NICU
Primer for Pharmacists

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Dedication

In memory of my dad who taught me the value of hard work.

To my mom and my sister Debbie who are always there for me; to my sweet daughter Abby for being the best cheerleader a girl could have and for all the time you’ve sacrificed with mom so I could work on “the book”; to all the students and residents who have challenged me to broaden my understanding; and to all the babies who have inspired and amazed me with their resilience.

Special thanks to Brock Harris and the other authors who were willing to come along on this journey with me.
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreword</td>
<td>vii</td>
</tr>
<tr>
<td>Preface</td>
<td>xi</td>
</tr>
<tr>
<td>Contributors</td>
<td>xiii</td>
</tr>
<tr>
<td>Reviewer</td>
<td>xv</td>
</tr>
<tr>
<td>Common Abbreviations in Neonatal Medicine</td>
<td>xvii</td>
</tr>
</tbody>
</table>

**Chapter 1.** General NICU Considerations ............................................................. 1  
*Megan Lunberry, PharmD, and Miyuki Nakayama Shouse, RPh, MS*

**Chapter 2.** Developmental Pharmacology, Pharmacokinetics, and Pharmacodynamics ............................................................. 17  
*John Brock Harris, PharmD, BCPS*

**Chapter 3.** Parenteral Nutrition ............................................................. 27  
*Ying-Tang Ng, PharmD*

**Chapter 4.** Drugs in Lactation ............................................................. 43  
*Amy P. Holmes, PharmD*

**Chapter 5.** Neonatal Abstinence Syndrome ............................................................. 55  
*Amy P. Holmes, PharmD*

**Chapter 6.** Apnea of Prematurity ............................................................. 65  
*John Brock Harris, PharmD, BCPS*

**Chapter 7.** Respiratory Distress Syndrome and Bronchopulmonary Dysplasia ......... 77  
*Julia Lau, PharmD, BCPS*

**Chapter 8.** Patent Ductus Arteriosus ............................................................. 93  
*Betsy Walters Burkey, PharmD, BCPS*

**Chapter 9.** Pain and Sedation ............................................................. 111  
*Ashley McCallister, PharmD, and Amy P. Holmes, PharmD*

**Chapter 10.** Neonatal Bacterial Sepsis and Meningitis ............................................................. 131  
*John Brock Harris, PharmD, BCPS*
Chapter 11. TORCH Infections ................................................................. 141
Amy P. Holmes, PharmD

Chapter 12. Respiratory Syncytial Virus .............................................. 155
Betsy Walters Burkey, PharmD, BCPS, and Michelle F. F. Poole, PharmD

Chapter 13. Necrotizing Enterocolitis .................................................. 167
John Brock Harris, PharmD, BCPS

Chapter 14. Gastrointestinal Disorders ............................................... 179
John Brock Harris, PharmD, BCPS

Chapter 15. Vaccine Use in Infants ....................................................... 187
Amy P. Holmes, PharmD

Chapter 16. Persistent Pulmonary Hypertension of the Newborn ............ 197
Julia Lau, PharmD, BCPS

Chapter 17. Neonatal Seizures .............................................................. 209
John Brock Harris, PharmD, BCPS

Chapter 18. Extracorporeal Membrane Oxygenation .............................. 215
Wyn Wheeler, PharmD, FCCM

Index ........................................................................................................ 229
Foreword

As pharmacists take on increasing responsibility for care of critically ill patients, providing pharmaceutical care for critically ill newborns in neonatal ICU can be particularly challenging. What other practice includes patients with weights that may vary 10-fold (i.e., 500 grams to 5,000 grams at birth) or can be expected to more than quadruple their weight while concurrently going through organ maturation and periods of organ damage during their hospital stay? Add to this the challenge of multiple concurrent diseases, changing therapeutic strategies based on conflicting scientific data, and NICU-specific pharmaceutical products or compounded preparation requirements using drugs with concentrations designed for administration to older patients. Consequently, it is readily apparent why a book such as the *NICU Primer for Pharmacists* can be a useful, rapid resource for practicing hospital pharmacists who serve a NICU in addition to all the other patient populations within the hospital.

When I started NICU practice in 1977, there was virtually nothing to guide clinicians regarding best doses or practices for treating neonatal diseases; later evidence demonstrated that much of what we did was actually harmful to the newborn. Most NICUs had little to offer newborns below 28 weeks gestation, before surfactant became available, and mortality rates were extremely high. The increasing survival rates for preterm infants as young as 24 weeks gestation means that clinicians are confronted with a whole new set of challenges to maximize the likelihood of not only survival, but survival without serious long-term damage and neurodevelopmental delays.
As methods to optimize outcomes evolve, timely interventions are likely required to interrupt the cascade of physiologic and biochemical events that produce damage. In many cases, this will mean optimal drug selection at the correct dose delivered to the patient within hours of recognizing the problem. For the pharmacist, it will require an excellent knowledge of drugs and diseases, or at least a reference that provides concise and pragmatic information, such as provided in this book. No doubt the information will come as a welcome resource when the pharmacist tries to deal with an array of rapid and complicated decisions.

In much of my career, lack of products specifically manufactured for neonatal care and the ever-present danger of dosing errors, often reflecting decimal place errors, made the possibility for drug-related complications unacceptably high and required constant vigilance by the healthcare team. Today’s pharmacists are confronted with additional, unique challenges to optimal care. This includes the dilemma of drug shortages and consequent use restrictions, which require pharmacists to have creative approaches to deliver the desired products to the most vulnerable patients. It also involves managing inventory and availability of very expensive new products needed to treat uniquely neonatal diseases. Other important functions include overseeing dosing adjustments as patients mature, increase or lose body weight, or suffer organ damage that alters drug elimination or results in changes in drug distribution. When situations arise where rapid administration of drugs to the patient is required to reduce mortality or long-term damage, drug distribution systems will need to adapt and procedures to be in place to ensure such orders are processed and delivered in a timely manner to the bedside. Pharmacists must be facile in detecting and correcting product dilutions to verify the correct dose because drugs often come in different strengths and different dilutions may need to be made. Many considerations must go through pharmacists’ minds as they collaborate with the healthcare team to promote safe and effective drug therapy.

The *NICU Primer for Pharmacists* provides a valuable overview of several common diseases, drug therapy, and critical preparation or administration considerations. The disclaimer in the front of the text wisely cautions the reader to consider whether the information remains current in this rapidly changing field. Nevertheless, even if the facts change, there is a logical organization and thought process reflected throughout this book that will provide pharmacists with a strategy for dealing with NICU patients.
and therapeutic approaches needed to care for them. This makes the book a useful resource for pharmacists, especially those who do not specialize in NICU, and students and residents who may do clinical clerkships in NICU.

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Many pharmacists working in hospital pharmacies today have little or no formal training in neonatology, yet they are faced with dispensing medications to this fragile NICU population. Some units have neonatal specialists who oversee medication-use practices; however, many units are too small to justify having the full time support of a specialist. Even in units where there is a specialist, they are not available 24/7 to verify orders, mix IVs, and dispense medications. This book is meant as an introduction to the world of the NICU for those front-line pharmacists who serve neonatal patients. Beyond checking for accuracy of weight-based dosing, this book strives to provide an overall understanding of the most common disease states in the neonatal population as well as the role of the most commonly used pharmaceutical agents in the NICU.

In addition, this book serves as an introduction to NICU for pharmacy learners. For years I have struggled with finding the right reading assignments for students and residents taking my NICU rotation. Many of the textbook chapters and journal articles that I have used assume some baseline knowledge of neonatal medicine. Even the learner who has opted to take an elective course in pediatrics has had little or no exposure to neonatology. This book serves as baseline information to familiarize those learners with this unique population and prepare them to delve into the primary literature.

Each chapter gives basic information on disease states specific to the neonatal population or describes scenarios that make common disease states different in neonates. At the end of every chapter, except the first one, you
will find a Suggested Reading list to dig further into a particular topic. (The Suggested Readings for Chapter 1 is the rest of the book!) Chapter 1 does include a list of recommended neonatal references. These are “go to” resources that may be helpful in researching neonatal topics not found in this book.

In reading and using the *NICU Primer for Pharmacists*, you will see that neonates are not just small adults. They are a very unique and specialized patient population warranting extra attention and care.

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Common Abbreviations in Neonatal Medicine

AA: Amino acid
AAP: American Academy of Pediatrics
ABG: Arterial blood gas
ACEI: Angiotensin-converting enzyme inhibitor
ACOG: American College of Obstetricians and Gynecologists
AED: Antiepileptic drugs
AEDF: Absent end diastolic flow
AGA: Appropriate for gestational age
AMPA: α-amino-3-hydroxyl-5-methyl-4-isoxazolepropionic acid
ANC: Absolute neutrophil count
AOP: Apnea of prematurity
APAP: Acetaminophen
APGAR: Appearance, Pulse, Grimace, Activity, and Respiration
ART: Antiretroviral treatment
ASHP: American Society of Health-System Pharmacists
A.S.P.E.N.: American Society for Parenteral and Enteral Nutrition
BBT: Baby’s blood type
BIO: Binocular indirect ophthalmoscope
BPD: Bronchopulmonary dysplasia
BSA: Body surface area
BUN: Blood urea nitrogen
cAMP: Cyclic adenosine monophosphate
CBC: Complete blood count
CDC: Centers for Disease Control and Prevention
CDH: Congenital diaphragmatic hernia
CGA: Corrected gestational age
cGMP: Cyclic guanosine monophosphate
Cl: Confidence interval
CLABSI: Central line-associated bloodstream infection
CLD: Chronic lung disease
CMV: Cytomegalovirus
CMV HIG: Cytomegalovirus hyperimmune globulin
CNS: Central nervous system
CoNS: Coagulase-negative staphylococci
CPAP: Continuous positive airway pressure
CPS: Canadian Paediatric Society
CRIES: Crying, Requires O₂ for SaO₂ <95%, Increased vital signs (blood pressure and heart rate), Expression, Sleeplessness
CRP: C-reactive protein
CS: Caesarean section
CSF: Cerebrospinal fluid
CVS: Congenital varicella syndrome
CYP: Cytochrome P450
DA: Ductus arteriosus
DART: Dexamethasone: A Randomized Trial
DC: Direct Coombs
DIC: Disseminated intravascular coagulation
DTaP: Diphtheria, tetanus, and pertussis
ECMO: Extracorporeal membrane oxygenation
EEG: Electroencephalogram
ELBW: Extremely low birth weight
EMLA: Eutectic mixture of local anesthetics
EOS: Early-onset sepsis
EPT: Extremely preterm
ET: Endotracheal or endothelial
FDA: Food and Drug Administration
FiO₂: Fraction inspired oxygen concentration
FTA-ABS: Fluorescent treponemal antibody-absorption
g: gram
GA: Gestational age
GABA: Gamma-aminobutyric acid
GBS: Group B Streptococcus
GC: Gonorrhea/chlamydia
GER: Gastroesophageal reflux
GERD: Gastroesophageal reflux disease
GFR: Glomerular filtration rate
GI: Gastrointestinal
GIR: Glucose infusion rates
GPA: gravida/para/abortus (obstetric history)
H₂RA: H₂-receptor antagonist
HBIG: Hepatitis B immune globulin
HEP: Hepatitis
HepB: Hepatitis B
Hib: Haemophilus influenza
HIV: Human immunodeficiency virus
HMF: Human milk fortifier
HSV: Herpes simplex virus
IAP: Intrapartum antibiotic prophylaxis
IDM: Infant of diabetic mother
IFALD: Intestinal failure-associated liver disease
IgG: Immunoglobulin G
IgM: Immunoglobulin M
IM: Intramuscular
iNO: Inhaled nitric oxide
INR: International normalized ratio
IPV: Inactivated polio virus
IUGR: Intrauterine growth restriction
IV: Intravenous
IVFE: Intravenous fat emulsion
IVH: Intraventricular hemorrhage
kg: kilogram
KMC: Kangaroo mother care
LBW: Low birth weight
LGA: Large for gestational age
LOS: Late-onset sepsis
LPT: Late preterm
M3G: Morphine-3-glucuronide
M6G: Morphine-6-glucuronide
MAP: Mean airway pressure
MAS: Meconium aspiration syndrome
MBT: Maternal blood type
MCT: Medium chain triglyceride
MDI: Metered dose inhaler
mm: Millimeter
mL: Milliliter
NAS: Neonatal abstinence syndrome
NEC: Necrotizing enterocolitis
NICU: Neonatal intensive care unit
NIH: National Institutes of Health
NIPS: Neonatal Infant Pain Scale
NMBA: Neuromuscular blocking agents
NMDA: N-methyl-D-aspartate
NO: Nitric oxide
N-PASS: Neonatal Pain, Agitation, and Sedation Scale
NPO: Nothing by mouth
NRFHT: Non-reassuring fetal heart trace
NSAIDs: Nonsteroidal anti-inflammatory drugs
OI: Oxygenation index
OR: Odds ratio
PAH: Pulmonary arterial hypertension
PAMF-TSL: Palo Alto Medical Foundation–Toxoplasma Serology Laboratory
PaO₂: Partial pressure of oxygen
PCR: Polymerase chain reaction
PCT: Procalcitonin
PDA: Patent ductus arteriosus
PDE: Phosphodiesterase
PDE₃: Phosphodiesterase type 3
PDE₅: Phosphodiesterase type 5
PEEP: Positive end-expiratory pressure
PGE₂: Prostaglandin E₂
PGI₂: Prostacyclin I₂
PICC: Peripherally inserted central catheter
PIPP: Premature Infant Pain Profile
PIV: Peripheral IV
PMA: Post-menstrual age
PN: Parenteral nutrition
PNA: Postnatal age
PNALD: Parenteral nutrition-associated liver disease
PNC: Prenatal care
PO: By mouth or oral
PPHN: Persistent pulmonary hypertension of the newborn
PPI: Proton-pump inhibitor
PPROM: Prolonged premature rupture of membranes
PPV: Positive pressure ventilation
PRBC: Packed red blood cell
PVL: Periventricular leukomalacia
PVR: Pulmonary vascular resistance
RDS: Respiratory distress syndrome
ROM: Rupture of membranes
ROP: Retinopathy of prematurity
ROS: Rule out sepsis
RPR: Rapid plasma reagin or reagent (screening test for syphilis)
RR: Relative risk
RSV: Respiratory syncytial virus
RUB: Rubella
SaO₂: Arterial oxygen saturation
SEM: Skin, eyes, and mouth
SGA: Small for gestational age
SIDS: Sudden infant death syndrome
SP-B: Surfactant protein B
SP-C: Surfactant protein C
SQ: subcutaneous
SSRI: Serotonin discontinuation syndrome
SVR: Systemic vascular resistance
TD: Tardive dyskinesia
TIPP: Trial of Indomethacin Prophylaxis in Preterm
TOF: Train-of-four
TORCH: Toxoplasmosis, Rubella, Cytomegalovirus, and Herpes Simplex
TP-EIA: Treponema pallidum enzyme immunoassay
TPN: Total parenteral nutrition
TP-PA: Treponema pallidum particle agglutination
TTN: Transient tachypnea of the neonate
UAC: Umbilical artery catheter
UVC: Umbilical venous catheter
VariZIG: Varicella zoster immune globulin
Vd: Volume of distribution
VD: Vaginal delivery
VEGF: Vascular endothelial growth factor
VKDB: Vitamin K deficiency bleeding
VLBW: Very low birth weight
VPT: Very preterm
WAT-1: Withdrawal Assessment Tool-1
WBC: White blood cell