Rh Blood Group System

NAHLA BAKHAMIS

Introduction

- Most imp blood gp Sys after ABO
- Much more complex
- More than 50 Ags, most imp ones are; D,C,E,c and e
- expressed on polypeptides
- Ags developed before birth (detected in 6-week-old fetus)

Table 15.11 Antigens of the Rh system.

Number	*Alternative names*	*Frequency**	*Number*	*Alternative names*	*Frequency**
RH1	D	Polymorphic	RH31	hr^B	Polymorphic
RH2	C	Polymorphic	RH32	R^N	Low
RH3	E	Polymorphic	RH33	Har	Low
RH4	c	Polymorphic	RH34	Hr^B	High
RH5	e	Polymorphic	RH35	R^N-like	Low
RH6	ce, f	Polymorphic	RH36	Be^a	Low
RH7	Ce	Polymorphic	RH37	Evans	Low
RH8	C^w	Polymorphic	RH39	C-like	Polymorphic
RH9	C^x	Low	RH40	Tar	Low
RH10	V	Polymorphic†	RH41	Ce-like	Polymorphic
RH11	E^w	Low	RH42	Cce^s	Polymorphic†
RH12	G	Polymorphic	RH43	Crawford	Low
RH17	Hr_o	High	RH44	Nou	High
RH18	Hr	High	RH45	Riv	Low
RH19	hr^s	Polymorphic	RH46	Sec	High
RH20	VS	Polymorphic†	RH47	Dav	High
RH21	C^G	Polymorphic	RH48	JAL	Low
RH22	CE	Low	RH49	STEM	Low
RH23	D^w	Low	RH50	FPTT	Low
RH26	c-like	Polymorphic	RH51	MAR	High
RH27	cE	Polymorphic	RH52	BARC	Low
RH28	hr^H	Polymorphic†	RH53	JAHK	Low
RH29	Total Rh	High	RH54	DAK	Low
RH30	Go^a	Low	RH55	LOCR	Low
			RH56	CENR	Low

Postgraduate hematology

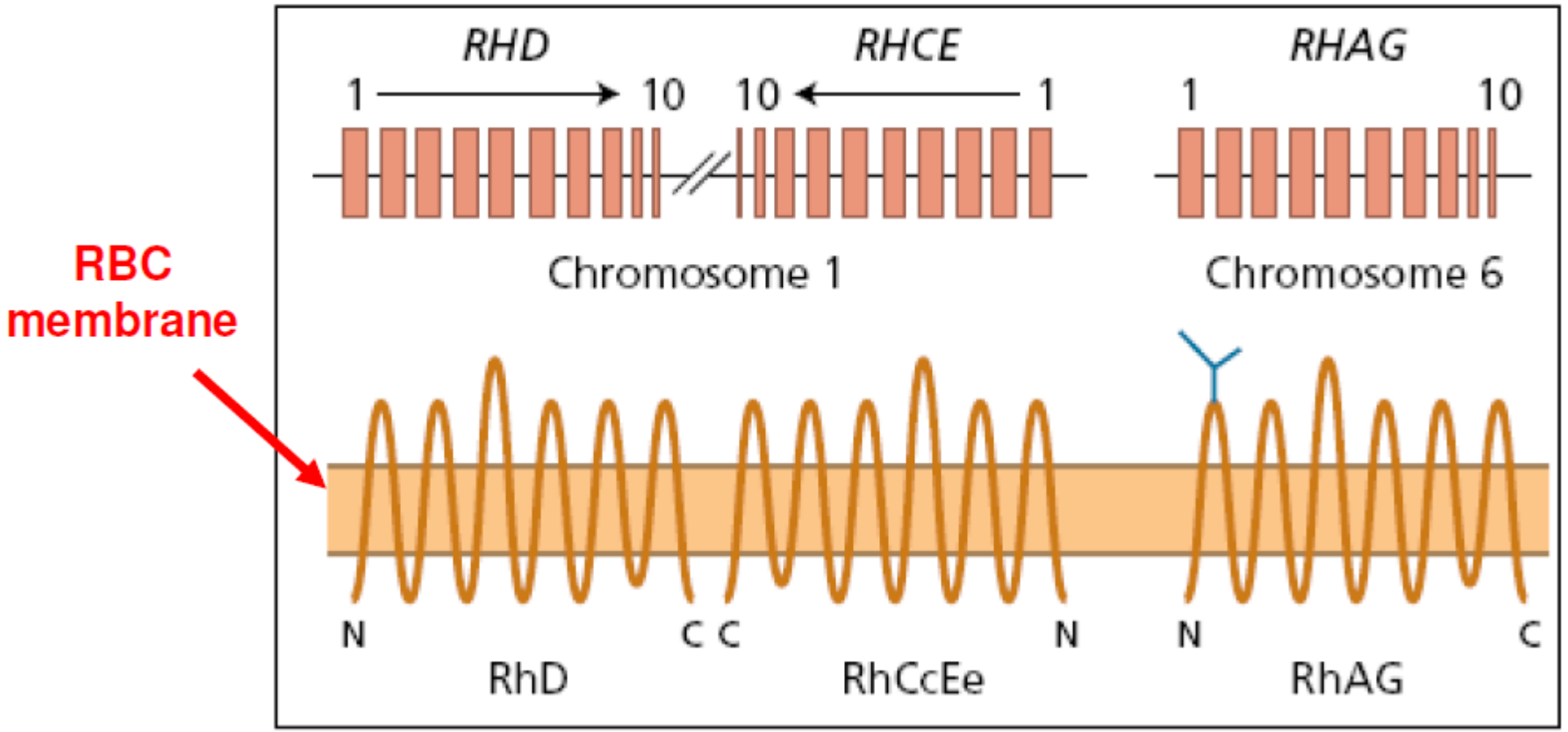
Rh genes

- 2 closely linked genes at Rh locus on Chromosome 1; RHD, RHCE
- RHD encodes D Ag (most immunogenic non-ABO)

  D>c>E>C>e
- RHCE encodes C,c and E,e Ags
- called Rh gene complex
- One Rh gene complex is inherited from each parent

Rh genes

- Both genes produce 2 separate proteins (polypeptides) located next to each other on the surface of RBC forming a complex of Ags
- around 400 aa/ proteins
- requires homologous RHAG Rh-associated glycoproteins (chromosome 6) for expression



Rh genes and the polypeptides they encode

Fisher-Race

- **3 loci carry Rh genes are so closely linked that never separate but are inherited as a unit or gene complex**

So according to Fisher-Race proposal, each person inherits a set of Rh genes from each parent (one D or d + one C or c and one E or e)

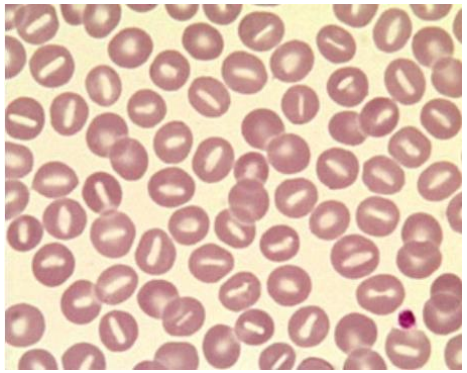
Rh antigens

- 3 integral membrane proteins:
    1. RhD
    2. Rh CcEe
    3. Rh-associated glycoprotein (Rh50,RHAG)

Rh null

- cells have no Rh Ags sites
- Genotype written ---/---
- the lack of Ag cause abnormal conditions of the RBC membrane;

  Reticulocytosis, stomatocytosis, haematocrit haemolytic anemia

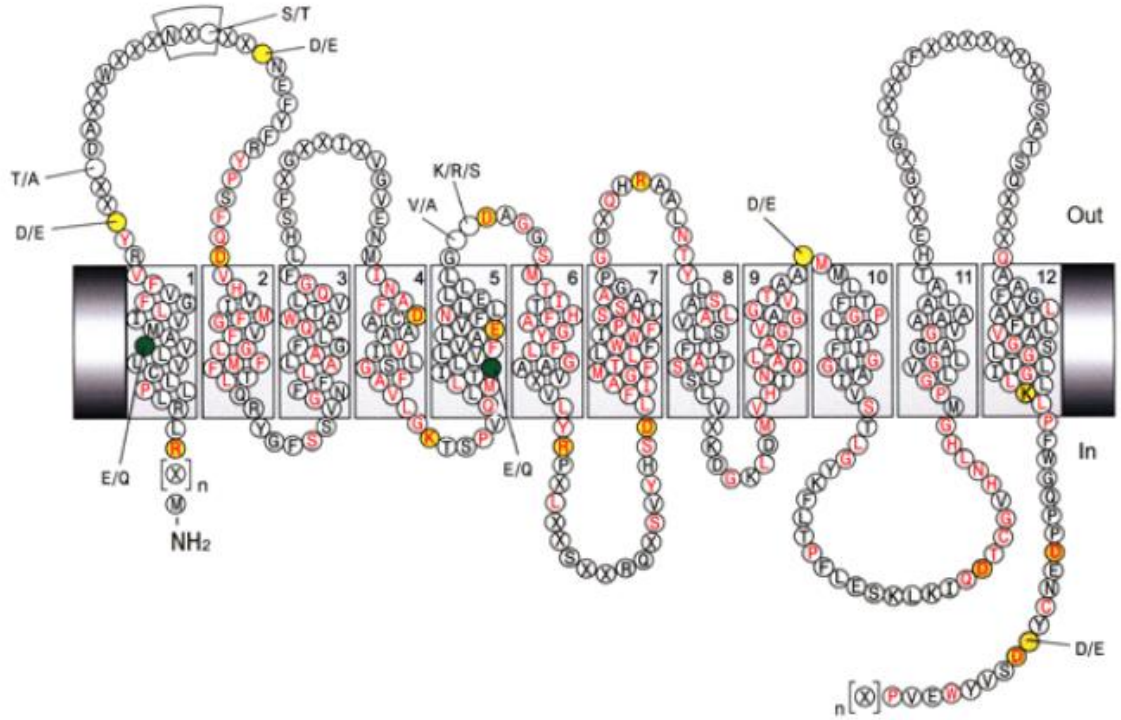


Rh null phenotype

- regulator type: Rh genes (RhD RHCE) inherited but not expressed (due to molecular defect in RHAG)

- Amorph type: RhD gene is absent (due to deletion or mutation) so RHCE will not express

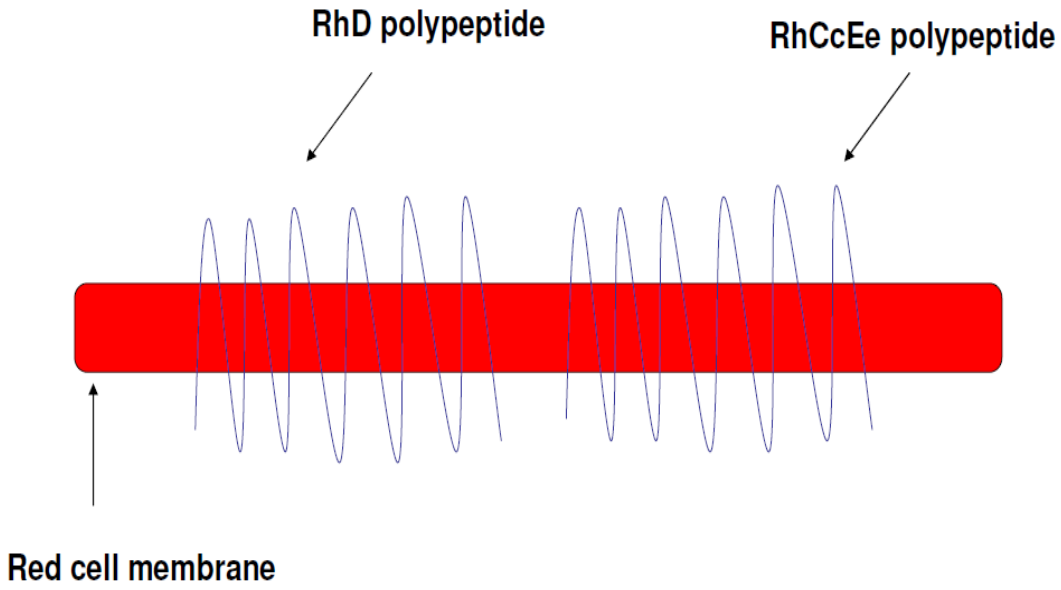
RhD gene



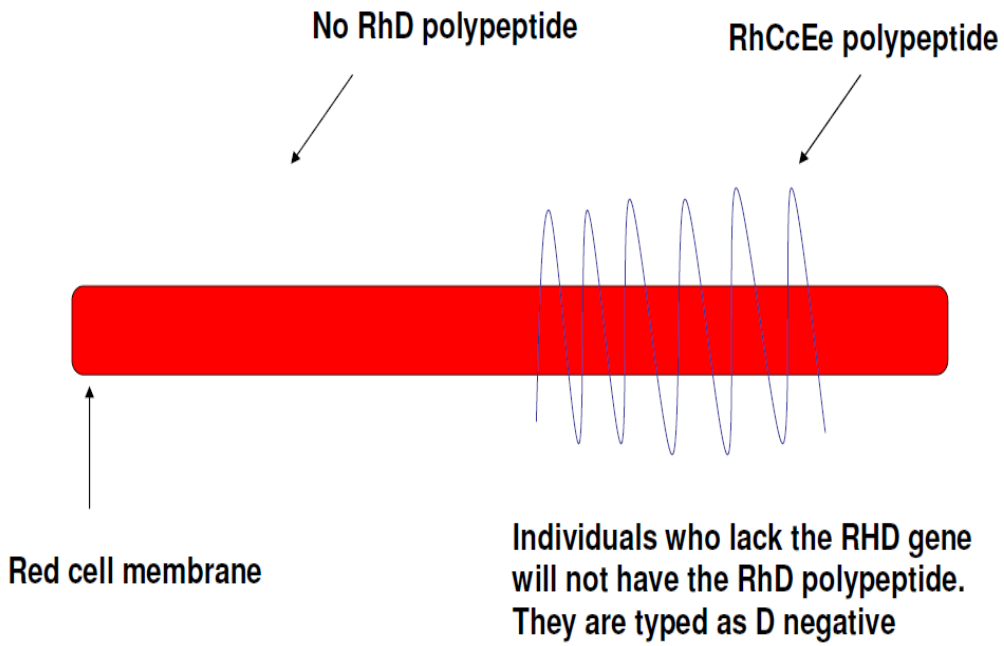
RHD gene

- Produce D Ag
- individual may inherit 2 RHD genes from both parents (homozygous)

  or 1 gene from either parent
- D negative individual don’t have the RHD gene (no RhD protines on RBC surface)
- the symbol ‘d’ indicate absence of D gene



RhD positive



RhD negative

RHCE gene

- ce, Ce, cE or CE depending on the allele present on the RHCE locus
- all of these alleles are Co-dominant
- one allele inherited from each parent

eg; one inherits CE from father & ce from mother all 4 Ag will expressed in the RBC surface C, c, E and e

	Rh genes present		Gene complex/haplotype	Shorthand nomenclature
	RHD gene	*RHCE gene*		
RhD pos	*D*	*Ce*	*DCe*	R_1
	D	*cE*	*DcE*	R_2
	D	*ce*	*Dce*	R_o
	D	*CE*	*DCE*	R_z
RhD neg	*d*	*Ce*	*dCe*	r^I
	d	*cE*	*dcE*	r^{II}
	d	*ce*	*dce*	r
	d	*CE*	*dCE*	r^y

Remember you inherit 1 Rh gene complex (haplotype) from each parent, so you will have 2 of any of the complexes in the table (DCE/dCe)

The 8 possible gene complex or **haplotypes** of the Rh system

CDE terminology

- An individual's Rh phenotype is reported as **DCE** because C/c locus is lies between D/d and E/e loci
- It is essential to remember that d doesn't represent an Ag but an absence of D Ag
- c, e represent actual Ags recognized

CDE terminology

- RhD +: DD or Dd
- RhD negative : dd
- Anti E negative : no E Ag present so it is ee genotype
- Anti E and Anti e +: both E and e Ag are present so the genotype is DC.?./Dc.?. Or DC.?./dc.?.

DCE/Dce or DCE/dce

Rh-Hr terminology (Wiener)

- R = D Ag, r = absence of D = d
- C : indicated by 1 or a single (‘)
- c : when there is no 1 or (‘)
- E : indicated by 2 or (‘’)
- e : no 2 or (‘’)

Rh-Hr terminology (Wiener)

Examples:

- R1 = DCe
- R0 = Dce
- r’ = dCe
- R2 = DcE
- r’’ = dcE
- When both C and E are present the letter Z or Y is used RZ= DCE rY=dCE

D positive Haplotypes	D negative Haplotypes
R1: Dce	r1: dCe
R2: DcE	r’’: dcE
R0: Dce	r: dce
R2: DCE	ry: dCE

Rh Phenotype/Genotype

- Anti-D, anti-C, anti-c, anti-E and anti-e is tested with pt RBC
- if specimen gives the following reaction: D+,C+, E-, c+,e +

  the phenotype would be DCce

  Genotype: DCe/dce (R1/r0) (common on white population)

  or: DCe/Dce (R1/R0) (common on black population)

Reactions with anti-					*Common genotypes*
D	*C*	*c*	*E*	*e*	
+	+	+	−	+	*DCe/dce**
					DCe/Dce
+	+	−	−	+	*DCe/DCe**
					DCe/dCe
+	−	+	+	+	*DcE/dce**
					DcE/Dce
+	−	+	+	−	*DcE/DcE**
					DcE/dcE
+	+	+	+	+	*DCe/DcE**
					DCE/dce
					DcE/dCe
					DCe/dcE
					DCE/Dce
−	−	+	−	+	*dce/dce*

*Probable genotype.

The phenotype of the Rh system is usually determined in the lab with Anti-D, anti-C, anti-c, anti-E anti-e

Rh D Ag frequency

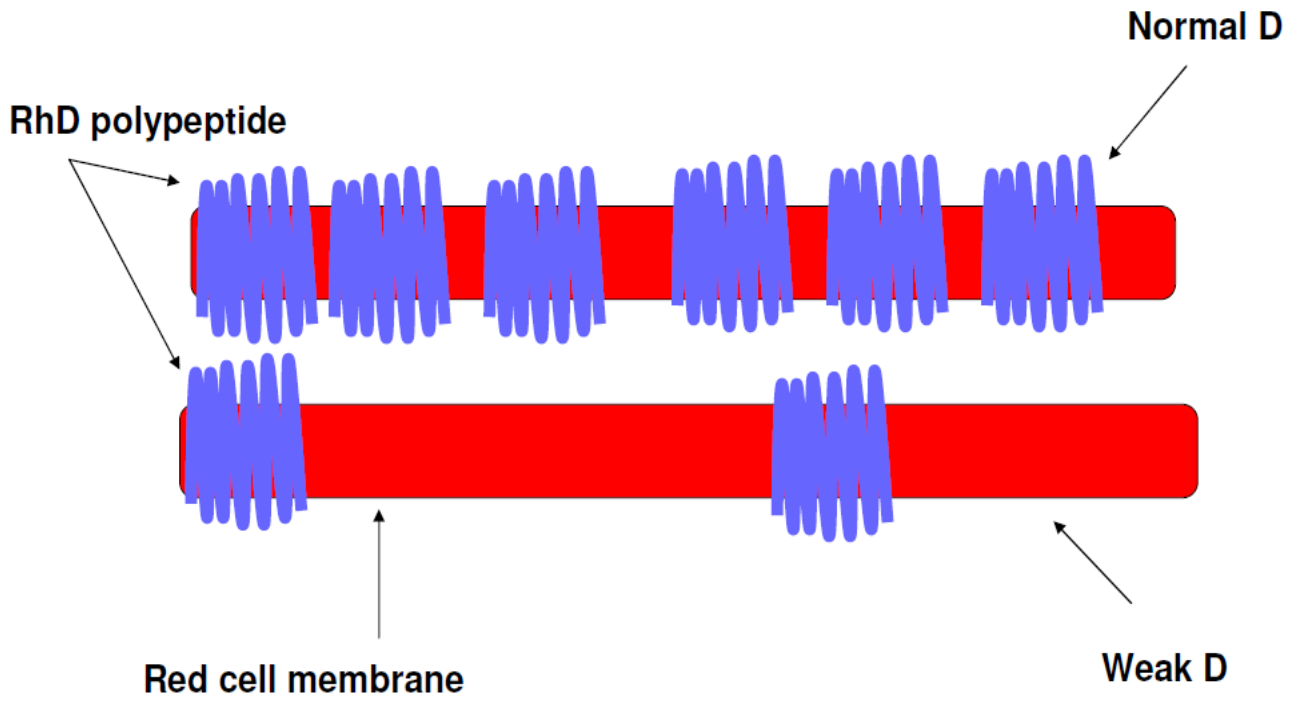
	% pos	% neg
Europe	83	17
West Africa	97	3
India	90	10
Japan	99.7	0.3
China	93	7
Saudis	**92.8**	**7.2**

RhD Ag

- extremely immunogenic
- transfusion of RhD + RBC to individual with RBC RhD – results in SEVER haemolytic transfusion reaction, particularly in the second exposure
- most clinically significant as it also cause HDNB

Weak D

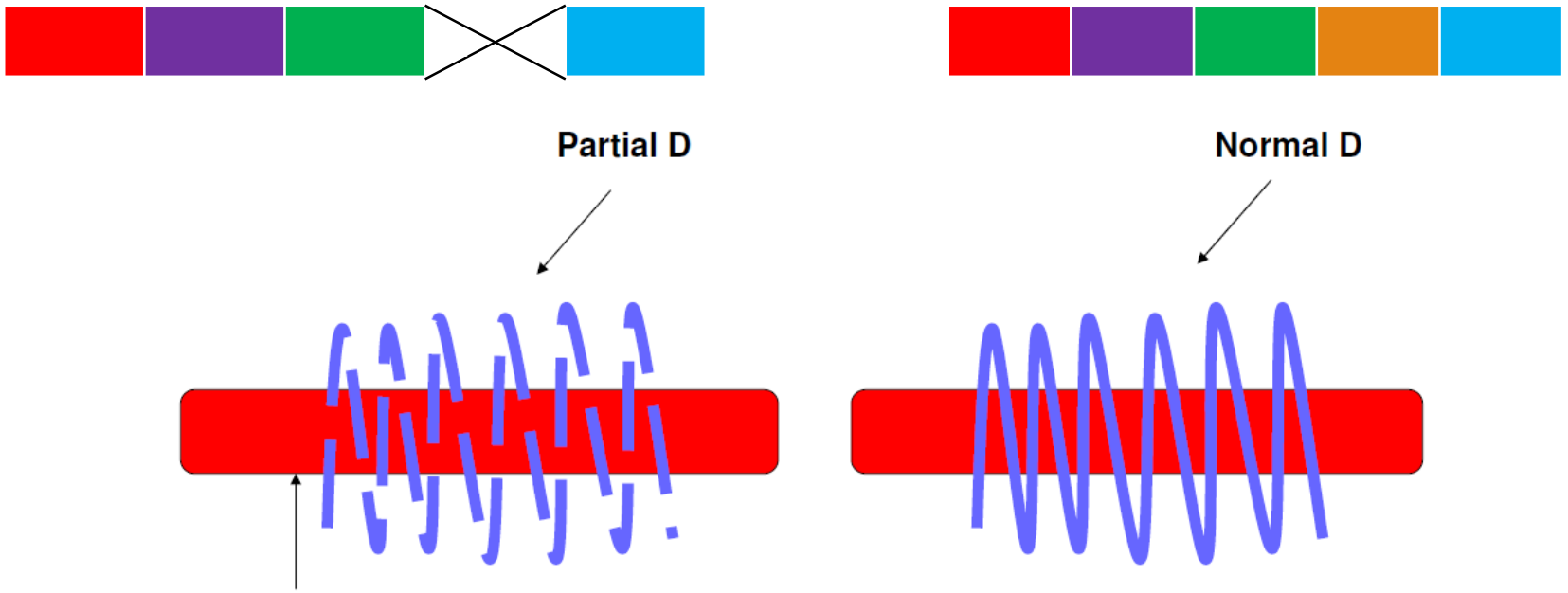
- weaker form of D+
- less Ag sites on RBC compared to D+ (D+ =10 000 to 30 000 Ag site/cell)
- common on African population (very rare on others)
- Agglutinate weakly or not at all at immediate spin (false –ve for RhD –ve)
- it is imp to be able to detect weak D in the lab (to prevent false –ve RhD result)
- agglutinate strongly at AHG test



Weak D

Partial D

- In 1953 was a report of D + individual who had anti-D in his serum/plasma
- Since then, many similar examples have been reported although it is generally rare
- The term ‘partial D’ used to describe the phenotype of those rare individuals who lack 1 or more of D epitope



Partial D lack many epitopes present in the normal D, therefore, individuals with partial D can produce antibodies to the epitopes they lack and present in the normal D

Partial D

- If some epitopes are missing, individual make Ab specific to the missing epitopes when exposed to normal D+ cells (have all epitopes)
- anti D produced react with normal D but not with their own cells or cells of the same partial D types
- Lab ID of partial D:

  panel of monoclonal anti-D Abs are now available to detect partial D

Clinical significance of weak and partial D

- weak D individual don't usually produce anti-D
- In contrast, partial D individuals may develop clinically significant anti-D if transfused with normal D positive blood
- blood donors should be tested for weak D before transfused to negative D recipient (weak D donor can be transfused to D + but not to D-)
- partial D donors should typed as D +

Clinical significance of the Rh system

- Rh Ab are nearly always immune type IgG

  (stimulated by exposure to foreign cells by pregnancy or exposure)
- generally, no naturally occurring Ab against Rh Ag (so previous exposure is perquisite)
- second to ABO system in causing sever reaction
- transfusion of D+ to D- MUST be avoided as D Ag is highly immunogenic
- group O - considered as universal donor

Clinical significance of the Rh system

- C, c, E and e are less immunogenic than D
- If incompatible blood for C, c, E and e is transfused, the recipient may occasionally produce Abs to the Ag he lacks
- In case of multi-transfused patients or patients who require frequent transfusion, Rh compatible (D, C, c, E and e) should be provided

Thanks for your patience any Questions ?