

Table of Contents

Ductal Closure After Birth – Morphological Aspects and New Insights	1
<i>R. Bökenkamp</i>	
Introduction	2
Developmental Background	2
Ductal Maturation	2
Postnatal Anatomical Remodelling	4
PDA in Premature Infants – Morphologic Aspects	4
Signalling Related to Ductal Closure	5
Genetic and Environmental Risk Factors for PDA in Premature Infants	5
Prevention of DA Closure in Neonates with CHD	5
Conclusion	7
References	8
Treatment Results After Ductal Closure in Extremely Low Gestational Age Infants	11
<i>P. Koehne</i>	
Factors Determining Outcome of Very Low Birth Weight Infants	12
Impact of Patent Ductus Arteriosus Intervention for Outcome	12
Prophylactic Cyclooxygenase Inhibitor Treatment	13
Prophylactic Ligation of the Ductus Arteriosus	18
Therapeutic Use of Cyclooxygenase Inhibitors for Patent Ductus Arteriosus Intervention	20
Surgical Ligation of Patent Ductus Arteriosus After Failed Pharmacological Intervention	27
Conclusions and Perspectives	31
References	31
Echocardiographic Assessment of the Patent Ductus Arteriosus in the Preterm Infant	37
<i>N. Evans</i>	
Introduction	38
Doppler Ultrasound	38

Is the Ductus Arteriosus Patent?	39
How Wide is the Ductus Arteriosus?	41
What is the Direction and Velocity of the Shunt?	42
What is the Hemodynamic Significance of the PDA?	43
Impact of the Ductal Shunt on the Lungs	46
Impact of the Ductal Shunt on the Systemic Circulation	48
Prediction of Spontaneous and Therapeutic Ductal Closure	50
Summary	52
References	53

**Evaluation of the Open Duct Using Systolic Time Intervals
and Doppler Sonography of Peripheral Arteries** 55

E. Robel-Tillig

Systolic Time Intervals	56
Definitions of the Ejection Time and the Pre-Ejection Period	56
How to Measure the Ejection Time and the Pre-Ejection Period?	58
Reference Ranges for the Ejection Time and the Pre-Ejection Period	59
Doppler Sonographic Blood Flow Parameters of Peripheral Arteries	60
Measurement of Blood Flow Parameters of Peripheral Arteries	60
Descending Aorta	60
Anterior Cerebral Artery	61
Superior Mesenteric Artery	61
Renal Artery	63
Summary and Conclusion	63
References	63

Competitive Inhibition of Bilirubin-Albumin Binding

by Ibuprofen	65
-------------------------------	----

L. Desfrere, C. Huon

Introduction	66
Hyperbilirubinemic Encephalopathy in Preterm Infants	66
Measurement of Unbound Bilirubin Concentrations	67
Bilirubin-Albumin Binding and Bilirubin Displacers	68
IBU Concentrations During Treatment of hsPDA	69
Bilirubin-Albumin Displacing Effect of IBU in Vitro	72

Bilirubin-Albumin Displacing Effect of IBU in Vivo	74
Conclusions	76
References	76
Controversies Around Treatment of the Open Duct	81
<i>B. Van Overmeire</i>	
Introduction	82
Fluid Restriction for PDA?	82
Which Drug Should Be Used?	83
A Choice Based on Side Effects?	84
Optimal Dosing of Indomethacin and Ibuprofen?	85
Is There a Role for Prophylaxis?	87
Conclusion	87
References	88
High-Dose Therapy with Cyclooxygenase-Inhibitors for Symptomatic Persistent Ductus Arteriosus in Preterms	93
<i>B. Beedgen</i>	
Treatment Options	94
Pharmacological Treatment	94
High-Dose Therapy with Indomethacin	96
Effectiveness and Side Effects of Escalating High-Dose Therapy	98
Long-Term Follow-up	101
Follow-up Results	103
Conclusions	106
Critical Perspective Concerning High-Dose Therapy with Indomethacin	107
High-Dose Therapy with Ibuprofen	109
Outlook	110
References	111
Risks and Benefits of Aggressive and Conservative Approaches to the Management of the Patent Ductus Arteriosus in Premature Infants	115
<i>S. Aliaga, M.M. Laughon</i>	
Introduction	116
PDA and Clinical Outcomes	117

PDA and Bronchopulmonary Dysplasia	117
PDA and Necrotizing Enterocolitis	119
PDA and Neurodevelopmental Impairment	121
Other systematic reviews	122
Risks of Treatment	122
Indomethacin	123
Ibuprofen	123
Surgical Ligation	124
Center (Centre) Variation in Treatment of the PDA	125
Conclusion	126
References	127
 Missing Data for an Evidence-Based Approach to the Treatment of a Patent Ductus Arteriosus	
A Small Selection of What We Do not Know Yet	131
<i>A. Franz</i>	
Prophylactic Interventions	133
Therapeutic Interventions	135
The Problem of Indications for Treatment, i.e., the Definition of a PDA Requiring Therapy	135
The Problem of Contamination	136
The Lack of Data on Long-Term Outcome	137
Further Open Questions	137
Summary	138
References	139
 Summary of the Discussions During the International Workshop on “Controversies Around Treatment of the Patent Ductus Arteriosus”	
<i>P. Herrmann</i>	
Subject Index	157