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Terminology for red cell antigens—1999 update

G. Daniels

Key Words: blood groups, terminology, red cells, antigens

Over 250 blood group antigens have been recognized since the discovery of the ABO blood groups in 1900. The significance of these red cell surface antigens in transfusion medicine has made an internationally agreed upon nomenclature important. Such a nomenclature has been devised and is now maintained by the International Society of Blood Transfusion (ISBT) Working Party on Terminology for Red Cell Surface Antigens.[1] This is a numerical nomenclature that can also be partially expressed in letters as an aid to memory. In addition to being a nomenclature, it is also a genetic classification to assist in the understanding of the genetic relationships that exist between the antigens. The terminology was last described in detail in 1995[1] and has been updated twice since that time.[2,3] The purpose of this article is to tabulate the current status of blood group terminology.

Blood Group Systems

A blood group system consists of one or more antigens governed either by a single gene or by a cluster of two or more very closely linked homologous genes with virtually no recombination occurring between them. Each system is genetically discrete from every other blood group system. There are 25 systems (Table 1; see page 96). Each system has a unique three-digit number (e.g., 006) and symbol (KEL). Every antigen within a system has a three-digit number, which, when written after the system number or symbol, gives the antigen a unique label (006003 or KEL3).

Blood Group Collections

Collections are sets of antigens that are genetically, biochemically, or serologically related but are not eligible for system status, usually because they have not been shown to be genetically discrete from all existing systems. There are five collections (Table 2). Eleven collections were created, but six of these have subsequently been declared obsolete, either because they formed a new system or because they joined an existing system. Like the systems, each collection has a three-digit number (e.g., 205) and symbol (COST). Obsolete numbers are never reused.

Table 2. Collections of antigens

Collection		Antigen number		
		001	002	003
205	COST	Cs^a	Cs^b	
207	I	I	i	
208	ER	Er^a	Er^b	
209	GLOB	P	P^k	LKE
210		Le^c	Le^d	

Obsolete collections: 201 Gerbich, 202 Cromer, 203 Indian, 204 Auberger, 206 Gregory, 211 Wright

Blood Group Series

The remaining antigens, which have not been shown to be eligible for system or collection status, are almost all of very low or high frequency in most populations. The antigens of low frequency (< 1%) form the 700 series, which contains 23 antigens (Table 3; see page 97). The high-frequency antigens form the 901 series, which contains 12 antigens, all with a frequency > 99 percent, with the exception of 901012, which has a frequency of about 91 percent (Table 4; see page 97). Many numbers of the 700 and 901 series have become obsolete, either because the antigen has joined a system or because the reagents required for definition of the antigen are no longer available.

An Alternative Terminology Within the ISBT Classification

The six-digit terminology for blood group antigens (e.g., 001001) is intended only for use in cataloging data, especially in computers, and as a framework for the genetically based classification of red cell antigens. The system or collection symbol followed by the specificity number (with sinistral zeros removed; e.g., KEL4) is far more suitable for use in publications on blood groups. Many scientists prefer a more traditional notation for everyday use and even in publications. Therefore, a pop-

Table 1. Antigens of the blood group systems

System		Antigen number 001	002	003	004	005	006	007	008	009	010
001	ABO	A	B	A, B	A1	. . .*					
002	MNS	M	N	S	s	U	He	Mi^{a}	M^{c}	Vw	Mur
003	P	P1	. . .	. . .							
004	RH	D	C	E	c	e	f	Ce	C^{w}	C^{x}	V
005	LU	Lu^{a}	Lu^{b}	Lu3	Lu4	Lu5	Lu6	Lu7	Lu8	Lu9	...
006	KEL	K	k	Kp^{a}	Kp^{b}	Ku	Js^{a}	Js^{b}	. . .	. . .	Ul^{a}
007	LE	Le^{a}	Le^{b}	Le^{ab}	Le^{bH}	ALe^{b}	BLe^{b}				
008	FY	Fy^{a}	Fy^{b}	Fy3	Fy4	Fy5	Fy6				
009	JK	Jk^{a}	Jk^{b}	Jk3							
010	DI	Di^{a}	Di^{b}	Wr^{a}	Wr^{b}	Wd^{a}	Rb^{a}	WARR	ELO	Wu	Bp^{a}
011	YT	Yt^{a}	Yt^{b}								
012	XG	Xg^{a}									
013	SC	Sc1	Sc2	Sc3							
014	DO	Do^{a}	Do^{b}	Gy^{a}	Hy	Jo^{a}					
015	CO	Co^{a}	Co^{b}	Co3							
016	LW	. . .	. . .	. . .	. . .	LW^{a}	LW^{ab}	LW^{b}			
017	CH/RG	Ch1	Ch2	Ch3	Ch4	Ch5	Ch6	WH			
018	H	H									
019	XK	Kx									
020	GE	. . .	Ge2	Ge3	Ge4	Wb	Ls^{a}	An^{a}	Dh^{a}		
021	CROM	Cr^{a}	Tc^{a}	Tc^{b}	Tc^{c}	Dr^{a}	Es^{a}	IFC	WES^{a}	WES^{b}	UMC
022	KN	Kn^{a}	Kn^{b}	McC^{a}	Sl^{a}	Yk^{a}					
023	IN	In^{a}	In^{b}								
024	OK	Ok^{a}									
025	RAPH	MER2									

System		Antigen number 011	012	013	014	015	016	017	018	019	020
002	MNS	M^{g}	Vr	M^{e}	Mt^{a}	St^{a}	Ri^{a}	Cl^{a}	Ny^{a}	Hut	Hil
004	RH	E^{w}	G	. . .	. . .	. . .	. . .	Hr$_{o}$	Hr	hr^{S}	VS
005	LU	Lu11	Lu12	Lu13	Lu14	. . .	Lu16	Lu17	Au^{a}	Au^{b}	Lu20
006	KEL	K11	K12	K13	K14	. . .	K16	K17	K18	K19	Km
010	DI	Mo^{a}	Hg^{a}	Vg^{a}	Sw^{a}	BOW	NFLD	Jn^{a}	KREP	Tr^{a}†	
017	CH/RG	Rg1	Rg2								

System		Antigen number 021	022	023	024	025	026	027	028	029	030
002	MNS	M^{v}	Far	s^{D}	Mit	Dantu	Hop	Nob	En^{a}	ENKT	‘N’
004	RH	C^{G}	CE	D^{w}	. . .	. . .	c-like	cE	hr^{H}	Rh29	Go^{a}
006	KEL	Kp^{c}	K22	K23	K24	VLAN	TOU				

System		Antigen number 031	032	033	034	035	036	037	038	039	040
002	MNS	Or	DANE	TSEN	MINY	MUT	SAT	ERIK	Os^{a}	ENEP	ENEH
004	RH	hr^{B}	Rh32	Rh33	Hr^{B}	Rh35	Be^{a}	Evans	. . .	Rh39	Tar

System		Antigen number 041	042	043	044	045	046	047	048	049	050
002	MNS	HAG	ENAV	MARS							
004	RH	Rh41	Rh42	Crawford	Nou	Riv	Sec	Dav	JAL	STEM	FPTT

System		Antigen number	051	052
004	RH	MAR	BARC	

*obsolete
†provisional

Table 3. The 700 series: low-frequency antigens

Number	Symbol
700002	By
700003	Chr^a
700005	Bi
700006	Bx^a
700015	Rd
700017	To^a
700018	Pt^a
700019	Re^a
700021	Je^a
700026	Fr^a
700028	Li^a
700039	(Milne)
700040	RASM
700041	SW1
700043	Ol^a
700044	JFV
700045	Kg
700047	JONES
700049	HJK
700050	HOFM
700052	SARA
700053	LOCR
700054	REIT

Table 4. The 901 series: high-frequency antigens

Number	Symbol
901001	Vel
901002	Lan
901003	At^a
901005	Jr^a
901007	JMH
901008	Emm
901009	AnWj
901012	Sd^a
901013	(Duclos)
901014	PEL
901015	ABTI
901016	MAM

ular alternative terminology (e.g., A, Kp^a, Cs^a, Vel), within the framework of the genetic classification, is provided and shown in Tables 1–4. The ISBT Working Party recommends that when applying the traditional terminology, only those symbols shown in Tables 1–4 should be used in order to reduce the multiplicity of symbols used to describe red cell antigens.

Phenotype Designation

In the ISBT terminology, phenotypes are written with the system symbol (or number) followed by a colon and then by a list of antigens present, each separated by a comma. If an antigen is known to be absent, its number is preceded by a minus sign (e.g., KEL:–1,2,–3,4).

In order to achieve a level of standardization of phenotype designations when the more traditional antigen symbols are used, the ISBT Working Party recently has published a list of examples of recommended designations (shown below).[3] Generally, *either* the ISBT numerical terminology *or* the alternative terminology for antigens and phenotypes should be used; they should *not* be mixed. Some names of phenotypes, however, such as Mi.III, GP.Mur, Rh_{null}, or Inab phenotype, are suitable for use together with the numerical terminology. Examples of phenotypes are shown below, with the ISBT numerical terminology shown in square brackets.

ABO

A [ABO:1, –2, 3]; B [ABO: –1, 2, 3]; O [ABO: –1, –2, –3]; AB [ABO: 1, 2, 3]; A_1 [ABO: 1, –2, 3, 4]; A_2 [ABO: 1, –2 , 3, –4].

MNS

M+ N+ S– s+ U+ He– Mi(a+) (listed in ISBT order) [MNS:1, 2, –3, 4, 5, –6, 7]. Alternatively, use Miltenberger or GP terminology:[4] e.g., Mi.III or GP.Mur. Null phenotypes: M^k [MNS:–1, –2, –3, –4, –5, etc.]; En(a–) [MNS:–1, –2, 3, 4, 5, etc.]; U– or S– s– U–[MNS:1, 2, –3, –4, –5, etc.].

P

P1+ [P:1]; P1– [P:–1]. P_2 can only be used as an alternative to P1– when the cells have been shown to be P+.

Rh

D+ C+ E– c+ e+ C^w– Rh:–32, 33 Be(a–) (listed in ISBT order) [RH:1, 2, –3, 4, 5, –8, –32, 33, –36]. The order D C c E e would be an acceptable alternative. It is also acceptable to use probable genotypes as phenotypes, providing it is made clear that they are only probable genotypes based on haplotype frequencies; e.g., R_1R_2 or DCe/DcE; R_1r C^w+ or DCe/dce C^w+. Null and mod phenotypes: Rh_{null} [RH:–1, –2, –3, –4, –5, –29, etc.]; Rh_{mod}.

Lutheran

Lu(a–b+) Lu:3, 4 [LU:–1, 2, 3, 4]. Null phenotype: Lu_{null} or Lu(a–b–) [LU:–1, –2, –3, etc.].

Kell

K– k+ Kp(a–b+c–) Ku+ Js(a–b+) K:11, 12, 13, –17 [KEL:–1, 2, –3, 4, 5, –6, 7, 11, 12, 13, –17, –21]. Null and mod phenotypes: K_0 (zero) or $Kell_{null}$ [KEL:–1, –2, –3, –4, –5, etc.]; K_{mod}.

Lewis

Le(a–b+) Le(ab+) [LE:–1, 2, 3]; Le(a–b–) Le(ab–) [LE:–1, –2, –3].

Duffy

Fy(a+b+) Fy:3 [FY:1, 2, 3]; Fy(a–b–) Fy:–3 [FY:–1, –2, –3]. Fy^x may be used as a phenotype.

Kidd

Jk(a+b–) Jk:3 [JK:1, –2, 3]; Jk(a–b–) Jk:–3 [JK:–1, –2, –3].

Diego

Di(a+b+) Wr(a–b+) Wd(a–) Rb(a–) WARR– [DI:1, 2, –3, 4, –5, –6, –7].

Yt

Yt(a+b–) [YT:1, –2].

Xg

Xg(a+) [XG:1].

Scianna

Sc:1, –2, 3 [SC:1, –2, 3].

Dombrock

Do(a+b+) Gy(a+) Hy+ Jo(a+) [DO:1, 2, 3, 4, 5].

Colton

Co(a+b–) Co:3 [CO:1, –2, 3]; Co(a–b–) Co:–3 [CO:–1, –2, –3].

Landsteiner-Wiener

LW(a+b–) LW(ab+) [LW:5, 6, –7]; LW(a–b–) LW(ab–) [LW:–5, –6, –7].

Chido/Rodgers

Ch:1, 2 WH– Rg:1, 2 [CH/RG:1, 2, –7, 11, 12].

Hh

H+; H–. The symbol O_h may be used for the true Bombay phenotype (red cells totally H-deficient, ABH nonsecretors). Otherwise, the terms “red cell H-deficient secretor” and “red cell H-deficient nonsecretor” are recommended.

Kx

Kx+ [XK:1]; Kx– or McLeod [XK:–1].

Gerbich

Ge:2, 3, 4 Wb– Ls(a–) An(a–) Dh(a–) [GE:2, 3, 4, –5, –6, –7, –8]. Gerbich phenotype may be used instead of Ge:–2, –3, 4 [GE:–2, –3, 4]; Yus phenotype may be used instead of Ge:–2, 3, 4 [GE:–2, 3, 4]; Leach phenotype may be used instead of Ge:–2, –3, –4 [GE:–2, –3, –4].

Cromer

Cr(a+) Tc(a+b–c–) Dr(a+) Es(a+) IFC+ WES(a–b+) UMC+ [CROM:1, 2, –3, –4, 5, 6, 7, –8, 9, 10]. Null phenotype: Inab phenotype [CROM:–1, –2, –3, –4, –5, –6, –7, –8, –9, –10].

Knops

Kn(a+b–) McC(a+) Sl(a+) Yk(a+) [KN:1, –2, 3, 4, 5]. “Null” phenotype: Helgeson phenotype.

Indian

In(a–b+) [IN:–1, 2].

Ok

Ok(a+) [OK:1].

RAPH

MER2+ [RAPH:1].

Cost

Cs(a+b–) [COST:1, –2].

Ii

I adult; i adult; cord. The numerical designations for these phenotypes have not been provided as they are to be modified in the near future.

Er

Er(a+b–) [ER:1, –2].

GLOB

p; P_1^k; P_2^k; LKE+. The numerical designations for these phenotypes have not been provided as they are to be modified in the near future.

700 Series

By– Chr(a–) Bi– Bx(a–) (listed in ISBT order) [700:–2, –3, –5, –6].

901 Series

Vel+ Lan+ At(a+) Jr(a+) (listed in ISBT order) [901:1, 2, 3, 5].

Conclusions

The current status of the ISBT terminology for red cell surface antigens is described in this review. This terminology can be used in several different formats within the framework of the genetic classification. The ISBT Working Party recommends that this terminology, within one of its forms, be used in all publications on blood groups.

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Serologic and molecular investigations of a chimera

N.A. Mifsud, A.P. Haddad, C.F. Hart, R. Holdsworth, J.A. Condon, M. Swain, and R.L. Sparrow

A chimeric individual possesses two or more genetically distinct cell populations. Although the chimerism may not be evident in all gene systems, various loci display greater numbers of alleles than genetically "normal" individuals. The proposita was referred for further laboratory investigation due to a mixed-field ABO blood group reaction following routine antenatal testing. Various molecular (HLA class II, ABO genotyping, and 10 short tandem repeat [STR] microsatellites) and serologic (HLA class I and red cell blood groups) typing techniques were employed to investigate a number of polymorphic loci located on different chromosomes. Chimerism was identified in 8 out of the 14 chromosomes tested: chromosome 1 (Duffy), 6 (HLA class I and II), 9 (ABO), 11 (*HUMTH01*), 12 (*HUMPLA2A1*), 15 (*HUMFES/FPS*), 18 (Kidd) and 21 (*D21S11*). The proposita was determined to be a probable dispermic chimera, based on the results of the serology and molecular studies. ***Immunohematology*** **1999;15:100–104.**

Precipitation of serum proteins by polyethylene glycol (PEG) in pretransfusion testing

J. Hoffer, W.P. Koslosky, E.S. Gloster, T.M. Dimaio, and M.E. Reid

Polyethylene glycol (PEG) is used as a potentiator of blood group antigen-antibody interactions. Although PEG is known to precipitate immunoglobulins, we could find no reports of this reagent entrapping red blood cells (RBCs) in irreversible clumps. The patient we describe here had hyperglobulinemia with a reversed albumin:globulin ratio and a diffuse immunoglobulin peak on serum protein electrophoresis. During preparation of serologic tests, a precipitate formed that entrapped the RBCs when PEG was added. Rapid recognition of this phenomenon could prevent delay in the selection of blood for transfusion by substituting PEG-indirect antiglobulin test (IAT) with another technique such as low-ionic-strength solution (LISS)-IAT, and by increasing the number of washes prior to addition of the antiglobulin reagent. ***Immunohematology*** **1999; 15:105–107.**

Hemochromatosis, iron, and blood donation: a short review

A.C. Fields and A.J. Grindon

Hereditary hemochromatosis (HH), an autosomal recessive disease of iron overload, is one of the most common inherited diseases. The candidate gene (*HFE*) for HH has been identified recently and a DNA-based test for the mutation is available. Treatment for HH patients with elevated iron stores include repeated phlebotomy. Left untreated, iron overload can lead to cirrhosis, organ failure, and a shortened life expectancy. In the past and present, blood collected for therapeutic purposes from patients with HH has been discarded. The aim of this article is to address whether blood collected from HH patients should be used for allogeneic transfusion in the future. ***Immunohematology*** **1999;15:108–112.**

Anti-Lu9: the finding of the second example after 25 years

K. Champagne, M. Moulds, and J. Schmidt

The first and only reported example of anti-Lu9 (an antibody directed at a low-incidence antigen in the Lutheran blood group system and allelic to the high-incidence antigen Lu6) was described in 1973 in the serum of a white female, Mrs. Mull. Her serum also contained anti-Lu1 (–Lu^a), and subsequently, an anti-HLA-B7 (–Bg^a) was identified. We report the second example of anti-Lu9 in a white male (GR), found 25 years later. The GR serum was reactive in the indirect antiglobulin test with Lu:–1,2,6,9 antibody-screening red blood cells (RBCs) using either a low-ionic-saline additive solution or polyethylene glycol for enhancement. Lu:6,9 RBCs were reactive with the serum when ficin- or EDTA/glycine-acid-treated, but nonreactive when trypsin- or α-chymotrypsin-treated. Six known examples of Lu:9 RBCs were reactive with the GR serum. His serum did not contain anti-Lu^a, anti-HLA-B7 (–Bg^a) or antibodies to 34 low-incidence antigens tested. We have identified the second example of anti-Lu9 that was likely stimulated by transfusion. Because only one of 200 donors was found to be Lu:9, our study suggests that the incidence of the Lu9 antigen may be less than originally thought. ***Immunohematology*** **1999;15:113–116.**

AMERICAN RED CROSS MEDICAL AND SCIENTIFIC UPDATE

Allogeneic peripheral blood stem cell transplantation

J.C. Whitehead and C.D. Hillyer

Peripheral blood stem cell (PBSC) transplantation has been used effectively in the autologous setting for many years. More recently, allogeneic PBSC transplantation also has been used as a primary treatment for a variety of hematologic malignancies. This transition from autologous to allogeneic PBSC transplantation has several advantages. First, a healthy donor's PBSCs can be easily and efficiently mobilized and transfused to the recipient without major complications. These allogeneic PBSCs engraft rapidly. Second, allogeneic PBSCs may induce an immunologic graft-versus-tumor effect without a significant difference in the incidence of acute graft-versus-host disease (GVHD) as has been observed in allogeneic bone marrow transplant (BMT).[1] Finally, the use of a large donor pool consisting of HLA-matched unrelated donors as well as HLA-mismatched donors allow for increased accessibility to allogeneic PBSC transplantation. This review focuses on the characteristics, mobilization, and engraftment of allogeneic PBSCs. In addition, specific donor issues and the incidence and significance of GVHD in the allogeneic PBSC recipient are discussed.