinary NEC Taskforce. A One-Year Review
Katherine Kuniyoshi, Marina Hernandez, Phuong Bui, Lucy Chen, Amanda Heinemann, Crystal Tran, Jody King

Amniotic Fluid Stem Cells Reprogram the Intestinal Epithelium during Experimental Necrotizing Enterocolitis
Bo Li, Carol Lee, Yuhki Koike, Alison Hock, Paolo De Coppi, Simon Eaton, Augusto Zani, Agostino Pierro

Regulatory T Cells in Experimental Necrotizing Enterocolitis
Peng Lu, Chhinder P. Sodhi, Hongpeng Jia, Qinjie Zhou, William B. Fulton, Yukihiro Yamaguchi, Thomas Prindle Jr., Sanxia Wang, and David J. Hackam*

Using Stool Calprotectin Levels in the "Rule Out Necrotizing Enterocolitis" Evaluation and Describing its Microscopic Source
Brianna C MacQueen, Robert D Christensen, Diane K Lambert, Vickie L Baer, Julyn G Shepard, Mark J Sheffield, Erick Gerday, Philip V Gordon, Robert Schlaberg, Jonathan Lowe, Mark J Cody, Christian C Yost

Reduction in Necrotizing Enterocolitis after Quality Initiatives by A Multidisciplinary Team
Lynn Miller, Michelle Feinberg, Ann Lewis, Barbara Engers, Kathy Bigelow, Shannon Brinker, Fran Kurland, Elizabeth Pothoff, Melynda Wallin, Alfonso Pantoja, John Britton, MD

Maternal omega-3 fatty acids enriched maternal diet attenuates the neonatal intestinal inflammatory response and prevents the development of necrotizing enterocolitis
Hiromu Miyake, Pekka Maattanen, Bo Li, Yuhki Koike, Carol Lee, Yong Chen, Philip M Sherman, Agostino Pierro

Stem Cell Therapy for Necrotizing Enterocolitis
Christopher J McCulloh, Jacob K Olson, Yu Zhou, Yijie Wang, Gail E. Besner

Comprehensive Feeding Bundle to Reduce the Incidence of Necrotizing Enterocolitis in Premature Neonates
Sudha Rani Narasimhan, Alganesh Kifle, Robin Wu, Angela Huang, Priya Jegatheesan

Intestinal oxygen delivery in preterm lambs: effect of enteral feeds, anemia and red cell transfusions
Jayasree Nair, Sylvia Gugino, Carmon Koenigsknecht, Justin Helman, Satyan Lakshminrusimha

Retinoic Acid Improves Incidence and Severity of Necrotizing Enterocolitis by Modulating Lymphocyte Balance and Preventing Lgr5+ Intestinal Stem Cell Loss
Diego F. Niño, Chhinder P. Sodhi, Charlotte E. Egan, Qinjie Zhou, Joyce Lin, Peng Lu, Yukihiro Yamaguchi, Hongpeng Jia,Laura Y. Martin, Misty Good, William B. Fulton, Thomas Prindle Jr, John A. Ozolek, and David J. Hackam

Necrotizing enterocolitis in moderate preterm infants
Jayasree Nair, Rachel Longendyke, Satyan Lakshminrusimha

Noninvasive Biomarkers to Diagnose Necrotizing Enterocolitis in Preterm Infants: A Pilot Case-Control Study
Leanne Nantais-Smith, Sravani Avula, Krishna Kosuru, Lizbeth Lockwood, Ranjan Monga, Mark Kadrofske

Enriched Probiotic Biofilms Enhance Survival and Prevent Intestinal Damage in an Experimental Model of Necrotizing Enterocolitis
Jacob K. Olson, Christopher J. McCulloh, Jason B. Navarro, Lauren Mashburn-Warren, Sarah Gartner, Steven D. Goodman, Gail E. Besner

A Long-Term Quality Improvement Project to Promote Growth and to Decrease NEC in VLBW Infants
Alfonso Pantoja, Michelle Feinberg, John Britton, Ann Lewis, Lynn Miller

Protease-Digested Casein Protects Cells from Death by Exposure to Free Fatty Acids: A Novel Mechanism By Which Breast Milk Protects Against NEC?
Alexander H. Penn, Karen R. Dobkins, Geert W. Schmid-Schönbein

The Current State of NEC Prevention Practices in the NICU
Megan Quinn, Sheila Gephart

Fatty Acids Found in Expressed Breast Milk are Associated with NOX1 Activity in Intestinal Epithelial Cell Culture
Kathryn Rubey, Lisa Brock, Liyun Zhang, Pippa Simpson, David Gourlay, and Scott Welak

Low Citrulline-Arginine-Nitric Oxide Production Rates are Associated with Necrotizing Enterocolitis in the Premature Piglet
Jason L Robinson, Victoria A Smith, Stephanie M Cruz, Patricio E Lau, Oluyinka O Olutoye, Barbara Stoll, Juan C Marini, Douglas G Burrin

GutCheckNEC to predict NEC in infants from 501-1500 grams and relationships to the pediatric early warning score
Janet Rothers, Michelle Fleiner, Sheila M. Gephart

The Role of Metabolic Regulators in the Etiology of NEC
Manasa Srivillibhuthur, Namit Kumar, Shilpy Joshi, Katherine D. Walton, Anbo Zhou, William J. Faller, Ansu O. Perekatt, Owen J. Sansom, Deborah L. Gumucio, Jinchuan Xing, Edward M. Bonder, Nan Gao, Eileen White, and Michael P. Verzi

Bacteroides thetaiotaomicron cross-feeds pathobionts: a possible mechanism for Necrotizing Enterocolitis
Ishita M. Shah, Steven A. Frese, Gege Xu, Carlito B. Lebrilla, Juliana Maria Leite Nobrega De Moura Bell, Daniela Barile, David A. Mills

Metabolic Dysfunction and Bioenergetic Failure in Neonatal Necrotizing Enterocolitis
Tiffany J Sinclair, Dongyan Zhang, Yungliang Chen, Bruce X Ling, Claudia M Mueller, Harvey J Cohen, Reese H. Clark, Karl G Sylvester

A single nucelotide polymorphism in the dual specificity phosphatase-6 gene is associated with a decreased risk of developing necrotizing enterocolitis in preterm infants
Maria M. Talavera, Yi Jin, Kim McBride, Leif D. Nelin

Characterization of the infantile mucosal immune system and microbiome in health and disease
Amy Tsou, Sarah Walls, Catherine J Hunter, Esi Lamousé-Smith and Scott Snapper

Does the Initial Procedure for Surgical NEC Really Matter?
Yanowitz T, Walek S, Zaniletti I, Sharma J, Brozanski B, Sullivan K, DiGeronimo R, Piazza AJ, Wadhawan R, Murthy K

The following posters were authored by NEC-impacted families and are available to view at www.NECsociety.org/nec-family-posters/

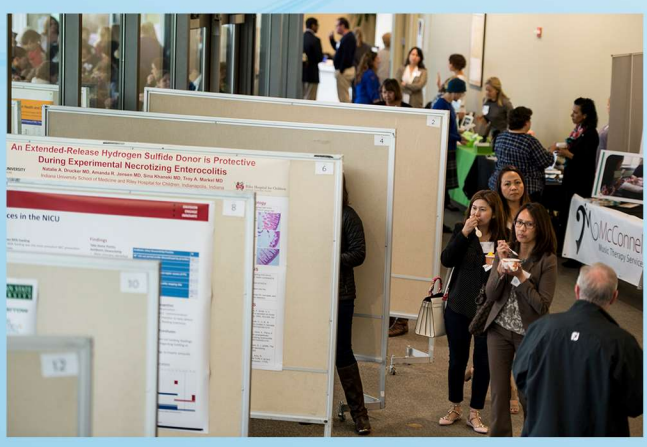
What I Wish I Could Tell You: Grayson's Story
Laurel and Jerome Grayson

What I Wish I Could Tell You: Hope's Story
Kari Gregerson and Joe Luchsinger

What I Wish I Could Tell You: Reid's Story
Heather Denchik

What I Wish I Could Tell You: Carol and Lydia's Story
Carol and Lydia's family

What I Wish I Could Tell You: Thoughts from 30 NEC-Impacted Families



Patient-Family Advocates

Patient-Family Advocates contributed to every aspect of the 2017 NEC Symposium from the earliest visions of the meeting to the future planning and next steps. The NEC Society is grateful to the patient-family advocates who dedicated their time and shared their stories, resulting in the NEC Symposium's success:

Jennifer Canvasser
Noah Canvasser
Julie Cavellini
Heather Denchik
Kari Gregerson
Cristal Grogan
Kathleen Jachnycky
Heidi Kapferer
Jerome Kapferer
Laurel Kapferer
Lynn Eve Komaromi
Kristy Love
Joe Luchsinger
Marlayna McBride
Mary Midolo
Leslie Napolitano
Elaine Nell
Brooke Propst
Michael Propst
Ryan Raab
Simone Rosito
Keira Sorrells
Jill Specht
Nicholas Specht
Heather Tanner
Christine Tester
Erin Umberger
Stephanie Vaughan

Exhibitors

The 2017 NEC Symposium featured 12 nonprofit exhibitor organizations. Each of these nonprofits are focused on advancing the needs of families in the NICU and encouraging best practices in NICU care.

Hand to Hold
Human Milk Banking Association of North American
Morgan Leary Vaughan Fund
NEC Society
NEC Society Research Collaborative
National Association of Neonatal Nurses (Northern CA)
National Perinatal Association
NICU Helping Hands
Preemie Parent Alliance
San Jose Mothers Milk Bank
Sutter Children's Hospital Music Therapy
Team Grayson

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