

# Contents

## Preface — vii

### **1 Accuracy Goals for Laboratory Tests — 1**

- 1.1 Accuracy and Precision — 1
  - 1.1.1 Definition — 1
  - 1.1.2 Imprecision as a Form of Error — 2
- 1.2 Types of Error — 2
  - 1.2.1 Bias — 2
  - 1.2.2 Impact of Bias — 4
- 1.3 Interference as a Type of Bias — 6
- 1.4 References — 8

### **2 Nature of Interferences — 11**

- 2.1 Definition — 11
- 2.2 Nature of Interferences — 11
- 2.3 Instrumentation — 12
- 2.4 The Chemistry of the Absorbance of Light — 15
- 2.5 References — 20

### **3 The Nature of Icteric Interference — 21**

- 3.1 Source Information on Bilirubin Interference — 21
- 3.2 Allen Correction as a Source of Bilirubin Interference — 21
- 3.3 Bilirubin Interference with Oximetry — 22
  - 3.3.1 Co-oximetry Interference — 24
  - 3.3.2 Pulse Oximetry — 25
  - 3.3.3 Cerebral Oximetry — 26
  - 3.3.4 Interference with Methemoglobin — 27
- 3.4 Chemical Reactions as a Cause of Bilirubin Interference — 28
  - 3.4.1 Bilirubin Reaction with Creatinine Methods — 29
  - 3.4.2 Bilirubin Reactions with Peroxidase Methods — 31
- 3.5 References — 32

### **4 The Nature of Lipemic and Turbidity Interferences — 35**

- 4.1 Types of Interferences — 35
- 4.2 Lipemia Causes Turbidity — 36
- 4.3 Lipemia Interference Mechanisms — 37
  - 4.3.1 Light Scattering — 37
  - 4.3.2 Lipoprotein Particles — 40
  - 4.3.3 Intralipid® and Lipemia Simulation — 42
  - 4.3.4 Empirical Studies in Lipemia Turbidity — 43

4.4	Lipoprotein Particles and Lipemia —	44
4.5	References —	45
<b>5</b>	<b>Measurement of Interference —</b>	<b>47</b>
5.1	A Typical Commercial Study —	47
5.2	Guidelines for Interference Studies —	48
5.3	Bilirubin —	49
5.4	Intralipid® —	50
5.5	Procedure to Make Five Concentrations —	52
5.6	Interference Criteria —	52
5.7	Data Analysis —	54
5.8	References —	60
<b>6</b>	<b>Origin of Icteric Samples —</b>	<b>63</b>
6.1	The Origin of Bilirubin —	63
6.2	Bilirubin Toxicity —	65
6.3	Transport of Bilirubin in the Blood —	65
6.4	Uptake of Bilirubin by the Liver —	66
6.5	Clinical Aspects of Bilirubin —	66
6.6	Neonatal Jaundice —	67
6.7	Cholestasis —	69
6.8	Hepatitis —	70
6.9	Alcoholic Liver Disease —	70
6.10	Hemolysis —	71
6.11	Drug Induced Hyperbilirubinemia —	71
6.12	Summary —	72
6.13	References —	72
<b>7</b>	<b>Impact of Icterus —</b>	<b>75</b>
7.1	Introduction —	75
7.2	Estimated Impacts Based on Interference Studies —	75
7.3	Differential Interference with Different Bilirubin Isoforms —	77
7.4	Non-spectrophotometric Icterus Interference —	79
7.5	Resolving Icterus Interference —	80
7.6	Summary —	81
7.7	References —	81
<b>8</b>	<b>Origin of Lipemia and Turbidity —</b>	<b>83</b>
8.1	Lipoprotein Pathways —	83
8.2	Classification of Hypertriglyceridemia —	85
8.2.1	Frederickson Classification of Dyslipidemias —	85
8.2.2	Obesity, Metabolic Syndrome and Diabetes —	87

8.2.3	Alcohol —	88
8.2.4	Nonalcoholic Fatty-liver Disorder —	89
8.2.5	Medications —	89
8.2.6	HIV Infection —	89
8.2.7	Renal Disease —	90
8.3	References —	91
<b>9</b>	<b>Impact of Lipemia/Turbidity —</b>	<b>93</b>
9.1	Introduction —	93
9.2	Estimated Impacts Based on Interference Studies —	95
9.2.1	Interference by Light Scattering —	95
9.2.2	Interference by Volume Displacement —	96
9.2.3	Interference by Lipid Partitioning —	99
9.3	Summary —	99
9.4	References —	99
<b>10</b>	<b>Endogenous Interferences in Clinical Laboratory Tests: Icteric, Lipemic and Turbid Samples —</b>	<b>101</b>
10.1	Interference Indices —	101
10.2	Generating Interference Indices —	101
10.2.1	Preparation of Standards —	102
10.2.2	Data Collection and Deconvolution of Non-Target Interferences —	103
10.2.2.1	Subtraction Using Selected Wavelengths —	104
10.2.2.2	Index Calculation Using Derivative Spectrometry —	105
10.2.3	Establishing Indices and Defining Ranges —	107
10.3	Limitations —	110
10.4	Summary —	110
10.5	References —	111
<b>11</b>	<b>Reporting of Results —</b>	<b>113</b>
11.1	Introduction —	113
11.2	Procedures for Handling Samples with Interference Within the Laboratory —	113
11.3	Reporting of Results in Icteric and Turbid Samples —	115
11.4	Autoverification and Reporting Algorithms —	116
11.5	Practical Issues: Education and Implementation —	117
11.6	References —	118
<b>12</b>	<b>Analyte-dependent Interference —</b>	<b>119</b>
12.1	Complex Interferences —	119
12.1.1	Model for Analyte-dependent Interference —	120
12.1.2	Examples of Analyte-Dependent Interference —	121

<b>12.2</b>	<b>Statistical Testing for Significance — 129</b>
<b>12.3</b>	<b>Failure to Design the Interference Study — 133</b>
<b>12.4</b>	<b>Advantages of Using Multiple Regression Analysis — 133</b>
<b>12.5</b>	<b>Concluding Remarks — 135</b>
<b>12.6</b>	<b>References — 137</b>

<b>Index — 139</b>
--------------------