Steven M. Donn
Sunil K. Sinha *Editors*

Manual of Neonatal Respiratory Care

Third Edition

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To all those parents in the past 30 years
who have entrusted me with the care
of their most precious possessions

Steven M. Donn

To all those who have pursued careers
in the care of newborn infants

Sunil K. Sinha

Foreword

A successful transition from fetal to neonatal life is dependent upon the profound cardiorespiratory adaptations occurring at this time. Unfortunately, these events frequently require medical intervention, especially in preterm infants. The consequences of the resultant pathophysiologic changes and therapeutic interventions in such neonates may have long lasting effects on the developing respiratory system and even the neurodevelopmental outcome of this high-risk population.

Recognition of the importance of neonatal respiratory management was an early milestone in the history of neonatology. The role of surfactant deficiency in the etiology of neonatal respiratory distress syndrome was sealed over 50 years ago, and this paved the way for the introduction of assisted ventilation for this population in the 1960s. I was privileged to be introduced to neonatal pediatrics in the early 1970s at a time when the advent of continuous positive airway pressure demonstrated how physiologic insight can be translated into effective therapy. The decade of the 1970s offered so many other innovations in neonatal respiratory care. These included noninvasive blood gas monitoring, xanthine therapy for apnea, and our first real understanding of the pathogenesis and management of meconium aspiration syndrome, group B streptococcal pneumonia, and persistent fetal circulation or primary pulmonary hypertension of the newborn, three frequently interrelated conditions. The decade ended in remarkable fashion with the introduction of exogenous surfactant therapy and recognition that the novel new technique of high-frequency ventilation allows effective gas exchange in sick neonates.

The last 30 years have enabled us to build drastically on the foundation of this earlier period in neonatal respiratory management. The improved survival of extremely low birth weight infants has been nothing short of spectacular. For preterm infants, the focus is now clearly to reduce the unacceptably high incidence of bronchopulmonary dysplasia. However, many key questions in neonatal respiratory care still need to be addressed. What constitutes optimal ventilatory strategy and optimal targets for gas exchange as reflected in levels of PaO_2 and $PaCO_2$? What is the risk/benefit ratio of current and future pharmacologic adjuncts to ventilatory

support, such as inhaled nitric oxide, xanthine, or antioxidant therapy, to name a few? How can we safely support ventilation and provide pharmacotherapy in the most noninvasive manner?

For preterm or term infants with malformations of the respiratory system, advances in pre- and postnatal imaging and surgical techniques hold promise for improved outcome. Great strides are being made simultaneously in our understanding of the molecular basis for normal and abnormal lung development. Furthermore, it is being increasingly recognized that genotypic characteristics may greatly influence the consequences of subsequent environmental exposures on lung development. These scientific advances need to be translated into improving adverse neonatal outcomes, such as the unacceptably high rate of wheezing disorders and asthma in the survivors of neonatal intensive care. As care providers to neonates, it is our responsibility to encourage clinical trials and other patient-based investigation that will allow us to optimize the outcome of neonatal respiratory care.

The third edition of the *Manual of Neonatal Respiratory Care* is comprehensive and provides an important educational tool to address many of these challenges. It is, again, thoroughly edited by the accomplished trans-Atlantic team of Steven Donn and Sunil Sinha. Once again, they have assembled physician/scientist leaders in the field of Developmental Pulmonology who provide a true international perspective to neonatal respiratory care. Both prior and new contributors provide a concise overview that spans neonatal physiology, pathogenesis of disease, and unique approaches to management of both simple and complex neonatal respiratory disorders. The result is a comprehensive text that provides a strongly international insight into neonatal respiratory care in a user-friendly, practical format.

Cleveland, OH, USA Richard J. Martin, MBBS, FRACP

Preface

It is indeed a privilege for us to edit the third edition of the *Manual of Neonatal Respiratory Care*, and we were honored when Springer Science+Business Media approached us to do this.

In the years that have passed since the second edition, much has transpired, some technological and some philosophical. Microprocessor-based technology continues to refine the equipment at our disposal and to offer us almost limitless ways to manage neonatal respiratory failure. At the same time, there has been a resurgence in the philosophy of minimal intervention, giving rise to the new popularity of continuous positive airway pressure and noninvasive ventilation. We have entered the age of evidence-based medicine, emphasizing the importance of the randomized, controlled trial. We have seen enormous growth in information technology and worldwide access to it. Therapeutic options also continue to expand, but greater care must be taken as survival of even more premature babies accentuates their toxicities and complications.

We have maintained the same outline format for the third edition, appreciating the positive feedback we have received from many that this is conducive to bedside use. We have not only updated previous chapters, we have added newer ones to reflect changes in practice, equipment, and science. Some of these include an expanded focus on oxygen toxicity, control of oxygen delivery, use of nasal cannula therapy, noninvasive ventilation, newer ventilators, management of hemodynamics, home ventilation, interpreting medical literature, medico-legal issues, and an expansive contemporary bibliography on neonatal respiratory care.

Our list of contributors represents a world-class group of scientists, clinicians, and experts in their respective fields. We are indebted to them for taking the time and effort to provide their insights and knowledge. The *Manual of Neonatal Respiratory Care* would also not have been possible without the efforts of many "behind the scenes" individuals, including our development editor, Mike Griffin, and our acquisitions editor, Shelley Reinhardt, both of Springer; Vicky Hall in Middlesbrough; and Susan Peterson in Ann Arbor, who coordinated the efforts of more than 50 contributors,

and somehow managed to get all 85 chapters formatted the same way (an incredible feat!). Lastly, we acknowledge our wives, Paula Donn, and Lalita Dean, for their patience and sacrifices while we put the *Manual* together.

Change will continue to occur at a rapid pace. What we hope this edition accomplishes is the establishment of fundamentals that will enable the clinician to develop the ability to assimilate change in a physiologically sound way while providing the best possible care to his or her patients.

Ann Arbor, MI, USA — Steven M. Donn
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List of Abbreviations

μm	Micrometer
°C	Degrees Celsius (Centigrade)
°K	Degrees, Kelvin
A	Alveolar
a	Arterial
a/A	Arterial/alveolar ratio
A/C	Assist/control
AAC	Automatic airway compensation
A-aDO_2	Alveolar–arterial oxygen gradient
ABG	Arterial blood gas
ACT	Activated clotting time
ADP	Adenosine diphosphate
AH	Absolute humidity
ALTE	Apparent life-threatening event
AM	Morning
AMP	Adenosine monophosphate
Ao	Aortic
AOI	Apnea of infancy
AOP	Apnea of prematurity
AP	Anteroposterior
ARDS	Adult (or acute) respiratory distress syndrome
ASD	Atrial septal defect
ATP	Adenosine triphosphate
ATPS	Ambient temperature and pressure, saturated with water vapor
BAER	Brainstem audiometric-evoked responses
BP	Blood pressure
BPD	Bronchopulmonary dysplasia
BPM (bpm)	Beats or breaths per minute
BR	Breath rate
BTPS	Body temperature and pressure, saturated with water vapor

C	Compliance
C20	Compliance over last 20% of inflation
CCAM	congenital cystic adenomatoid malformation
cAMP	Cyclic adenosine monophosphate
CBF	Cerebral blood flow
CBG	Capillary blood gas
cc	Cubic centimeter
C_D or C_{DYN}	Dynamic compliance
CDH	Congenital diaphragmatic hernia
CDP	Constant distending pressure
CF	Cystic fibrosis
cGMP	Cyclic guanosine monophosphate
CHAOS	Congenital high airway obstruction syndrome
CHD	Congenital heart disease
C_L	Compliance
CLD	Chronic lung disease
CLE	Congenital lobar emphysema
cm	Centimeter
CMV	Conventional mechanical ventilation
CMV	Cytomegalovirus
CNS	Central nervous system
CO	Cardiac output
CO_2	Carbon dioxide
CO-Hb	Carboxyhemoglobin
COPD	Chronic obstructive pulmonary disease
CPAP	Continuous positive airway pressure
CPL	Congenital pulmonary lymphangiectasia
CPR	Cardiopulmonary resuscitation
CPT	Chest physiotherapy
CRP	C-reactive protein
CSF	Cerebrospinal fluid
C_{ST}	Static compliance
CT	Computed tomography
CVP	Central venous pressure
CXR	Chest X-ray (radiograph)
D	End-diastole
D5W	Dextrose 5% in water
DCO_2	Gas transport coefficient for carbon dioxide
DIC	Disseminated intravascular coagulation
dL	Deciliter
DNA	Deoxyribonucleic acid
DPG	Diphosphoglycerate
DPPC	Dipalmitoyl phosphatidyl choline
DR	Delivery room

E	Elastance
ECG	Electrocardiogram
ECMO	Extracorporeal membrane oxygenation
EDRF	Endothelial-derived relaxing factor
EEG	Electroencephalogram
EF	Ejection fraction
ELBW	Extremely low birth weight
EMG	Electromyogram
EMLA	Eutectic mixture of Lidocaine and Prilocaine
ERV	Expiratory reserve volume
ET	Endotracheal
$ETCO_2$	End-tidal carbon dioxide
ETCPAP	Endotracheal continuous positive airway pressure
ETT	Endotracheal tube
F or f	Frequency
F or Fr	French
FCV	Flow control valve, flow-cycled ventilation
FDA	Food and Drug Administration (US)
FDP	Fibrin degradation products
FGF	Fibroblast growth factor
FIO_2	Fraction of inspired oxygen
FiO_2	Fraction of inspired oxygen
FOE	Fractional oxygen extraction
FRC	Functional residual capacity
FSP	Fibrin split products
FTA	Fluorescent treponemal antibody
g	Gauge
g	Gram
G	Gravida
GA	Gestational age
GBS	Group B streptococcus
GER	Gastro-esophageal reflux
GERD	Gastro-esophageal reflux disease
GIR	Glucose infusion rate
gm	Gram
GNP	Gross national product
GTP	Guanosine triphosphate
GUI	Graphics user interface
h or hr	Hour
H_2O	Water
Hb	Hemoglobin
HCH	Hygroscopic condenser humidifier
HCO_3^-	Bicarbonate

HFJV	High-frequency jet ventilation
HFNC	High flow nasal cannula
HFO	High-frequency oscillation
HFOV	High-frequency oscillatory ventilation
HFV	High-frequency ventilation
Hg	Mercury
Hgb	Hemoglobin
HME	Heat and moisture exchanger
HR	Heart rate
HSV	Herpes simplex virus
Hz	Hertz
I	Inertance
I:E	Inspiratory:expiratory ratio
IC	Inspiratory capacity
Ig	Immunoglobulin
IL	Interleukin
IMV	Intermittent mandatory ventilation
INO	Inhaled nitric oxide
IO	Intraosseous
IP	Inspiratory pressure
IPPV	Intermittent positive pressure ventilation
IRV	Inspiratory reserve volume
IUGR	Intrauterine growth restriction
IV	Intravenous
IVC	Inferior vena cava(l)
IVH	Intraventricular hemorrhage
IVS	Interventricular septum
K	Constant
kDa	Kilodalton
kg	Kilogram
kPa	Kilopascal
L	Liter
LA	Left atrium
LBW	Low birth weight
LCD	Liquid crystalline display
LED	Light emitting diode
LHR	Ratio of lung diameter to head circumference
LOS	Length of stay
LPM (lpm)	Liters per minute
LVEDD	Left ventricular end-diastolic dimension
LVID	Left ventricular internal diameter
LVIDD	Left ventricular internal diameter at diastole
LVIDS	Left ventricular internal diameter at systole
LVO	Left ventricular output

m	Meter
MAP	Mean arterial pressure
MAS	Meconium aspiration syndrome
mcg	Microgram
MD	Minute distance
mEq	Milliequivalent
MetHb	Methemoglobin
mg	Milligram
MIC	Mean inhibitory concentration
min	Minute
mL (ml)	Milliliter
mm	Millimeter
MMV	Mandatory minute ventilation
mOsm	Milliosmoles
MRI	Magnetic resonance imaging
MSAF	Meconium-stained amniotic fluid
MV	Minute ventilation
NAVA	Neurally adjusted ventilatory assist
NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care unit
NIPPV	Noninvasive positive pressure ventilation
NIRS	Near-infrared spectroscopy
NO	Nitric oxide
NO_2	Nitrogen dioxide
NOS	Nitric oxide synthase
O_2	Oxygen
OI	Oxygenation index
P	Para
P	Pressure
P50	Point of 50% saturation of hemoglobin with oxygen
$PACO_2$	Partial pressure of carbon dioxide, alveolar
$PaCO_2$	Partial pressure of carbon dioxide, arterial
PAO_2	Partial pressure of oxygen, alveolar
PaO_2	Partial pressure of oxygen, arterial
PAV	Proportional assist ventilation
Paw	Airway pressure
Pāw	Mean airway pressure
PB	Periodic breathing
PC	Pressure control
PCA	Postconceptional age
PCR	Polymerase chain reaction
PDA	Patent ductus arteriosus
PE	Elastic pressure