RHESUS BLOOD GROUP:
ABRIEF INSIGHT AND NOMENCLATURE

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OBJECTIVE

- Introduction: background/history of Rhesus blood group antigen
- Describe 5 major Rhesus antigens
- Characteristic of Rhesus antibodies
- Variants of D
- Translate 5 major Rhesus antigens and genotypes from Fisher-Race to Wiener nomenclature
- Introduction to Rosenfield ans ISBT nomenclature

INTRO:BACKGROUND

In 1939, Mrs Seno, a group O patient, had miscarriage of her second pregnancy in Bellevue hospital. She had serious transfusion reaction after receiving group O blood from her husband. Serum drawn from the patient after the transfusion reaction was found to agglutinate the husband's cells as well as 80 of 104 red cell samples.

Levine and Stetson suggested that the woman had produced an antibody specific for a fetal antigen genetically transmitted from the father and this antibody was responsible for the transfusion reaction. No name was given to the antibody.

Meanwhile there were more cases of HDN and HTR in ABO compatible transfusion.

In search of more blood groups, in 1940 Landsteiner and Wiener immunized rabbits with blood of Rhesus monkey and found that the rabbit anti–Rhesus antibody agglutinated approximately 85% of human red blood cells tested.

Rh–positive and Rh–negative refer to the presence or absence of a single red blood cell antigen,respectively.

INTRO:BACKGROUND

- In 1941 Levine found in over 90% of erythroblastosis fetalis cases , the mother was Rh negative and the father was Rh positive.
- Human anti-Rh and animal anti Rh are not the same
- However, "Rh" was adapted into blood group antigen terminology
- The animal anti-Rh antibody was renamed "anti-LW" for Landsteiner and Wiener.

RH BLOOD GROUP

- Rh Blood group has over 50 antigens one of very complex system due to high polymorphism of the autosomal genes.
- D, C, c , E, e are most important.
- Rh system is second most important blood group after ABO because it is extremely immunogenic.
- It causes the production of anti-D in 50 - 70% of Rh(D) negative people who are exposed to the D antigen. Moreover, anti-D is the most common cause of severe HDN and can cause in utero death.
- Because of this, in blood transfusion, the patient and donor are matched for Rh(D) type as well as ABO groups.
- Rh proteins are non-glycosylated glycoprotein, maintains structural integrity of RBC membrane. They may have a role in ammonia or bicarbonate transportation in blood.
- Immunogenicity:

D > c > E >C > e

Antigen	Frequency
D	85%
c	80%
C	70%
e	98%
E	30%

RH ANTIBODIES

- All Rh antibodies are immune in nature, developed after immunizing event.
- Anti- D is the most immunogenic. Anti-c is the second most important.
- Anti-E is frequently a naturally occurring antibody and it is more common than anti-c.
- Anti-c and anti-e only occur after antigenic stimulus.
- React at 37 degree celcius but most frequently detected by IAT.
- Generally do not react at room temperature in saline suspended cell (IS)
- Most are IgG in nature and therefore can cross the placenta. But some may have minor IgM
- Generally, do not fix complement and cause extravascular hemolysis. RBCs hemolyzed by the tissue macrophage system.
- All are important in HDN and delayed HTR

VARIANT OF D

Weak D Phenotype

Most D positive RBC's react macroscopically with Reagent anti-D at immediate spin

-These patients are referred to as Rh positive

- Reacting from 1+ to 3+ or greater

HOWEVER, some D-positive rbc's DO NOT react (do NOT agglutinate) at Immediate Spin using Reagent Anti-D.

These require further testing (37degC and/or AHG) to determine the D status of the patient.

Variants of D

Weak expression of the Rh system on the RBC or D^u

D^u red cells can be classified into three categories according to the mechanism that account for the Weak D

Categories of D^u red cells

1 - Acquired D^u(Position Effect)

2 – D^u Variant (Partial D)

3 - Hereditary D^u (Genetically Transmissible)

CATEGORIES OF DU RED CELLS

1 - Acquired Du (Position Effect)

C allele in trans position to D allele – Example: Dce/dCe, DcE/dCE

In both of these cases the C allele is in the trans position in relation to the D allele.

D antigen is normal, C antigen appears to be crowding the D antigen. (Steric hindrance)

Does NOT happen when C is in cis position I Example: DCe/dce

Can safely transfuse D positive blood components.

2 - Du Variant (Partial D)

The D- Ag consists of at least 4 parts

Missing one or more PARTS (epitopes) of the D antigen,remaining Ag is weakly expressed

Alloantibodies are produced to the missing parts

Du variants should receive Rh –ve blood when transfused

3 - Hereditary Du (Genetically Transmissible)

The RHD gene codes for weakened expression of D antigen in this mechanism.

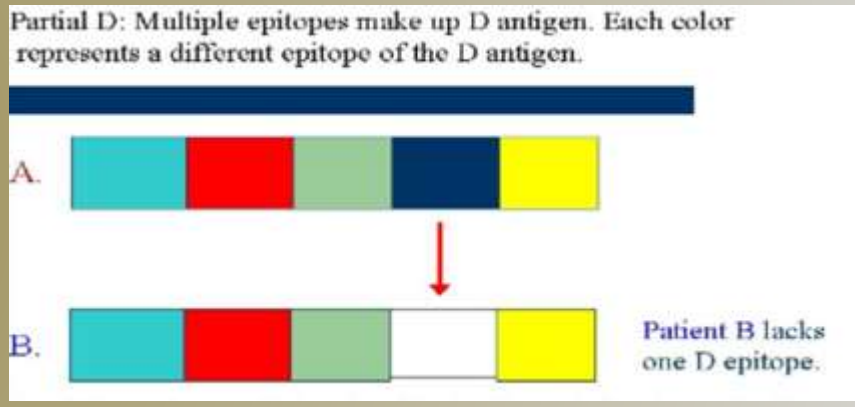
D antigen is complete, there are just fewer D Ag sites on the RBC.

Common in Black population (usually Dce haplotype). Very rare in White population.

Agglutinate weakly or not at all at immediate spin phase.

Agglutinate strongly at AHG phase.

Can safely transfuse D positive blood components.



Example of of partial D: Multiple epitopes make up D antigen. Each color represents a different epitope of the D antigen.
Patient B lacks one D epitope. The difference between Patient A and Patient B is a single epitope of the D antigen. The problem is that Patient B can make an antibody to Patient A even though both appear to have the entire D antigen present on their red blood cell's using routine anti-D typing reagent

RH NOMENCLATURE

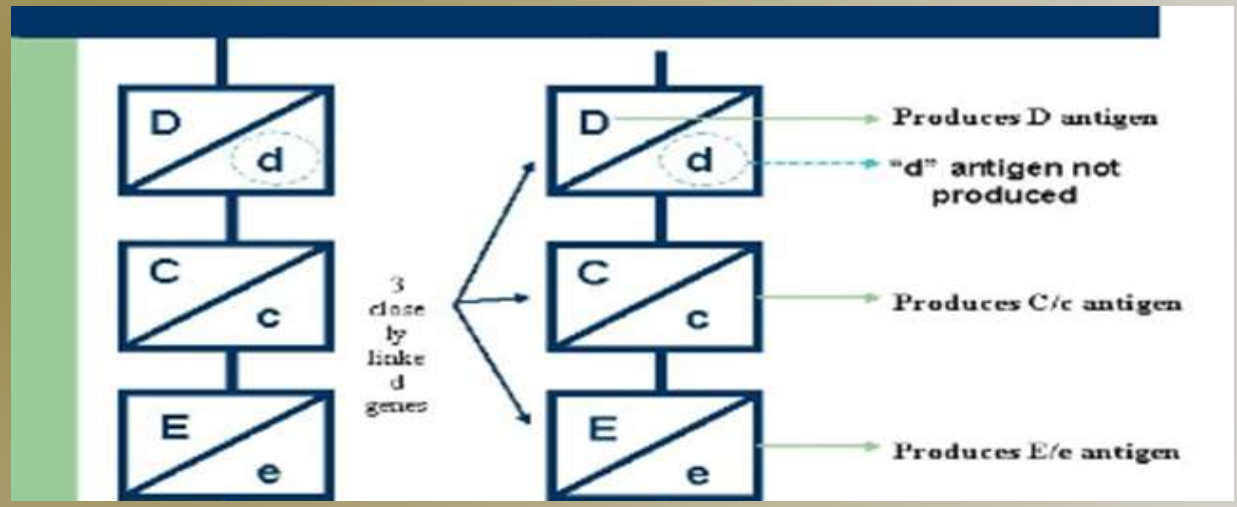
There are 4 types nomenclature for Rh with each serves different purposes

- Fisher –Race: genetics and serology
- Wiener: shorthand
- Rosenfield: presence or absence of a given antigen
- ISBT: catalogue each antigen within a blood group system

FISHER-RACE NOMENCLATURE

Fisher-Race Theory

- Rh inheritance is controlled by 3 closely linked loci on each chromosome of a homologous pair
- Each locus has its own set of alleles which are: Dd , Cc , and Ee.
- The D gene is dominant to the d gene, but Cc and Ee are co-dominant.
- The 3 loci are so closely linked that crossing over does NOT occur, and the 3 genes on one chromosome are always inherited together.



FISHER-RACE NOMENCALTURE

- Rh phenotype is designated by the presence or absence of Rh antigens: D, C, c, E, e
- little d: Indicates the ABSENCE of the D antigen and nothing more.
- There is NO little d antigen or allele.
- Many blood bankers today are leaving the 'd' out the nomenclature entirely.

Gene combination	Antigen
Dce	D, c. e
DCe	D, C, e
DcE	D, c, E
DCE	D, C,E
dce	c, e
dCe	C, e
dcE	c, E
dCE	C, E

WIENER NOMENCLATURE

- **Good for describing phenotype**
- **There is one Rh locus at which occurs one Rh gene, but this gene has multiple alleles.**
- **For example, one gene R 1 produces one agglutinogen (antigen) Rh which is composed of three "factors" The three factors are analogous to C, D, and e respectively**
- **The main difference between the Fisher-Race and Wiener theories is that the Fisher-Race theory has three closely linked loci, the Wiener theory has only one gene locus at which multiple alleles occur**
- Wiener further theorized that 8 major genes led to different combinations of antigens (D, C, E, c, e):
- R^0, R^1 , R^2 , R^z
- r, r′, r″, r^y

WIENER NOMENCLATURE

Wiener nomenclature is expressed by the use of a single letter. Below is the conversion of Wiener to Fisher -Race

R	D present
r	D absent
0 or no symbol	Implies c and e
1 or ‘	Implies C and e
2 or “	Implies c and E
z or y	Implies C and E

Gene combination	Antigen	Weiner (gene)
Dce	D, c. e	R^0
DCe	D, C, e	R1
DcE	D, c, E	R2
DCE	D, C, E	R^z
dce	c, e	r
dCe	C, e	r’
dcE	c, E	r”
dCE	C, E	r^y

	Fisher-Race	Wiener
Rh positive	Dce DCe DcE DCE	R0 R1 R2 RZ
Rh negative	dce dCe dcE dCE	r r’ r” ry

TIPS

One easy approach to interpret Wiener into Fisher-Rice is by remembering the word d-ce (or dice)

D/d	c	e
	Position 1	Position 2
R =capital D	**1 =this position must be capital**	**2 =this position must be capital**
r= little d (no antigen)	**’ = this position must be in capital**	**” = this position must be in capital**
	Z or y : both position 1 and 2 must be in capital	
	0 =both must be little	

ROSENFIELD

- This system describes the presence or absence of the antigen on the RBC. There is no genetic basis
- D=1, C=2, E=3, c=4, e=5
- Example: R1r (Dce/ dce) is interpreted as Rh:1,2,-3,4,5

-when E is not present, it is therefore designated as -3

ISBT

- International Society of Blood Transfusion Numeric Terminology
- Rh blood group is assigned the prefix 004
- Each antigen assigned to the Rh blood group is given a unique number to complete the six digit number
- Example: E antigen 004003
- Advantage over Rosenfield is that it is purely numeric system, easier for data processing

THE END