

CLINICAL BIOCHEMISTRY

2nd EDITION

R. LUXTON

Contents

Preface	xiii
Abbreviations	xv

Clinical biochemistry

1 What is clinical biochemistry?	1
1.1 The role of the clinical biochemistry laboratory	2
1.2 What does the result mean?	3
Analytical factors affecting a result	3
Physiological factors affecting a result	5
1.3 Reference ranges	5
1.4 Clinical utility	5
1.5 Blood samples	10
1.6 Units of measurement	10
Commonly measured analytes	12
Methods used in clinical biochemistry	12
Suggested further reading	14
Self-assessment questions	14

Input

2 Nutrition and drugs	15
2.1 Composition of the body	15
2.2 Macronutrients	16
Water	16
Carbohydrate	17
Fats	17
Protein	19
2.3 Micronutrients	20
Vitamins	20
Vitamin A	21
Vitamin D	21
Vitamin E	21
Vitamin K	21
Vitamin B ₁	21
Vitamin B ₂	21
Vitamin B ₅	22
Vitamin B ₁₂	22
Vitamin C	22
Niacin	22
Folic acid	23

	Biotin	23
	Pantothenic acid	23
2.4	Minerals and trace elements	23
2.5	Assessment of nutritional status	24
2.6	Toxicology	25
	Therapeutic drug monitoring	25
	Drug overdose	26
2.7	Laboratory measurement of nutrients and drugs	27
2.8	Spectroscopy and colorimetry	28
	Suggested further reading	30
	Self-assessment questions	31
3	Digestion	33
3.1	The food we eat	34
	Proteins	34
	Carbohydrate	34
	Fat	34
3.2	The digestive process	34
3.3	Gut hormones	36
3.4	Clinical disorders	37
	Stomach	37
	Intestine	38
	Pancreas	38
	Gall bladder	39
3.5	Investigation of malabsorption	39
	Suggested further reading	40
	Self-assessment questions	40
Control		
4	Genetic control	41
4.1	DNA and genetic information	42
4.2	Proteins from DNA	43
4.3	Genetic damage	46
	Ionizing radiation	46
	Mutagens and carcinogens	47
	Viruses	47
4.4	Cancer and tumour markers	48
4.5	Genetic disease and the clinical biochemistry laboratory	50
	Suggested further reading	52
	Self-assessment questions	52
5	Endocrinology – chemical control	53
5.1	Transport of hormones	56
5.2	Action of hormones	56
5.3	Control of hormone production	56
5.4	The hypothalamic–pituitary axis	57
5.5	Endocrine disorders	59
5.6	Investigation of endocrine disease	61

Stimulation tests	61
Suppression tests	63
Stress tests	63
5.7 Measurement of hormones	63
Competitive immunoassay	64
Non-competitive immunoassay (sandwich assay)	65
Lateral flow immunoassay	67
Suggested further reading	68
Self-assessment questions	69
6 Thyroid hormones	71
6.1 The thyroid gland	72
6.2 Thyroid hormones	72
6.3 Action of thyroid hormones	73
6.4 Thyroid hormone homeostasis	74
6.5 Thyroid disease	75
Hyperthyroidism	75
Hypothyroidism	76
Congenital hypothyroidism	78
6.6 Measurement of thyroid hormones	78
Suggested further reading	80
Self-assessment questions	80
7 Control of water and electrolyte metabolism	81
7.1 Water balance	82
7.2 The importance of sodium	84
7.3 Control of osmolality	85
Arginine vasopressin	85
Aldosterone	86
7.4 Disorders of water and electrolyte balance	87
Hypernatraemia	87
Hyponatraemia	88
7.5 Potassium	90
7.6 Disorders of potassium metabolism	91
Hyperkalaemia	91
Hypokalaemia	92
7.7 Measurement of sodium and potassium	93
Electrolyte exclusion effect	93
Flame emission spectroscopy	94
Ion-selective electrodes	94
Sodium electrodes	95
Potassium electrodes	95
Suggested further reading	95
Self-assessment questions	96
8 Control of calcium metabolism	97
8.1 Calcium	97
8.2 Calcium control	98

	Parathyroid hormone	98
	1,25-Dihydroxycholecalciferol	100
	Calcitonin	101
8.3	Phosphate	102
8.4	Disorders of calcium metabolism	102
	Hypercalcaemia	104
	Hypocalcaemia	105
8.5	Measurement of calcium	107
	Atomic absorption spectrophotometry	107
	Dye-binding techniques	108
	Electrochemical methods	108
	Suggested further reading	109
	Self-assessment questions	109
9	Control of carbohydrate metabolism	111
9.1	Glucose homeostasis	112
9.2	Insulin	114
9.3	Disorders of carbohydrate metabolism	114
	Hyperglycaemia	115
	Hypoglycaemia	117
9.4	The investigation of glucose disorders	118
	Glucose	118
	Insulin	121
	C-peptide	121
	Glycated proteins	121
	Suggested further reading	122
	Self-assessment questions	122

Processing

10	Enzymes	123
10.1	Isoenzymes and isoforms	125
10.2	Clinically important enzymes	126
	Aspartate aminotransferase and alanine aminotransferase	126
	Creatine kinase	127
	Lactate dehydrogenase	127
	Alkaline phosphatase	128
	Acid phosphatase	130
	γ -Glutamyltransferase	130
	Amylase	130
10.3	Enzymes and tissue damage	131
	Cardiac enzymes	131
	Liver enzymes	132
	Muscle enzymes	133
	Inborn errors of metabolism	133
10.4	Principles of enzyme measurements	134
10.5	Biosensors	137
	Suggested further reading	138
	Self-assessment questions	138

11 Inborn errors of metabolism	141
11.1 Inheritance	142
11.2 Investigation of IBEM	144
Screening	145
Investigation of suspected IBEM	146
11.3 Prenatal diagnosis	147
11.4 Phenylketonuria	147
11.5 Cystic fibrosis	148
11.6 Chromatography	149
Suggested further reading	151
Self-assessment questions	152

Transport and storage

12 Plasma proteins	153
12.1 Total protein	155
12.2 Protein groups	156
12.3 Specific proteins	157
Albumin	157
Caeruloplasmin	158
Transferrin	158
α -Fetoprotein	158
Prostate specific antigen	159
C-reactive protein	159
Immunoglobulin	159
Enzymes	160
Tumour markers	160
12.4 Measurement of plasma proteins	160
Total protein	161
Electrophoresis	161
Suggested further reading	164
Self-assessment questions	164

13 Lipids and lipoproteins	165
13.1 Lipids and lipoproteins	166
Chylomicrons	168
Very-low-density lipoprotein	168
Intermediate-density lipoprotein	168
Low-density lipoprotein	168
High-density lipoprotein	168
13.2 Lipid transport	168
Exogenous lipid	168
Endogenous lipid	169
13.3 Lipid disorders	170
Primary hyperlipidaemias	171
Secondary hyperlipidaemias	172
Hypolipidaemia	172
13.4 Atherosclerosis	172
13.5 Laboratory investigations of lipid	173

Suggested further reading	174
Self-assessment questions	175

14 Acid-base balance and blood gases	177
14.1 Control of pH	179
Respiratory control	179
Metabolic control	179
14.2 Normal pH	181
14.3 Disorders of acid-base balance	182
Compensation	183
14.4 Pathophysiology	184
Metabolic acidosis	184
Respiratory acidosis	185
Metabolic alkalosis	185
Respiratory alkalosis	186
Mixed acid-base disturbances	186
14.5 Anion gap	186
14.6 Blood gases	186
14.7 Blood gas measurements	187
Suggested further reading	189
Self-assessment questions	189

Defence

15 Immunoglobulins	191
15.1 Antibodies	192
15.2 Disorders associated with antibodies	195
Hypergammaglobulinaemia	195
Hypogammaglobulinaemia	196
15.3 Laboratory investigation of antibodies	197
Total antibody	197
Antibody isotypes	197
15.4 Laboratory techniques in the investigation of antibodies	198
Immunoprecipitation	198
Immunofixation	200
Suggested further reading	201
Self-assessment questions	201

16 Proteins of the innate immune system	203
16.1 Complement proteins	204
16.2 Acute-phase proteins	205
C-reactive protein	207
Haptoglobin	207
α -Antitrypsin	208
16.3 Interferons	208
16.4 Clinical biochemistry and the innate immune system	209
Complement investigations	209
Acute-phase proteins and interferons	210

Suggested further reading	210
Self-assessment questions	210
Output	
17 Kidney function	213
17.1 Kidney structure and function	214
Glomerulus	216
Proximal tubule	216
Loop of Henle	216
Distal tubule	217
Collecting ducts	217
17.2 Kidney disease	217
17.3 Glomerular function	219
17.4 Tubular function	221
17.5 Proteinuria	222
Protein analysis	224
Urine analysis	225
17.6 Renal stones	226
Suggested further reading	226
Self-assessment questions	227
18 Liver function	229
18.1 Liver structure	230
18.2 Bilirubin metabolism	232
18.3 Jaundice	233
Pre-hepatic jaundice	234
Hepatic jaundice	234
Post-hepatic jaundice	234
Congenital hyperbilirubinaemia	236
18.4 Liver disease	236
Hepatitis	238
Chronic hepatitis	238
Cirrhosis	238
Alcoholic liver disease	239
Cholecystitis	239
18.5 Investigation of liver disease	240
Bilirubin	240
Other analytes	241
Suggested further reading	241
Self-assessment questions	241
Answers to self-assessment questions	243
Index	247