

# NICU

## Primer for Pharmacists

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# Dedication

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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.



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# Foreword

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**A**s 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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# Preface

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**M**any 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.

*Amy P. Holmes*

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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:**  $\alpha$ -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

**CI:** Confidence interval

**CLABSI:** Central line-associated blood stream 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 O<sub>2</sub> for SaO<sub>2</sub> <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

**FiO<sub>2</sub>:** 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:** grvida/para/abortus (obstetric history)

**H<sub>2</sub>RA:** H<sub>2</sub>-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

<b>IPV:</b> Inactivated polio virus	<b>OI:</b> Oxygenation index
<b>IUGR:</b> Intrauterine growth restriction	<b>OR:</b> Odds ratio
<b>IV:</b> Intravenous	<b>PAH:</b> Pulmonary arterial hypertension
<b>IVFE:</b> Intravenous fat emulsion	<b>PAMF-TSL:</b> Palo Alto Medical Foundation-Toxoplasma Serology Laboratory
<b>IVH:</b> Intraventricular hemorrhage	<b>PaO<sub>2</sub>:</b> Partial pressure of oxygen
<b>kg:</b> kilogram	<b>PCR:</b> Polymerase chain reaction
<b>KMC:</b> Kangaroo mother care	<b>PCT:</b> Procalcitonin
<b>LBW:</b> Low birth weight	<b>PDA:</b> Patent ductus arteriosus
<b>LGA:</b> Large for gestational age	<b>PDE:</b> Phosphodiesterase
<b>LOS:</b> Late-onset sepsis	<b>PDE<sub>3</sub>:</b> Phosphodiesterase type 3
<b>LPT:</b> Late preterm	<b>PDE<sub>5</sub>:</b> Phosphodiesterase type 5
<b>M3G:</b> Morphine-3-glucuronide	<b>PEEP:</b> Positive end-expiratory pressure
<b>M6G:</b> Morphine-6-glucuronide	<b>PGE<sub>2</sub>:</b> Prostaglandin E <sub>2</sub>
<b>MAP:</b> Mean airway pressure	<b>PGI<sub>2</sub>:</b> Prostacyclin I <sub>2</sub>
<b>MAS:</b> Meconium aspiration syndrome	<b>PICC:</b> Peripherally inserted central catheter
<b>MBT:</b> Maternal blood type	<b>PIPP:</b> Premature Infant Pain Profile
<b>MCT:</b> Medium chain triglyceride	<b>PIV:</b> Peripheral IV
<b>MDI:</b> Metered dose inhaler	<b>PMA:</b> Post-menstrual age
<b>mm:</b> Millimeter	<b>PN:</b> Parenteral nutrition
<b>mL:</b> Milliliter	<b>PNA:</b> Postnatal age
<b>NAS:</b> Neonatal abstinence syndrome	<b>PNALD:</b> Parenteral nutrition-associated liver disease
<b>NEC:</b> Necrotizing enterocolitis	<b>PNC:</b> Prenatal care
<b>NICU:</b> Neonatal intensive care unit	<b>PO:</b> By mouth or oral
<b>NIH:</b> National Institutes of Health	<b>PPHN:</b> Persistent pulmonary hypertension of the newborn
<b>NIPS:</b> Neonatal Infant Pain Scale	<b>PPI:</b> Proton-pump inhibitor
<b>NMBA:</b> Neuromuscular blocking agents	<b>PPROM:</b> Prolonged premature rupture of membranes
<b>NMDA:</b> N-methyl-D-aspartate	<b>PPV:</b> Positive pressure ventilation
<b>NO:</b> Nitric oxide	<b>PRBC:</b> Packed red blood cell
<b>N-PASS:</b> Neonatal Pain, Agitation, and Sedation Scale	<b>PVL:</b> Periventricular leukomalacia
<b>NPO:</b> Nothing by mouth	
<b>NRFHT:</b> Non-reassuring fetal heart trace	
<b>NSAIDs:</b> Nonsteroidal anti-inflammatory drugs	

**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

**SaO<sub>2</sub>:** 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:** **T**oxoplasmosis, **R**ubella,  
Cytomegalovirus, and **H**erpes  
**S**implex

**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