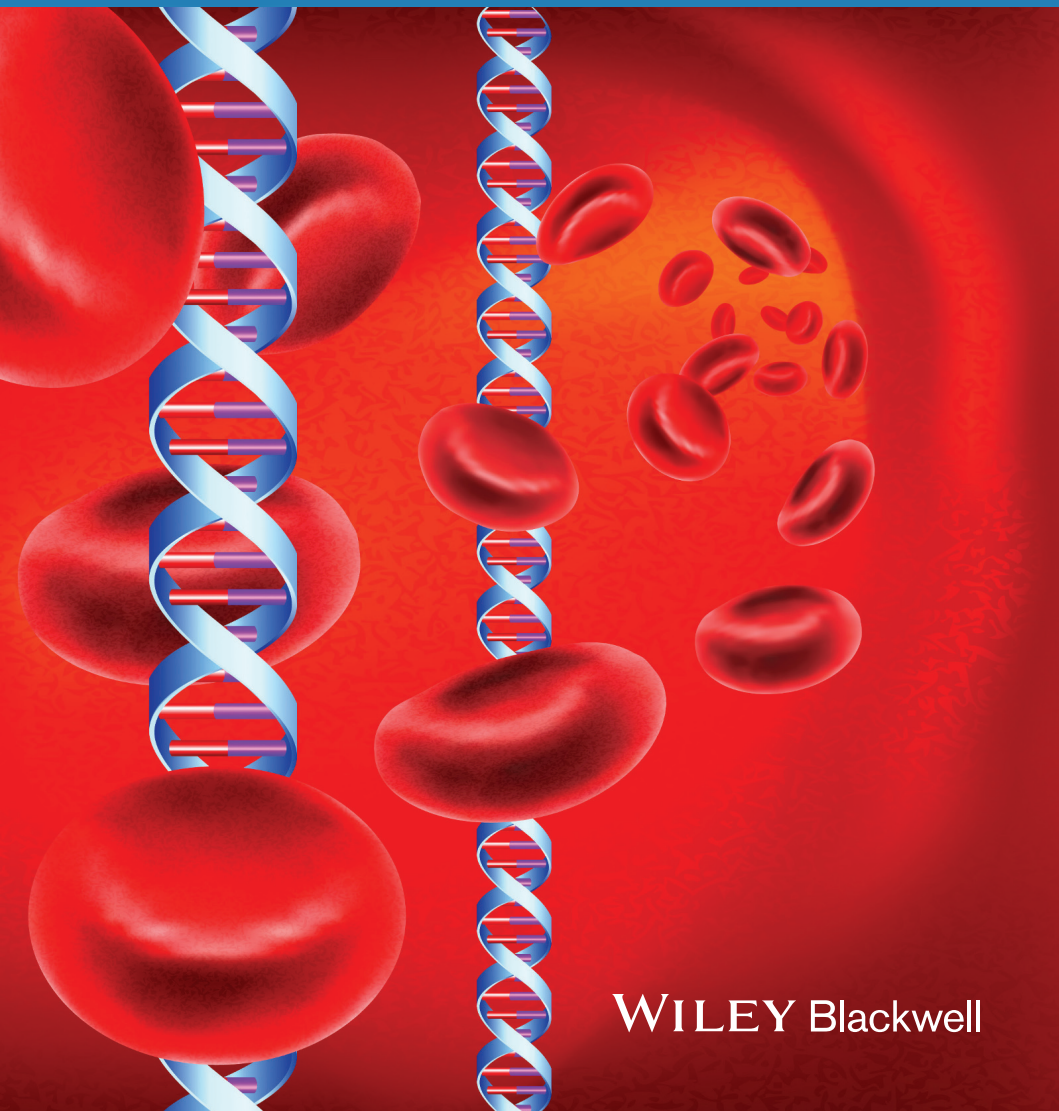
THIRD EDITION

Essential Guide to Blood Groups

GEOFF DANIELS AND IMELDA BROMILOW



WILEY Blackwell

Essential Guide to Blood Groups

Essential Guide to Blood Groups

THIRD EDITION

Geoff Daniels, PhD, FRCPath
Consultant Clinical Scientist and Head of Diagnostics
IBGRL, Bristol Institute for Transfusion Services
NHS Blood and Transplant
Bristol, UK

Imelda Bromilow, MSc, CBiol
Scientific Consultant
Liverpool, UK

WILEY Blackwell

This edition first published 2014, © 2014 by John Wiley & Sons, Ltd

Registered Office
John Wiley & Sons, Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial Offices
9600 Garsington Road, Oxford, OX4 2DQ, UK
The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK
111 River Street, Hoboken, NJ 07030-5774, USA

For details of our global editorial offices, for customer services and for information about how to apply for permission to reuse the copyright material in this book please see our website at www.wiley.com/wiley-blackwell

Library of Congress Cataloging-in-Publication Data

Daniels, Geoff, author.
Essential guide to blood groups / Geoff Daniels, Imelda Bromilow. – Third edition.
p. ; cm.
Includes bibliographical references and index.
ISBN 978-1-118-68892-2 (pbk.)
I. Bromilow, Imelda, author. II. Title.
[DNLM: 1. Blood Group Antigens–Handbooks. WH 39]
QP91
612.1'1825–dc23
2013019571

A catalogue record for this book is available from the British Library.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Cover image: Bubaone

Set in 9/12pt Palatino by SPi Publisher Services, Pondicherry, India

1 2014

Contents

Abbreviations

2ME	2-mercaptoethanol
ADCC	antibody dependent cell-mediated cytotoxicity
AET	2-aminoethylisothiouronium bromide
AHG	anti-human globulin
AIHA	autoimmune haemolytic anaemia
AML	acute myeloid leukaemia
CAPA	corrective and preventive action
CGD	chronic granulomatous disease
CHAD	cold haemagglutinin disease
CLT	chemiluminescence test
CMV	cytomegalovirus
cv	co-efficient of variation
DAF	decay accelerating factor
DARC	Duffy antigen receptor for chemokines
DAT	direct antiglobulin test
DTT	dithiothreitol
EDTA	ethylenediaminetetraacetic acid
ETC	enzyme treated cells
FMH	feto-maternal haemorrhage
GP	glycophorin
GPI	glycosylphosphatidylinositol
HA	haemolytic anaemia
Hb	haemoglobin
HCT	haematocrit
HDFN	haemolytic disease of the fetus and newborn
HFA	high frequency antigen
HLA	human leucocyte antigen
HTR	haemolytic transfusion reaction
IAT	indirect antiglobulin test
ICAM	intercellular adhesion molecule
Ig	immunoglobulin

IL	interleukin
IS	immediate spin
ISBT	International Society of Blood Transfusion
IUT	intrauterine transfusion
LFA	low frequency antigen
LISS	low ionic strength saline
MAC	membrane attack complex
MCA	middle cerebral artery
MGSA	melanoma growth stimulatory activity
MMA	monocyte monolayer assay
NANA	N-acetylneuraminic acid
NISS	normal ionic strength saline
PBS	phosphate buffered saline
PCH	paroxysmal cold haemoglobinuria
PCR	polymerase chain reaction
PEG	polyethylene glycol
PNH	paroxysmal nocturnal haemoglobinuria
QA	quality assurance
QC	quality control
RBC	red blood cell
RCA	root cause analysis
SNP	single nucleotide polymorphism
SOP	standard operating procedure
TQM	total quality management
WAIHA	warm auto-immune haemolytic anaemia

An introduction to blood groups

CHAPTER 1

What is a blood group?

In 1900, Landsteiner showed that people could be divided into three groups (now called A, B, and O) on the basis of whether their red cells clumped when mixed with separated sera from other people. A fourth group (AB) was soon found. This is the origin of the term 'blood group'.

A blood group could be defined as, 'An inherited character of the red cell surface, detected by a specific alloantibody'. Do blood groups have to be present on red cells? This is the usual meaning, though platelet- and neutrophil-specific antigens might also be called blood groups. In this book only red cell surface antigens are considered. Blood groups do not have to be red-cell specific, or even blood-cell specific, and most are also detected on other cell types. Blood groups do have to be detected by a specific antibody: polymorphisms suspected of being present on the red cell surface, but only detected by other means, such as DNA sequencing, are not blood groups. Furthermore, the antibodies must be alloantibodies, implying that some individuals lack the blood group.

Blood group antigens may be:

- proteins;
- glycoproteins, with the antibody recognising primarily the polypeptide backbone;
- glycoproteins, with the antibody recognising the carbohydrate moiety;
- glycolipids, with the antibody recognising the carbohydrate portion.

Blood group polymorphisms may be as fundamental as representing the presence or absence of the whole macromolecule (e.g. RhD), or as minor as a single amino acid change (e.g. Fy^a and Fy^b) or a single monosaccharide difference (e.g. A and B).

Essential Guide to Blood Groups, Third Edition. Geoff Daniels and Imelda Bromilow.

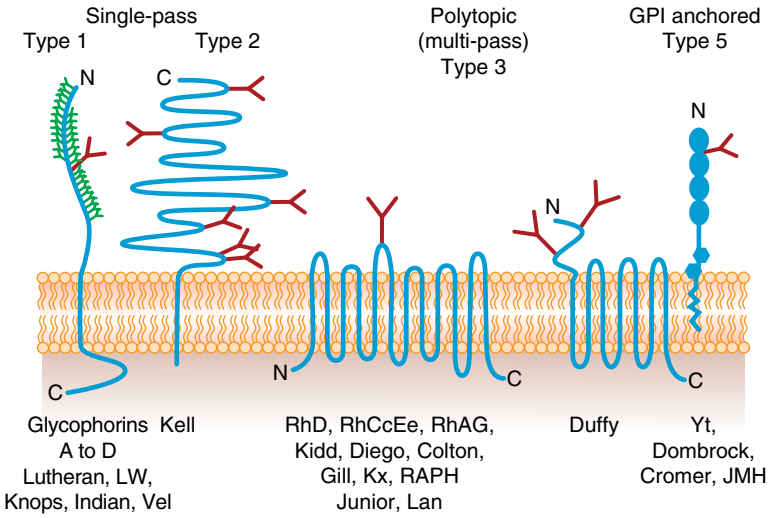


Fig. 1.1 Diagram of different types of blood group active proteins and glycoproteins based on their integration into the red cell surface membrane. Listed are examples of blood group antigens for each type. (Type 4 proteins are cytoplasmic and not present in red cells.)

Blood group proteins and glycoproteins are integral structures of the red cell membrane. Diagrammatic representations of some blood group proteins and glycoproteins in the membrane are shown in Fig. 1.1. Some pass through the membrane once. These generally have an external N-terminal domain and a cytoplasmic C-terminal domain (Type 1), though in one case (the Kell glycoprotein) the C-terminus is external and the N-terminus internal (Type 2). Some are polytopic (Type 3); that is, they cross the membrane several times. Usually both termini are cytoplasmic, but the Duffy glycoprotein has an odd number of membrane-spanning domains and an extracellular N-terminal domain. Finally, some have no membrane-spanning domain, but are anchored to the membrane by a lipid tail (called a glycosylphosphatidylinositol or GPI anchor), which is attached to the C-terminus of the protein through carbohydrate (Type 5). There are no Type 4 glycoproteins, which have no external domain, in the red cell membrane.

Most red cell surface proteins are glycosylated, the only exceptions being the Rh and Kx proteins. This glycosylation may be (1) N-glycosylation, large, branched sugars attached to asparagine residues of the amino acid backbone, or (2) O-glycosylation, smaller glycans (usually tetrasaccharides) attached to serine or threonine residues.

Blood group antibodies

Blood groups are antigens and, by definition, a molecule cannot be an antigen unless it is recognised by an antibody (or T cell receptor); therefore, all blood group specificities are defined by antibodies. Most adults have antibodies to the A or B antigens, or to both; that is, they have 'naturally occurring' antibodies to those ABO antigens they lack. For most other blood groups, corresponding antibodies are not 'naturally occurring', but are only formed as a result of immunisation by transfused red cells or by fetal red cells leaking into the maternal circulation during pregnancy or childbirth.

Blood group antibodies are usually IgM or IgG, although some may be IgA (Chapter 6). 'Naturally occurring' antibodies are usually predominantly IgM, whereas 'immune' antibodies are predominantly IgG. As a general rule, IgM antibodies will directly agglutinate antigen-positive red cells in a saline medium, whereas most IgG antibodies require potentiators or anti-human globulin to effect agglutination (Chapter 2).

Clinical importance of blood groups

Blood groups are of great clinical importance in blood transfusion and in transplantation. In fact, the discovery of the ABO system was one of the most important factors in making the practice of blood transfusion possible. Many blood group antibodies have the potential to cause rapid destruction of transfused red cells bearing the corresponding antigen, giving rise to a haemolytic transfusion reaction (HTR), either immediately or several days after the transfusion. At their worst, HTRs give rise to disseminated intravascular coagulation, renal failure, and death. At their mildest, they reduce the efficacy of the transfusion (Chapter 6).

IgG blood group antibodies can cross the placenta during pregnancy and haemolyse fetal red cells expressing the corresponding antigen. This may cause alloimmune fetal haemolytic anaemia, more commonly known as haemolytic disease of the fetus and newborn (HDFN). Many blood group antibodies have the potential to cause HDFN, but the most common culprits are D and c of the Rh system and K of the Kell system.

Biological importance of blood groups

The biological importance of many blood group antigens is either known or can be surmised from their structure. The following functions have been attributed to blood group antigens: transporters of biologically important molecules across the red cell membrane; receptors of external stimuli and cell adhesion; regulators of autologous complement to

prevent red cell destruction; enzymes; anchors of the red cell membrane to the cytoskeleton; and providers of an extracellular carbohydrate matrix to protect the cell from mechanical damage and microbial attack. Very little is known, however, about the functions of the blood group polymorphisms, but it is likely that they arose from selection pressures created by pathogens exploiting blood group molecules for attachment to the cells and subsequent invasion.

Blood group systems

The International Society of Blood Transfusion (ISBT) recognises 339 blood group antigens; 297 of these are classified into 1 of 33 blood group systems (Table 1.1 and see the Red Cell Immunogenetics and Blood Group Terminology Working Party area of the ISBT website: www.isbtweb.org). Each blood group system represents either a single gene or a cluster of two or three closely linked genes of related sequence and with little or no recognised recombination occurring between them. Consequently, each blood group system is a genetically discrete entity. The MNS system comprises three genes, Rh, Xg, and Chido/Rodgers, two genes each, and each of the remainder represents a single gene. Rh and MNS are the most complex systems, with 54 and 46 antigens, respectively; nine systems consist of just a single antigen.

Blood group terminology and classification

Since the discovery of the ABO system in 1900, a multitude of blood group antigens have been identified and many different styles of terminology have been used. These include the following to represent alleles: upper case letters (e.g. A, B; M, N); upper and lower case letters to represent antithetical antigens, the products of alleles (S, s; K, k); superscript letters (Fy^a, Fy^b), and numbers (Lu6, Lu9). A variety of different styles of terminology have been used even within one system (e.g. Kell system: K, k; Kp^a, Kp^b, Kp^c; K12, K13).

In 1980, the ISBT established a Working Party to devise a genetically based numerical terminology for blood groups. This terminology is based on the blood group systems (Table 1.1). Each system has a three-digit number plus a 3–5 upper case letter symbol. For example, the Kell system is 006 or KEL (Table 1.2). Each antigen within that system has a three-digit number. K is 001 and Kp^a is 003, and so become 006001 or KEL1 and 006003 or KEL3, respectively. The full numerical symbol is seldom used and the alphanumerical symbols, with the redundant zeros removed, are more commonly employed. Phenotypes consist of the system symbol, followed by a colon, followed by a list of antigens shown

Table 1.1 The blood group systems.

Number	Name	Symbol	Number of antigens	Gene name(s)*	CD number	Chromosome
001	ABO	ABO	4	*ABO*		9
002	MNS	MNS	46	*GYPA*, *GYPB*, *GYPE*	CD235	4
003	P1PK	P1	3	*A4GALT*		22
004	Rh	RH	54	*RHD*, *RHCE*	CD240	1
005	Lutheran	LU	20	*BCAM*	CD239	19
006	Kell	KEL	35	*KEL*	CD238	7
007	Lewis	LE	6	*FUT3*		19
008	Duffy	FY	5	*DARC*	CD234	1
009	Kidd	JK	3	*SLC14A1*		18
010	Diego	DI	22	*SLC4A1*	CD233	17
011	Yt	YT	2	*ACHE*		7
012	Xg	XG	2	*XG*, *CD99*	CD99	X/Y
013	Scianna	SC	7	*ERMAP*		1
014	Dombrock	DO	8	*ART4*	CD297	12
015	Colton	CO	4	*AQP1*		7
016	Landsteiner–Wiener	LW	3	*ICAM4*	CD242	19
017	Chido/Rodgers	CH/RG	9	*C4A*, *C4B*		6
018	H	H	1	*FUT1*	CD173	19
019	Kx	XK	1	*XK*		X
020	Gerbich	GE	11	*GYPC*	CD236	2
021	Cromer	CROM	18	*CD55*	CD55	1
022	Knops	KN	9	*CR1*	CD35	1
023	Indian	IN	4	*CD44*	CD44	11

(*Continued*)