

Contents

Foreword: The Lifelong Imprint of Early Nutrition **xv**

Lucky Jain

Preface: Maternal, Fetal, and Neonatal Nutrition Has Lifelong Implications **xix**

Akhil Maheshwari and Jonathan R. Swanson

Neonatal and Preterm Infant Growth Assessment **295**

Tanis R. Fenton, Susan Dai, Vikki Lalari, and Belal Alshaikh

The needs to assess preterm infant growth clinically differ from the needs to summarize growth for research. Clinically, growth assessments are used to understand individuals' growth relative to their individual genetic potential, morbidity status and nutrition care. Growth quantification for research purposes is used to quantify growth of groups using meaningful metrics. Historically, neonatology has lacked consistency in the use of growth metrics, over-used irrelevant categories and over-diagnosed growth failure. Understanding the numerous preterm infant expected growth patterns can help identify concerning growth.

Maternal Nutrition and Fetal/Infant Development **313**

Sangeeta Jain, Akhil Maheshwari, and Sunil K. Jain

Nutrition in pregnant mothers has long been known to be an important determinant of fetal/maternal outcomes. In general, the typical American diet shows opportunities for improvement. The intake of fruits, vegetables, whole grains, and fiber may be below recommended levels, but the relative proportion of sodium, fats, and carbohydrates seems high. In this review, we present current evidence on how the fetal/neonatal outcomes may be altered by maternal nutrition at the time of conception, fetal nutrition in utero, contribution of maternal dietary factors in fetal outcomes, weight gain during pregnancy, diabetes during pregnancy, fetal growth restriction (FGR), maternal nutritional status during later pregnancy, and pregnancy in adolescent mothers.

Human Milk Lipids Induce Important Metabolic and Epigenetic Changes in Neonates **331**

Keyur Donda and Akhil Maheshwari

Lipids are a major source of energy during the fetal/neonatal period. Most are received from the mother, transplacentally during the intrauterine period or via maternal milk after birth. However, in addition to the known nutritional roles, lipids are now known to bind a variety of cellular receptors to regulate specific patterns in metabolism and gene expression. The expression of these receptors is regulated by various genetic and environmental stimuli, and ligation can activate positive-feedback loops in the expression and the activity of downstream signaling pathways. The authors summarize the role of lipid ligands, cognate receptors, epigenetic regulation, and downstream signaling.

Parenteral Nutrition

355

Sharon Groh-Wargo and Stephanie Merlino Barr

Prematurity and other complications at birth are nutritional emergencies. Parenteral nutrition is a bridge to enteral nutrition for a few days or months, and sometimes the sole source of nutrition for life. Parenteral nutrition regimens are constructed to provide adequate and balanced energy, macronutrients, and micronutrients to support growth and prevent deficiencies. Neonatal parenteral nutrition regimens are complicated by periodic shortages of essential products, compatibility challenges, and contaminants. Newborns benefit from serial growth assessments, monitoring of biochemical status, nutrition-focused physical examinations, and management by a multidisciplinary team to ensure adequacy of parenteral nutrition and promote best outcomes.

Lipids and Long Chain Polyunsaturated Fatty Acids in Preterm Infants

381

Kristin Santoro and Camilia R. Martin

Fatty acids are critical bioactives for fetal and neonatal development. Premature delivery and current nutritional strategies pose several challenges in restoring fatty acid balance in the preterm infant. The impact on fatty acid balance and outcomes using lipid emulsions, enteral nutrition, and enteral supplements are reviewed, including a summary of the most recent large clinical trials of enteral fatty acid supplementation for the preterm infant. Research gaps remain in successfully implementing nutritional strategies to optimize fatty acid status in preterm infants.

Neonatal Glucose Homeostasis

393

Cynthia L. Blanco and Jennifer Kim

Hypoglycemia is a common condition in the newborn period. Several intrinsic and extrinsic factors play a role in the degree/duration of hypoglycemia. Multiple thresholds have been proposed as a potential point whereby hypoglycemia may have short and long-term adverse effects. Rather than a “numerical” threshold, treatment approaches should be individualized and tailored to the etiology, symptoms, and neonatal underlying conditions. Hyperglycemia in the newborn period is commonly seen in preterm infants and can exert gluco-toxic effects in organs at critical periods of development. Considering the peripheral insulin resistance (IR) of prematurity and contributing factors is key to achieving euglycemia.

Cerebral Effects of Neonatal Dysglycemia

405

Megan E. Paulsen and Raghavendra B. Rao

This article summarizes the available evidence reporting the relationship between perinatal dysglycemia and long-term neurodevelopment. We review the physiology of perinatal glucose metabolism and discuss the controversies surrounding definitions of perinatal dysglycemia. We briefly review the epidemiology of hypoglycemia and hyperglycemia in fetal, preterm, and term infants. We discuss potential pathophysiologic mechanisms contributing to dysglycemia and its effect on neurodevelopment. We highlight current strategies to prevent and treat dysglycemia in the context of neurodevelopmental outcomes. Finally, we discuss areas of future research and the potential role of continuous glucose monitoring.

Enteral Nutrition: The Intricacies of Human Milk from the Immune System to the Microbiome 427

Jaclyn B. Wiggins, Rachael Trotman, Patti H. Perks, and Jonathan R. Swanson

In 2012, the American Academy of Pediatrics stated that all preterm infant diets should consist of human milk (mother's own milk or pasteurized donor human milk). The clinical reasons supporting this policy are many, including reducing infections and retinopathy of prematurity, decreased neonatal intensive care unit length of stay, subsequent readmissions, a decrease in mortality, and improved neurodevelopmental outcomes. This article focuses on human milk, its composition and bioactive factors, and how it affects the gut-brain axis through the microbiome. We examine how differences between mother's own milk and pasteurized donor human milk affect the premature infant.

Human Milk Fortification: A Practical Analysis of Current Evidence 447

Erynn M. Bergner, Sarah N. Taylor, Laura A. Gollins, and Amy B. Hair

Human milk (HM) with appropriate fortification is the recommended nutrition for very low birth weight (VLBW) infants. Fortification provides additional nutrients, vitamins, and minerals to support the growing preterm infant during critical periods of development. This article discusses the variability of HM including differences between maternal and pasteurized donor human milk (DHM), fortification of HM through the use of single- and multi-nutrient fortifiers, and clinical controversies including the timing of fortification, volume of feedings, and future innovations in HM fortification.

Long-Term Impact of Early Nutritional Management 461

Catherine O. Buck and Angela M. Montgomery

Early nutritional management and growth monitoring of the preterm infant represents an opportunity to target normal brain growth and optimize neurodevelopmental outcomes. Optimization of early protein energy, use of human milk, and growth targets that follow measures over time rather than measures at discharge or term age are the strongest indicators of neurodevelopmental outcome in very preterm infants. Future research should target identification of body composition measures and postdischarge nutrition and growth patterns associated with neurodevelopmental outcomes in preterm infants. This article reviews the link between early nutrition and growth targets in extremely preterm infants with long-term clinical outcomes.

Infant Nutrition in Low- and Middle-Income Countries 475

Aamir Javaid and Sana Syed

The burden of infant malnutrition is greatest in low- and middle-income countries (LMICs). Infant malnutrition is defined based on distinct subcategories, among them stunting (low-height-for-age) and wasting (low-weight-for-height). Some experts are shifting more toward understanding the interplay between these overlapping phenotypes and other confounding factors such as maternal nutrition and environmental hygiene. Current guidelines emphasize appropriate breastfeeding and nutrition within the

1000 days from conception to a child's second birthday to optimize early development. Future research directed toward better biomarkers of malnutrition before acute clinical symptoms develop will help direct targeted efforts toward at-risk populations.

Nutritional Supplements to Improve Outcomes in Preterm Neonates

485

Mohan Pammi and Ravi M. Patel

Preterm infants are at higher risk of mortality and morbidity compared with those born at term. Nutrition-related morbidities include poor growth, immune deficiency, nutritional deficiencies, and adverse long-term neurodevelopment. In addition to macronutrients, many nutritional supplements have been used to enhance growth and development, and decrease infections. Nutrients can enhance preterm infants' immune status, optimize the microbiome, improve growth and development, and influence the risk of necrotizing enterocolitis, sepsis, and other outcomes.

Evidence-Based Approaches to Successful Oral Feeding in Infants with Feeding Difficulties

503

Kathryn A. Hasenstab and Sudarshan R. Jadcherla

Infants in the neonatal intensive care unit (NICU) frequently have feeding difficulties with the root cause remaining elusive to identify. Evaluation of the provider/parent/infant feeding process may provide objective clues to sources of feeding difficulty. Specialized testing may be necessary to determine if the infant's swallowing skills are dysfunctional, immature, or maldeveloped, and to determine the risk of feeding failure or chronic tube feeding. Current evidence-based diagnostic and management approaches resulting in successful oral feeding in the NICU infant are discussed.

Short Bowel Syndrome and Dysmotility

521

Muralidhar H. Premkumar

Due to recent advances, the mortality due to short bowel syndrome (SBS) has significantly decreased, but the morbidities are still high. Morbidities arising specifically due to dysmotility in SBS include feeding intolerance, prolonged dependence on parenteral nutrition, and associated complications such as intestinal failure associated liver disease, and bloodstream infections. The understanding of the pathogenesis of dysmotility in SBS has improved vastly. However, the tools to diagnose dysmotility in SBS in infants are restrictive, and the medical therapies to treat dysmotility are limited. Surgical techniques available for the treatment after failure of conservative management of dysmotility offer hope but carry their associated risks. The evidence to support either the medical therapies or the surgical techniques to treat dysmotility in SBS in children is scarce and weak. Development of newer therapies and efforts to build evidence to support currently available treatments in treating dysmotility in SBS is needed.

Malabsorption Syndromes and Food Intolerance

537

Jonathan Medernach and Jeremy P. Middleton

Feeding intolerance is ubiquitous in neonatal intensive care units with as many signs and symptoms as possible diagnoses. Optimizing nutrition is

paramount in both preterm and term infants. Determining the cause of feeding intolerance and adjusting nutrition interventions is an important part of the daily care of newborns. This review discusses the role of malabsorption and food intolerance as possible causes of nutrition difficulties in the newborn.

Nutritional Management of Short Bowel Syndrome

557

Muralidhar H. Premkumar, Amuchou Soraisham, Nitasha Bagga, L. Adriana Massieu, and Akhil Maheshwari

Short bowel syndrome (SBS) of infancy is a cause of prolonged morbidity with intolerance to enteral feeding, specialized nutritional needs, and partial/total dependence on parenteral nutrition. These infants can benefit from individualized nutritional strategies to support and enhance the process of intestinal adaptation. Early introduction of enteral feeds during the period of intestinal adaptation is crucial, even though the enteral feedings may need to be supplemented with an effective, safe, and nutritionally adequate parenteral nutritional regimen. Newer generation intravenous lipid emulsions can be effective in preventing and treating intestinal failure-associated liver disease. Prevention of infection(s), pharmaceutical interventions to enhance bowel motility and prevent/mitigate bacteria overgrowth, and specialized multidisciplinary care to minimize the injury to other organs such as the liver, kidneys, and the brain can assist in nutritional rehabilitation and lower the morbidity in SBS.