

## 2nd EDITION

# Contents

Preface	xiii
Preface to the first edition	xv
Abbreviations	xvi
Colour plates	xix
<b>1 The immune system</b>	<b>1</b>
1.1 Immunology and transfusion science	1
1.2 The immune system	2
1.3 Two types of immune defence	2
1.4 Non-specific defences	3
Complement	3
Interferons	4
Cytokines	5
Cells of the non-specific defences	5
1.5 Non-specific responses to tissue damage and infection	9
Inflammation	10
The acute phase response	10
1.6 The specific immune response	11
Immunogens	12
Relative importance of humoral and cell-mediated immunity	13
1.7 Cells of the specific immune response	14
Development of small lymphocytes	15
Role of T and B lymphocytes	16
Distinguishing T and B lymphocytes	16
Specificity of small lymphocytes	17
Activation of B lymphocytes	18
Cytokine involvement	19
Polyclonal response	19
Activation of T lymphocytes	20
Stimulation of T <sub>c</sub> cells	20
Stimulation of helper T cells	23
Suggested further reading	24
Self-assessment questions	24
<b>2 Antibodies and antigens</b>	<b>27</b>
2.1 History of antibodies	27
2.2 Antibodies are immunoglobulins	28
2.3 Kinetics of the antibody response	29
2.4 Immunoglobulin isotypes	31

2.5	Antibody structure	33
	Immunoglobulin domains	35
	Role of the Fab and Fc regions	35
	Hypervariable regions	36
	Structure of IgM	36
2.6	Binding of an antibody to an epitope	38
	Antibody affinity and avidity	39
2.7	Effector role of the antibody	40
	Physical changes	41
	Lysis	41
	Stimulation of inflammation	43
	Stimulation of phagocytosis	44
	Suggested further reading	45
	Self-assessment questions	45
<b>3</b>	<b>Complement</b>	<b>47</b>
3.1	Historical context	47
3.2	Complement is not a single entity	48
3.3	The classical pathway: activation to lysis	50
3.4	Other biological activities of complement	55
	Attraction of phagocytes, opsonization and clearance of immune complexes	56
	Stimulation of inflammation	57
3.5	Alternative pathway for complement activation	57
	The alternative pathway can feed into the lytic sequence	58
3.6	The lectin pathway	58
3.7	Physiological regulation of complement activation	59
3.8	Complement in transfusion science	59
	Establishing complement levels in sera	60
	Loss of complement activity in sera	60
	Significance of complement binding by anti-red blood cell antibodies	61
	Non-lytic complement-fixing antibodies	61
	Complement deficiencies	61
	Suggested further reading	62
	Self-assessment questions	63
<b>4</b>	<b>Genetics for blood groups</b>	<b>65</b>
4.1	Genetics and blood groups	65
4.2	DNA and chromosomes	66
4.3	The structure and role of genes	66
4.4	DNA replication and protein synthesis	68
4.5	Blood groups and molecular events in genes	68
4.6	Inheritance of blood group genes	70
	Mendelian laws and patterns of inheritance	71
	Zygosity: homozygous and heterozygous	71
	Genotype and phenotype	72
	Genes linked to the X chromosome	72
	Gene dominance	73
	Patterns of inheritance	73

Suggested further reading	74
Self-assessment questions	75
<b>5 Introduction to blood groups: the ABO blood group system</b>	<b>77</b>
5.1 Introduction	77
5.2 Blood group nomenclature	78
5.3 The ABO blood group system	79
5.4 The biochemical nature of the A and B antigens	81
5.5 Genes involved in the ABO system	83
5.6 Secretors of A, B and H sugars	85
5.7 The <i>FUT1</i> ( <i>H</i> ) gene and the Bombay blood groups	85
5.8 Inheritance and molecular genetics of the ABO groups	86
5.9 Subgroups of A and B blood groups	87
5.10 Population distribution of the ABO groups	88
5.11 The distribution of ABO-determining antigens	88
5.12 ABO blood group antibodies	89
Suggested further reading	90
Self-assessment questions	90
<b>6 Introduction to the Rh blood group system</b>	<b>91</b>
6.1 Introduction to the Rh system	91
6.2 Inheritance and nomenclature of the Rh system	93
6.3 Fisher's DCE system	94
6.4 The two-locus model	95
6.5 Qualitative differences in Rh antigens	98
The G antigen	99
Compound antigens	100
6.6 Quantitative differences in Rh antigens	100
Antigen dosage	100
Influence of other Rh antigens	100
Weaker forms of RH antigens	101
6.7 Laboratory aspects of Rh blood group typing	102
Rh D typing	102
Phenotyping and genotyping	103
Nature of RH antigens	104
Laboratory detection	104
Clinical significance	105
Suggested further reading	105
Self-assessment questions	106
<b>7 Other blood group systems</b>	<b>107</b>
7.1 Carbohydrate antigens	107
Lewis system	107
P system and globoside collection	111
Ii system	113
Compound carbohydrate antigens	114
7.2 Protein antigens	114
MNS system	114

Lutheran system	116
Kell system	118
Duffy system	121
Kidd system	122
7.3 Importance of other blood groups in transfusion science	123
Suggested further reading	123
Self-assessment questions	124
<b>8 Immune and autoimmune haematology disorders</b>	<b>125</b>
8.1 Mechanisms of red cell destruction	125
8.2 Causes and classification of immune haemolytic anaemia	127
8.3 Haemolytic transfusion reactions	127
8.4 Warm autoimmune haemolytic anaemia	128
Warm antibody types	128
8.5 Cold haemolytic anaemia	129
Chronic cold haemagglutinin disease	129
Cold auto-antibodies and infection	129
Paroxysmal cold haemoglobinuria	130
8.6 Underlying mechanisms which may cause immune/autoimmune haemolytic anaemia	130
8.7 Drug-induced haemolytic anaemia	131
Immune complex mechanism	131
Drug adsorption (haptens) mechanism	132
Drug-induced haemolytic anaemia caused by methyldopa	132
Membrane modification or non-immunological protein adsorption	133
8.8 Laboratory tests for diagnosis of autoimmune/immune haemolytic anaemia	133
8.9 Haemolytic disease of the newborn	134
Clinical effects of haemolysis on the foetus or neonate	135
Test to detect antibodies formed by the mother	136
Exchange transfusion	138
Prophylactic disease prevention	138
Quantitation of foetal maternal haemorrhage	139
Other antibodies and haemolytic disease of the newborn	140
8.10 Immune disorders affecting platelets	141
Autoimmune thrombocytopenic purpura	141
Alloimmune thrombocytopenic purpura	141
Mechanism of platelet antibody destruction	142
Suggested further reading	142
Self-assessment questions	142
<b>9 Blood products and components</b>	<b>145</b>
9.1 Introduction to blood components	145
9.2 Blood components for transfusion	147
Red cell concentrates	147
Leucocyte-depleted blood components	149
Washed red cells	150
Frozen red cells	150
9.3 Plasma-derived blood components	150
Plasma fractionation	151

Human albumin solution	152
Immunoglobulins	152
Coagulation factor concentrates	152
Other factor concentrates	155
9.4 Plasma-derived products from single donations	155
Cryoprecipitate	156
Platelet concentrates	157
9.5 Quality assurance procedures for blood and blood products	159
Suggested further reading	160
Self-assessment questions	160
<b>10 Haemagglutination and blood grouping methods</b>	<b>161</b>
10.1 Introduction	161
10.2 Haemagglutination	162
First stage of agglutination	162
Second stage of agglutination	165
Concentration of antigen and antibody	170
10.3 Methods	171
Direct agglutination	171
Indirect agglutination	174
Adsorption and elution	177
10.4 Technical considerations	177
Antiglobulin tests	177
Typing red cells with a positive DAT	178
Visualization of agglutination	178
10.5 Associated technical considerations	181
Enhancement of reactions	181
Serum versus plasma for antibody detection	182
Use of controls	182
Compatibility testing	183
Antibody identification	183
Suggested further reading	184
Self-assessment questions	184
<b>11 Adverse effects of transfusion</b>	<b>185</b>
11.1 General precautions	186
Donor selection	186
Donor testing	187
Collection and storage	188
Blood product selection, pre-treatment and pre-transfusion testing	188
Monitoring of transfusions and reporting of adverse incidents	189
11.2 Adverse effects caused by transmission of infectious agents	190
11.3 Adverse reactions due to the transfusion of red cells	191
11.4 Adverse reactions due to the transfusion of leucocytes	194
11.5 Adverse reactions due to the transfusion of platelets	195
11.6 Adverse reactions due to the transfusion of plasma	196
11.7 Adverse reactions due to other causes	198

11.8	Investigation of an alleged reaction to a red cell transfusion	198
11.9	Summary	201
	Suggested further reading	201
	Self-assessment questions	202
<b>12</b>	<b>Haemopoietic stem cell processing and transplantation</b>	<b>203</b>
12.1	Introduction	203
12.2	Some useful definitions	205
12.3	Clinical situations requiring a haemopoietic stem cell transplant	206
12.4	Sources of haemopoietic stem cells for transplant	207
	Bone marrow	208
	Peripheral blood stem cells	209
	Human umbilical cord blood	209
12.5	Pre- and post-transplant treatments	210
	Processing and storage of haemopoietic stem cells	210
	Conditioning treatment	211
	Transfusion support post-transplant	211
12.6	Problems associated with haemopoietic stem cell transplants	212
	Infections	213
	Graft-versus-host disease	213
	Rejection of the graft	214
12.7	The major histocompatibility complex	214
	MHC Class I and II proteins	216
12.8	The HLA system	217
	Polymorphisms within the HLA system	218
	The Class II region	218
	Discovery and naming of alleles	219
	HLA typing	219
12.9	Availability and choice of donors	221
	Factors affecting compatibility	222
	Suggested further reading	222
	Self-assessment questions	223
<b>13</b>	<b>Applications of molecular and immunological techniques</b>	<b>225</b>
13.1	Introduction	225
13.2	Molecular techniques for the identification of blood groups	226
	Technology using the polymerase chain reaction	226
	Restriction fragment length polymorphisms	227
	Sequence-specific oligonucleotide probing	227
	The source and quality of DNA	227
13.3	Applications of molecular techniques	228
	Microarray technology	228
	Limitations of DNA-based assays for blood groups	229
13.4	Further applications of molecular techniques	230
	PCR in HLA typing	230

PCR in the detection of viruses	230
Pre-natal foetal genotyping	230
13.5 Immunological techniques using flow cytometry	231
Platelet antibodies	232
Detection of Rh D positive foetal cells	233
Identification of transfused donor red cells	234
Assessing the quality of leucodepletion	235
Bacterial contamination of platelet concentrate	236
13.6 Conclusion	236
Suggested further reading	236
Self-assessment questions	236
 <b>Answers to self-assessment questions</b>	 <b>239</b>
 <b>Index</b>	 <b>245</b>