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# 14th PAN ARAB TRANSFUSION MEDICINE CONFERENCE QATAR 2024

**Inspiring Transfusion Excellence Across Arab Nations**

30 November to 2 December 2024

Sheraton Grand Doha Resort & Convention Hotel,
Doha, Qatar

14th PAN ARAB TRANSFUSION MEDICINE CONFERENCE QATAR 2024
Inspiring Transfusion Excellence Across Arab Nations

# Case Study:
# Genotype in multi-transfused patients

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## OPENING CEREMONY

Master of Ceremony:
**Dr. Javed Akhter** - Vice Chair of Operations, DLMP

| TIME | TOPIC | SPEAKER |
|---|---|---|
| 10:40 | Welcome Speech | Dr. Einas Al Kuwari |
| 10:45 | Remarks of League of Arab States | Ms. Maissa Hidmi |
| 10:50 | Remarks of Arab Authority of Blood Transfusion Services | Dr. Aysha Al Malki |
| 10:55 | Opening Remarks | Dr. Sara Adel |
| 11:00 | WHO Strategic Framework for Blood Safety and Availability | Dr. Yuyun Maryuningsih |

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# Disclosure of COI

**The scientific planning committee (SPC) :**

has reviewed all disclosed financial relationships of speakers, moderators, facilitators and/or authors in advance of this CPD activity and has implemented procedures to manage any potential or real conflicts of interest.

**The SPC members**

have no relationships to disclose.

# Disclosure Statement

I make the following declaration in relation to this CPD Activity :

- This complies with the Ministry of Public Health in Qatar Department of Healthcare Professions MoPH-DHP accreditation standards.
- There is NO Conflict of Interest.
- There is no plagiarism or copyright infringement.
- The content is balanced and free of bias, either commercial or non-commercial.

# Agenda

- Overview
- Genotyping in Multitransfused Patients
- 2 Case Scenarios

# Sickle cell /Thalassemia in Saudi Arabia

- Southern region
- Eastern region(sickle/ thalassemia)
- Complexity is becoming more complex due to:
  - Lack of centralized health system **(future plan exist)**
  - Patients travel and get transfusion at different levels of hospitals

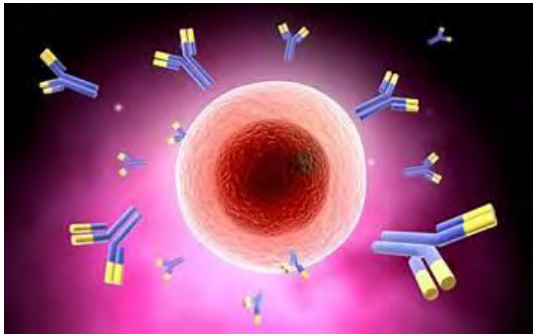
# Alloimmunization in Multi-Transfused Patients VS general Population

- General Population → 1-3 % alloimmunization rate
- Sickle Cell Patients
- Thalasemia Major
- Myelodysplastic Syndrome(MDS)

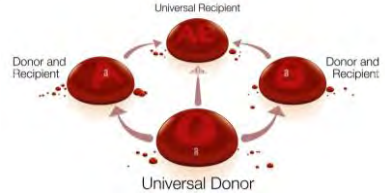
→ Up to 47 % alloimmunization rate

# Factors affecting rate of alloimmunization

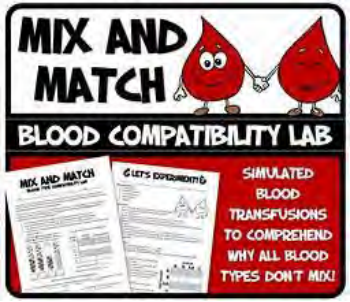
- Disparity between donor and patient antigentic profiles
- Ethnic differences
- Immunogenicity of the antigens
- Patient Clinical condition(immune system status)



# Mitigation Strategies




- ABO+D
- ABO+D+ RH(C,c,E,e)+ K, the most common
- ABO+D+ RH(C,c,E,e)+ K+ Duffy($Fy^a$/$Fy^b$)+ Kidd($Jk^a$/$Jk^b$)+ MNS(M,N,S,s)
- Genotype Match-**Potential future**



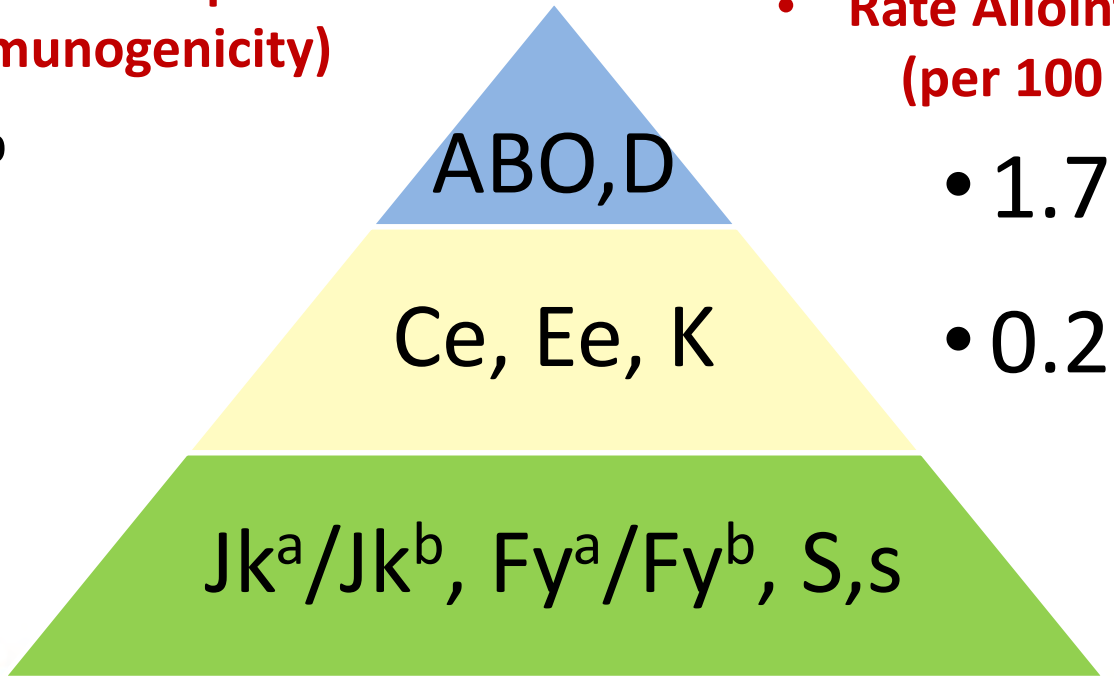
# Mitigation Strategies

**There is no univeral consensus about the best approach**

- Many factors play a role in choosing strategies
  - Financial factors and cost
  - Resources available
    - diverse phenotyped/genotyped blood
  - Difficulty to accommodate phenotype/genotype match
    - Availability of blood with different(rare phenotypes/genotypes)

# Alloimmunization prevalence and prevention in Sickle Cell Patients

- **Alloimmunization prevalence (Immunogenicity)**
  - 20-75 %
  - 5-27 %
  - 7%




- **Rate Allointibodies (per 100 units)**
  - 1.7-3.5
  - 0.26-0.5
  - 0.1

# How effective phenotyping/genotyping

- **Serologic phenotyping is inadequate to allelic diversity**
- **Genotypping is somehow effective in providing more accuarate match**
  - **Associated with challenges**
    - Avaialbaility of complete match
      - Diversity and polymorphism
        - Partial c, C-,
        - Uncommon phenotypes(O negative, c- or e- 1 in 20,000)

# Case No. 1

- 27-year-old sickle cell-trait pregnant patient, present to our hospital at antenatal clinic.
- No Red blood cells were ordered.
- Type and Screen is:

| Forward group | | | | Reverse Group | |
|---|---|---|---|---|---|
| Anti-A | Anti-B | Anti-D | Control | A1cells | B Cells |
| 4 | 0 | 4 | 0 | 0 | 4 |

| | Donor | Rh | | | | | | Kell | | | | Duffy | | Kidd | | Lewis | | P | MNS | | | | Lutheran | | Result | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | D | C | E | c | e | $C^W$ | K | k | $Kp^a$ | $Kp^b$ | $Fy^a$ | $Fy^b$ | $Jk^a$ | $Jk^b$ | $Le^a$ | $Le^b$ | $P_1$ | M | N | S | s | $Lu^a$ | $Lu^b$ | AHG | ENZ | RT |
| 1 | 14122964 | + | + | 0 | + | + | + | 0 | + | 0 | 0 | 0 | 0 | + | 0 | 0 | + | 0 | 0 | + | 0 | 0 | 0 | + | 3 | | |
| 2 | 25191834 | + | 0 | + | + | 0 | 0 | 0 | + | 0 | + | 0 | + | + | + | 0 | 0 | + | + | + | + | + | 0 | + | 3 | | |
| 3 | 18887661 | + | + | + | + | + | 0 | 0 | + | 0 | + | + | 0 | 0 | + | 0 | 0 | + | + | 0 | + | + | 0 | + | 3 | | |
| Pt | | | | | | | | | | | | | | | | | | | | | | | | | | | |

# Case No. 1, Continued

| | Donor | Rh | | | | | | Kell | | | | Duffy | | Kidd | | Lewis | | P | MNS | | | | Lutheran | | Result | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | D | C | E | c | e | $C^w$ | K | k | $Kp^a$ | $Kp^b$ | $Fy^a$ | $Fy^b$ | $Jk^a$ | $Jk^b$ | $Le^a$ | $Le^b$ | $P_1$ | M | N | S | s | $Lu^a$ | $Lu^b$ | AHG | ENZ | RT |
| 1 | 14122964 | + | + | 0 | 0 | + | 0 | 0 | + | 0 | + | + | 0 | + | 0 | 0 | + | 0 | 0 | + | 0 | + | 0 | + | 3 | 3 | |
| 2 | 25191834 | + | + | + | 0 | + | + | + | + | 0 | + | 0 | + | 0 | + | + | 0 | + | + | + | + | 0 | 0 | + | 3 | 3 | |
| 3 | 18887661 | + | 0 | + | + | 0 | 0 | 0 | + | 0 | + | + | 0 | 0 | + | 0 | + | + | + | 0 | + | + | 0 | + | 3 | 3 | |
| 4 | 2041861 | 0 | + | + | + | + | 0 | 0 | + | 0 | + | 0 | 0 | + | 0 | 0 | + | + | + | + | 0 | + | 0 | + | 3 | 3 | |
| 5 | 19231059 | 0 | 0 | 0 | + | + | 0 | + | + | 0 | + | + | 0 | + | + | + | 0 | + | + | 0 | + | + | 0 | + | 3 | 3 | |
| 6 | 16860868 | 0 | 0 | 0 | + | + | 0 | 0 | + | 0 | + | 0 | 0 | + | 0 | 0 | + | + | + | 0 | + | + | 0 | + | 3 | 3 | |
| 7 | 2959047 | 0 | 0 | 0 | + | + | 0 | 0 | + | 0 | + | + | 0 | + | 0 | 0 | 0 | + | + | 0 | + | + | 0 | + | 3 | 3 | |
| 8 | 3213456 | + | 0 | 0 | + | + | 0 | 0 | + | 0 | + | 0 | + | + | + | 0 | 0 | + | + | + | + | + | 0 | + | 3 | 3 | |
| 9 | 7654399 | + | 0 | 0 | + | + | 0 | 0 | + | 0 | + | + | 0 | + | 0 | 0 | 0 | + | + | 0 | + | + | 0 | + | 3 | 3 | |
| 10 | 8712345 | + | 0 | 0 | + | + | 0 | + | + | 0 | + | + | 0 | + | + | + | 0 | + | + | 0 | + | + | 0 | + | 3 | 3 | |
| 11 | 5567812 | 0 | 0 | 0 | 0 | + | 0 | + | + | 0 | + | + | 0 | + | + | + | 0 | + | + | 0 | + | + | 0 | + | 3 | 3 | |
| Pt | | | | | | | | | | | | | | | | | | | | | | | | | 0 | | |
| PT phenotype | | + | + | + | + | + | 0 | 0 | + | 0 | + | 0 | + | + | + | 0 | 0 | + | + | 0 | + | + | 0 | + | | | |

# Case No. 1, Continued

- No clue identified from the full phenotype
- Samples collected and sent out to Versiti(US)
  - Genotype results consistent with phenotype results
- Sample was tested against a number of antigen negative cells to high prevalence antignes in different blood groups systms. And they were found reactive at 37, IAT, PEG IAT, ficin IAT and AET.
- The only cell negative was:
  - **Lu(a-b-).**

# Case No. 1, Continued, molecular work

**Versiti Wisconsin, Inc.**
638 N 18 St • Milwaukee, WI 53233-2121
414.937.6250 • 800.245.3117 • Fax 414.937.6206
www.versiti.org • labinfo@versiti.org

Patient: **Almofleh, Afnan Mohammad**

Birth Date: 04/11/1996 Gender:Female
Patient ID: 25101510
Alt ID: 25101510
Client: Prince Sultan Military Medical City

## Immunohematology Molecular

### Red Cell Genotyping Panel

| Collected Date/Time |
|---|
| 03/06/2022 00:00 |

| Procedure | Result | Completed Date |
|---|---|---|
| Duffy Phenotype | Fy(a-b+) | 03/23/2022 |
| Kidd Phenotype | Jk(a+b+) | 03/23/2022 |
| Lutheran Phenotype | Lu(a-b+) | 03/23/2022 |
| Dombrock Phenotype | Do(a+b+)Jo(a+)Hy+ | 03/23/2022 |
| Colton Phenotype | Co(a+b-) | 03/23/2022 |
| Diego Phenotype | Di(a-b+) | 03/23/2022 |
| Yt Phenotype | Yt(a+b-) | 03/23/2022 |
| Cromer Phenotype | Cr(a+) | 03/23/2022 |
| Vel Phenotype | Vel+ | 03/23/2022 |

### Result Summary and Interpretation

| Procedure | Result | Collected Date/Time | Completed Date |
|---|---|---|---|
| Summary and Interpretation | See Below T1 | 03/06/2022 00:00 | 04/22/2022 |
| Summary and Interpretation | See Below T2 | 03/06/2022 00:00 | 03/23/2022 |
| Summary and Interpretation | See Below T3 | 03/06/2022 00:00 | 03/23/2022 |

Textual Result
T1: 03/06/2022 00:00 (Summary and Interpretation)
This sample was referred out for Lutheran blood group system (*LU*) genomic DNA nucleotide sequencing on a patient with a suspected antibody to a high prevalence antigen in the Lutheran blood group system. .

*LU* exons 5, 6, 11 and 12 were successfully sequenced and the following single nucleotide polymorphism(s) were detected:
c.611T>A

The c.611T>A change encodes a lysine at amino acid position 204 (p.Met204Lys). It expresses a Lu:-8 phenotype.

*LU* genotype: *LU*02.14/02.14*
Predicted phenotype: Lu(a-b+), LU:-8,14

Testing performed by New York Blood Center, Laboratory of Immunohematology and Genomics, Long Island, NY.

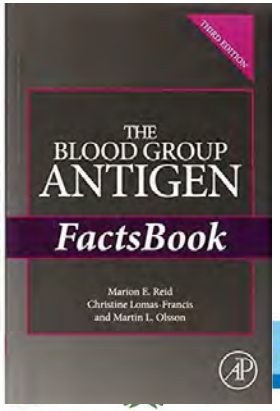
# Lutheran Blood Group System, The unusual

- There is a series of Lu antigens, whose people are Lu(a-b+), but when antibody is made by these people, only Lu(a-b-) is compatible 
- These people share serologic characteristics, but they are genotypically distinct.

# Lutheran Blood Group System, The unusual

| | Amino acid | nucleotide | Antigen negative |
|---|---|---|---|
| Lu4 | Arg175 in IgSF domain 2 | G at bp 524 in exon 5 | Gln175 and A at bp 524 |
| Lu5 | Arg109 in IgSF domain 1 | G at bp 326 in exon 3 | His109 and A at bp 326 |
| Lu6 | Ser275 in IgSF domain 3 | C at bp 824 in exon 7 | |
| Lu7 | Glu425in IgSF domain 4 | A at bp 1274 in exon 10 | Ala425 and C at bp 1274 |
| Lu8 | Meth204 in IgSF domain 2 | T at bp 611 in exon 6 | p.Meth204Lys c.611T>A |

Source: The Blood group Antigen Facts Book, By: Reid, M. E, Lomas-Francis, C, Olsson M.L 2012



# Case No. 1, Summary and lessons learned

- Understaning the blood group systmes in depth helps improving the blood banker's ability to resolve complex antibody IDs
- Although Serology is the gold standard in blood banks,
  - Molecular methods are becoming essential supplemet
    - Especially when no commercially available reagents (anti-sera) to determine antigen status
- Always share, consult colleagues and co-workers

# Case No. 2

- 18-year-old sickle cell disease female patient admitted with acute chest syndrome
- 2 Units of Red blood cells were ordered.
- Type and Screen is:

| Forward group | | | | Reverse Group | |
|---|---|---|---|---|---|
| Anti-A | Anti-B | Anti-D | Control | A1cells | B Cells |
| 0 | 0 | 4 | 0 | 4 | 4 |

| | Donor | Rh | | | | | | Kell | | | | Duffy | | Kidd | | Lewis | | P | MNS | | | | Lutheran | | Result | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | D | C | E | c | e | $C^w$ | K | k | $Kp^a$ | $Kp^b$ | $Fy^a$ | $Fy^b$ | $Jk^a$ | $Jk^b$ | $Le^a$ | $Le^b$ | $P_1$ | M | N | S | s | $Lu^a$ | $Lu^b$ | AHG | ENZ | RT |
| 1 | 14122964 | + | + | 0 | + | + | + | 0 | + | 0 | 0 | 0 | 0 | + | 0 | 0 | + | 0 | 0 | + | 0 | 0 | 0 | + | 2 | | |
| 2 | 25191834 | + | 0 | + | + | 0 | 0 | 0 | + | 0 | + | 0 | + | + | + | 0 | 0 | + | + | + | + | + | 0 | + | 0 | | |
| 3 | 18887661 | + | + | + | + | + | 0 | 0 | + | 0 | + | + | 0 | 0 | + | 0 | 0 | + | + | 0 | + | + | 0 | + | 2 | | |
| Pt | | | | | | | | | | | | | | | | | | | | | | | | | | | |

# Case No. 2, Continue

| | Donor | Rh | | | | | | Kell | | | | Duffy | | Kidd | | Lewis | | P | MNS | | | | Lutheran | | Result | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | D | C | E | c | e | $C^w$ | K | k | $Kp^a$ | $Kp^b$ | $Fy^a$ | $Fy^b$ | $Jk^a$ | $Jk^b$ | $Le^a$ | $Le^b$ | $P_1$ | M | N | S | s | $Lu^a$ | $Lu^b$ | AHG | ENZ | RT |
| 1 | 14122964 | + | + | 0 | 0 | + | 0 | 0 | + | 0 | + | + | 0 | + | 0 | 0 | + | 0 | 0 | + | 0 | + | 0 | + | 3 | 4 | |
| 2 | 25191834 | + | + | + | 0 | + | + | + | + | 0 | + | 0 | + | 0 | + | + | 0 | + | + | + | + | 0 | 0 | + | 3 | 4 | |
| 3 | 18887661 | + | 0 | + | + | 0 | 0 | 0 | + | 0 | + | + | 0 | 0 | + | 0 | + | + | + | 0 | + | + | 0 | + | 0 | 0 | |
| 4 | 2041861 | 0 | + | + | + | + | 0 | 0 | + | 0 | + | 0 | 0 | + | 0 | 0 | + | + | + | + | 0 | + | 0 | + | 2 | 4 | |
| 5 | 19231059 | 0 | 0 | 0 | + | + | 0 | + | + | 0 | + | + | 0 | + | + | + | 0 | + | + | 0 | + | + | 0 | + | 2 | 4 | |
| 6 | 16860868 | 0 | 0 | 0 | + | + | 0 | 0 | + | 0 | + | 0 | 0 | + | 0 | 0 | + | + | + | 0 | + | + | 0 | + | 2 | 4 | |
| 7 | 2959047 | 0 | 0 | 0 | + | + | 0 | 0 | + | 0 | + | + | 0 | + | 0 | 0 | 0 | + | + | 0 | + | + | 0 | + | 2 | 4 | |
| 8 | 3213456 | + | 0 | 0 | + | + | 0 | 0 | + | 0 | + | 0 | + | + | + | 0 | 0 | + | + | + | + | + | 0 | + | 2 | 4 | |
| 9 | 7654399 | + | 0 | 0 | + | + | 0 | 0 | + | 0 | + | + | 0 | + | 0 | 0 | 0 | + | + | 0 | + | + | 0 | + | 2 | 4 | |
| 10 | 8712345 | + | 0 | 0 | + | + | 0 | + | + | 0 | + | + | 0 | + | + | + | 0 | + | + | 0 | + | + | 0 | + | 2 | 4 | |
| 11 | 5567812 | 0 | 0 | 0 | 0 | + | 0 | + | + | 0 | + | + | 0 | + | + | + | 0 | + | + | 0 | + | + | 0 | + | 2 | 4 | |
| Pt | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 4 | |
| PT phenotype | | + | 0 | + | + | + | 0 | + | + | 0 | + | 0 | + | + | 0 | + | 0 | + | 0 | + | + | + | 0 | + | | | |

# Case No. 2, Continue

- Remember
  - C-, e+
  - Auto is weakly reactive
  - Not sure if the patient has auto anti-e
  - Or , this is an alloanit-e
  - Anti-e detected in the eluate.

# Case No. 2, Continue

- Samples sent out for further molecular analysis and investigations.
- Genotyping results(predicted phenotypes):
  - C-, partial c+, E-, partial e+, $hr^{B-}$, $hr^{S+}$
  - Conclusion
    - the patient is identified to have anti-C and anti-$hr^{B}$

# How do you feel?

# Case 2, continue
## What is hrB, hrS, ..etc?

- There are 4 similar antigens in name but genetically and serologically different.
- Hr(RH18)
- $Hr^{B}$(RH34
- $hr^{S}$(RH18)
- $hr^{B}$(RH31)

# Case 2, continue
# What is hrB, hrS, ..etc?

| Antigen name | ISBT name | Antibody specificity | Clinical Significance |
|---|---|---|---|
| **Hr** | **RH18** | Panreactive antibody, with all tested cells | yes |
| **$Hr^B$** | **RH34** | Panreactive antibody, with all tested cells | yes |
| **$hr^S$** | **RH19** | Anti-e-like or anti-ce(f)-like | Yes/no, little infortmation available |
| **$hr^B$** | **RH31** | Anti-Ce-like antibody | Little information available |

# Case 2, continue
## Lessons learned

- Not all e+ or C+ make autoanti-e/-C
- Think about possible antigen variants
- cE haplotypes do not express $hr^B$, so e- blood can be given to patients with anti-$hr^B$

# Thank you

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