

# Immune-hematological Challenges of Red Cell Concentrate Transfusion



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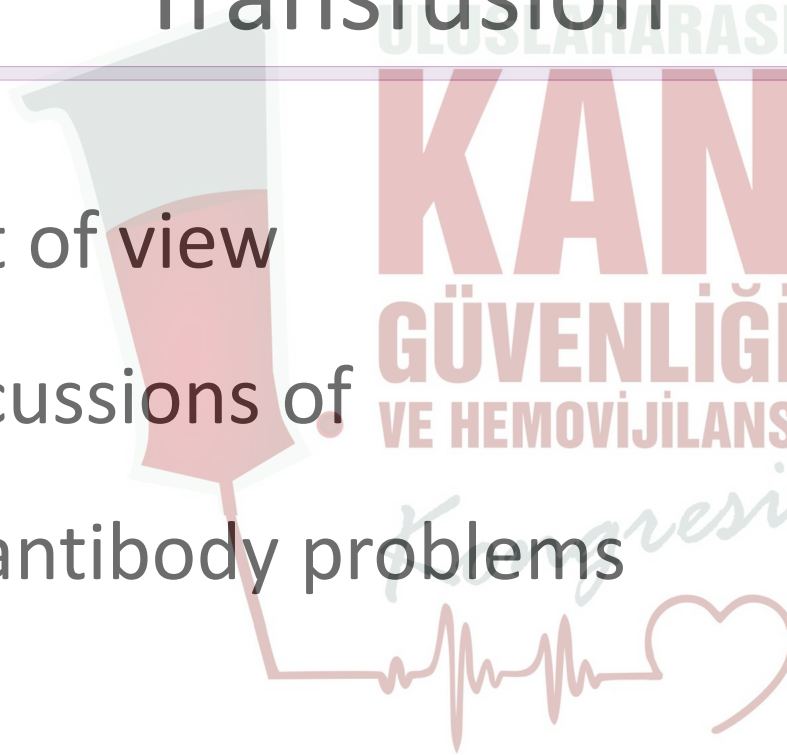
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# Immune-hematological Challenges of RCC

## Transfusion

- Clinician's point of view
- Case based discussions of
- Allo and auto- antibody problems



# Case 1

- 35 years old female patient
- Admitted to hospital for planned surgery for nasal septum deviation
- A Rh(D) negative 2 units of RCC are ordered for the next day
- Blood bank calls in:

‘We can not find compatible RCC tonight, we have already tried 40 units’



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# Case 1

- Patient is anxious: Is it something serious? Will surgery be postponed ?
- Chief of surgery is angry: I want my blood ready in the morning!!!
- On call resident is in panic: Can't we just spare O negative ? They probably won't use it anyway.

# Challenge

- Why CM is incompatible?
- Is there a way to find compatible RCC?
- What is the risk of hemolytic transfusion reaction if I transfuse incompatible RCC?
- Should I delay the surgery?

# Why CM is incompatible?

Acquired antibodies for red cell antigens

- Isohemagglutinins: Anti-A, B, AB
- Autoantibodies: against self antigens
- Allo-antibodies: against non-self antigens
- Drug associated antibodies

# Identifying the antibody –clinician's part

- Is there a previous transfusion/pregnancy history?

✓ Ever (Risk of exposure to foreign antigen(s))

✓ In 3 months (Risk of circulating foreign antigen positive RBC)



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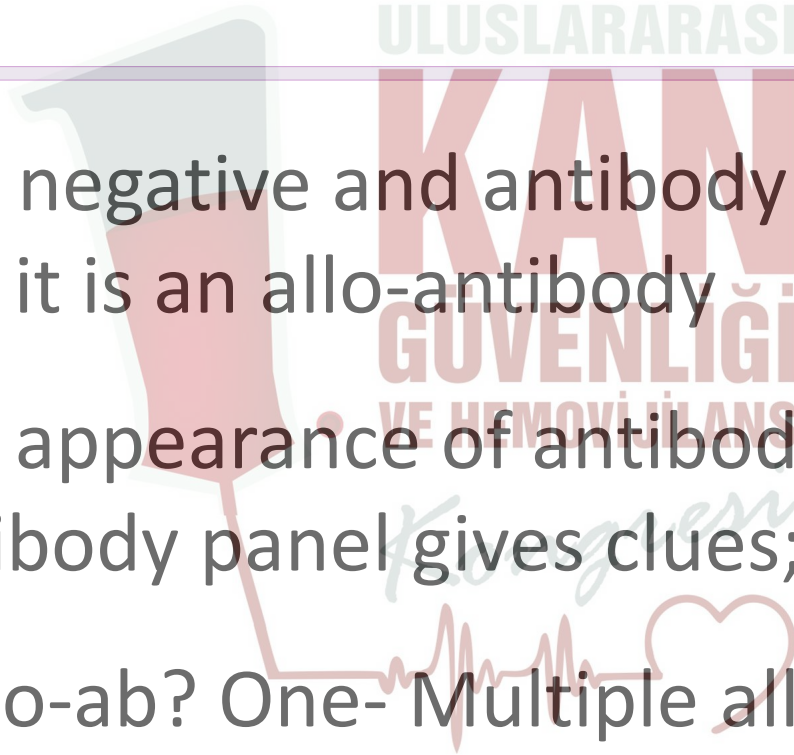
# Identifying the antibody –clinician's part

- Does the patient has hemolysis?
- Is transfusion urgent? Is it necessary?
- What are the DAT and antibody screen results?



# Identifying the antibody- blood bank's part

- If DAT is negative and antibody screen is positive it is an allo-antibody
- General appearance of antibody screen and antibody panel gives clues;
- Only allo-ab? One- Multiple allo? or maybe dosage effect?



# Allo-antibody panel



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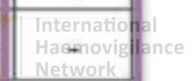
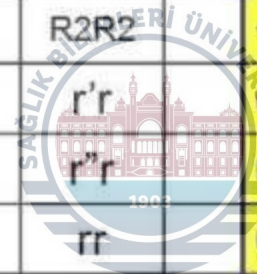
  
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# Multiple allo-antibody panel

	Lot #13015	Rh-Hr					Kell		Duffy		Kidd		P		MNSs				I S	PEG AHG
		D	C	E	c	e	K	k	Fy <sup>a</sup>	Fy <sup>b</sup>	Jk <sup>a</sup>	Jk <sup>b</sup>	P <sub>1</sub>	M	N	S	s			
1	R2R2	+	0	+	+	0	0	+	+	0	+	+	0	+	+	0	+	0	0	2+
2	r'r	0	+	0	+	+	0	+	0	+	+	0	+	+	+	+	+	0	0	4+
3	r'r	0	0	+	+	+	0	+	+	+	+	+	+	+	+	0	+	0	0	
4	rr	0	0	0	+	+	+	0	0	+	0	+	0	0	+	+	+	0	0	
5	R1R1	+	+	0	0	+	0	+	+	0	+	+	+	+	0	+	0	0	4+	
6	rr	0	0	0	+	+	0	+	0	+	0	+	0	+	0	0	+	0	0	
7	rr	0	0	0	+	+	0	+	+	0	+	0	+	0	+	0	+	0	0	
8	rr	0	0	0	+	+	0	+	0	+	+	+	+	+	+	+	0	0	0	
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# Transfusion in the presence of allo-antibody

- Identifying the allo-antibody
- Finding antigen negative RCC to the corresponding antibody
- Sometimes identifying the antibody can not be possible :
- Try as much cross matches as you can



# Allo-adsorbtion

- To solve multiple antibody problems
- To be sure that identified antibody is the right one
- Adsorbe allo-antibodies in the patients plasma one by one on different sets of RBC

# If compatible unit is not available

If the transfusion is urgent :

- Least incompatible RCC unit can be transfused 20-30 ml,
- If no signs of reaction after 30 min,
- Transfusion can be continued slowly and with close follow up
- This method is not recommended unless anemia is life threatening

- **Late hemolysis can occur.**

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# If compatible unit is not available

- Degree of incompatibility does not reliably predict the risk of hemolysis
- Autologous transfusion is an option for elective surgeries
- Other surgical techniques and local hemostatic agents which diminish the blood loss are advised



# If compatible unit is not available

- Type the patients RBC for the most immunogenic antigens:
- Cc, Ee, K, Fy, Jk, Ss
- Match the negative antigens of donor and the recipient
- Widely phenotyped donor pool would save time and energy



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# Preventing allo-antibody problems

- Type and screen the patient while performing other routine testing before scheduled surgery. Not at the last minute!
- If the patient is expected to have multiple transfusions perform phenotyping and
- Transfuse them with negative antigens matched RCC



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# Case 2

- 50 year of male patient
- Admitted to ER dizziness and shortness of breath
- Hb 5 gr/dl
- LDH and ID bilirubin is elevated, haptoglobin is low
- DAT is +4 polyspecific



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# Case 2

- Patient was diagnosed as auto-immune hemolytic anemia
- Prednisolone treatment was started
- Attending physician ordered 2 units of RCC
- Patients blood type is A Rh(D) positive



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# Case 2

- Blood bank personnel calls in:  
“We have cross matched 10 units of A Rh(D) positive RCC, they are all incompatible. We can release the RCC with the physicians written consent”

# Challenge

- Why CM is incompatible?
- Is transfusion necessary? - Is it urgent?
- Is transfusion safe?
- What is the risk of hemolytic transfusion reaction if I transfuse incompatible RCC?
- Should I wait for the compatible unit?



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# Why CM is incompatible?

- Autoantibodies are mostly against to public antigens
- They react with patients own RBC
- Excess antibody in the plasma bounds to donor RBC
- **and test +RBC**



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DAT +

CM +

AB  
screen +

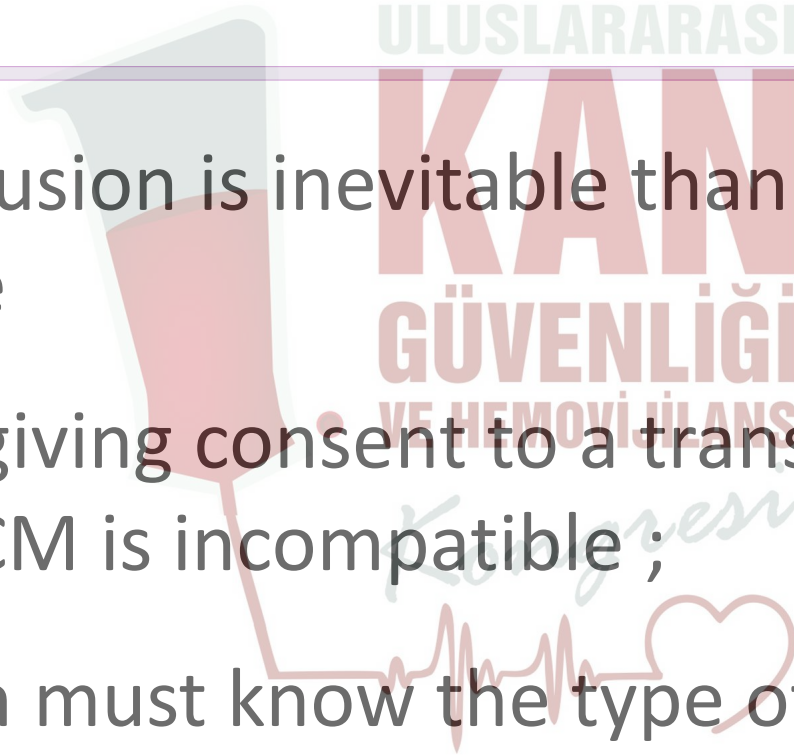
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# Safety of transfusion in AIHA

- If transfusion is inevitable than it should be done
- Before giving consent to a transfusion where CM is incompatible ;
- Clinician must know the type of antibody



# Is it auto-ab and auto-ab only?

- If the patient had no transfusion and/or pregnancy in the past 3 months and DAT is positive; it is auto-antibody
- Antibody screen and antibody panel is pan-reactive with the same degree of positivity

# Antibody panel of AIHA



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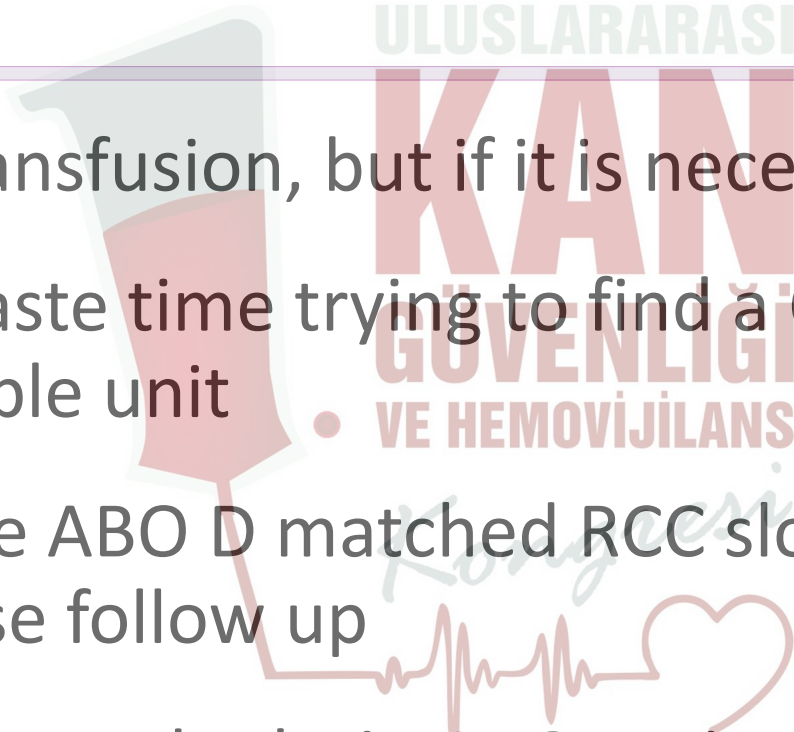
  
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# Transfusion in auto-antibody

- Avoid transfusion, but if it is necessary
- Don't waste time trying to find a CM compatible unit
- Transfuse ABO D matched RCC slowly and with close follow up
- If there is no doubt in ABO typing of the patient: O group transfusion is not



# Transfusion in auto-antibody

- Patient will hemolyse transfused RBC with the same speed that he/she hemolyzes his/her own
- Start treatment for hemolytic anemia
- Whether the auto-antibody is warm or cold would change the treatment so ..



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# Polyspecific coombs is not enough

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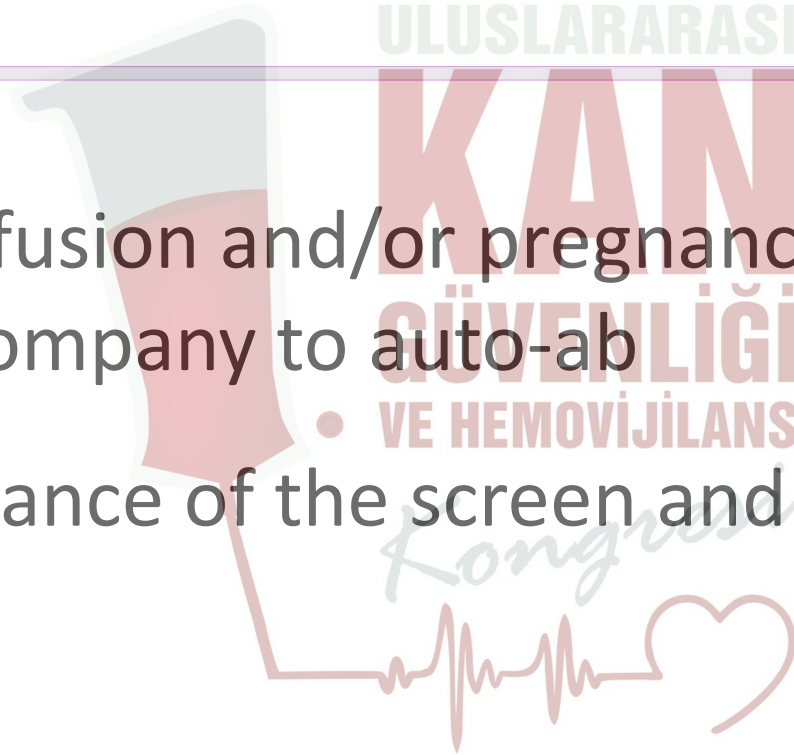
IgG C3d Ctl.

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# Is there a risk of + allo-ab?

- If there is transfusion and/or pregnancy in the past, allo-ab can accompany to auto-ab
- General appearance of the screen and panel can give a hint



# Panel of auto + allo-antibody

Cell	D	C	c	E	e	C <sup>w</sup>	K	k	Kp <sup>a</sup>	Kp <sup>b</sup>	Js <sup>a</sup>	Js <sup>b</sup>	Fy <sup>a</sup>	Fy <sup>b</sup>	Jk <sup>a</sup>	Jk <sup>b</sup>	Le <sup>a</sup>	Le <sup>b</sup>	P <sub>1</sub>	M	N	S	s	Lu <sup>a</sup>	Lu <sup>b</sup>	Xg <sup>a</sup>	AHG
1	+	+	0	0	+	0	+	+	0	+	0	+	+	+	+	0	0	+	0	+	0	+	0	0	+	+	4+
2	+	0	+	+	0	0	0	+	0	+	+	0	+	+	+	+	0	0	0	+	+	+	0	0	+	+	2+
3	+	+	0	0	+	+	0	+	0	+	+	+	+	+	0	0	0	0	0	+	0	+	0	0	+	+	4+
4	+	0	+	0	0	0	0	+	0	+	+	+	0	+	+	0	0	0	0	0	+	0	+	+	+	+	2+
5	0	+	+	0	+	0	0	+	0	+	+	+	0	0	+	0	+	0	0	+	0	0	+	0	+	+	4+
6	0	0	+	+	+	0	0	+	+	+	0	+	0	+	+	+	0	0	+	0	+	0	+	0	+	+	2+
7	0	0	+	0	+	0	0	+	0	+	+	+	0	0	+	+	0	0	+	+	0	0	+	0	+	0	2+
8	0	0	+	0	+	0	+	0	0	+	+	+	0	0	+	0	0	+	+	+	+	0	+	0	+	+	2+
9	+	+	+	0	+	0	0	+	0	+	0	+	+	0	+	+	+	0	+	+	+	0	+	0	+	0	4+
10	+	+	+	0	+	0	0	+	0	+	+	+	0	0	+	0	0	+	+	+	+	+	+	0	+	+	4+
11	0	0	+	0	+	0	0	+	+	+	0	+	+	0	0	+	0	+	+	0	+	+	+	0	+	+	2+
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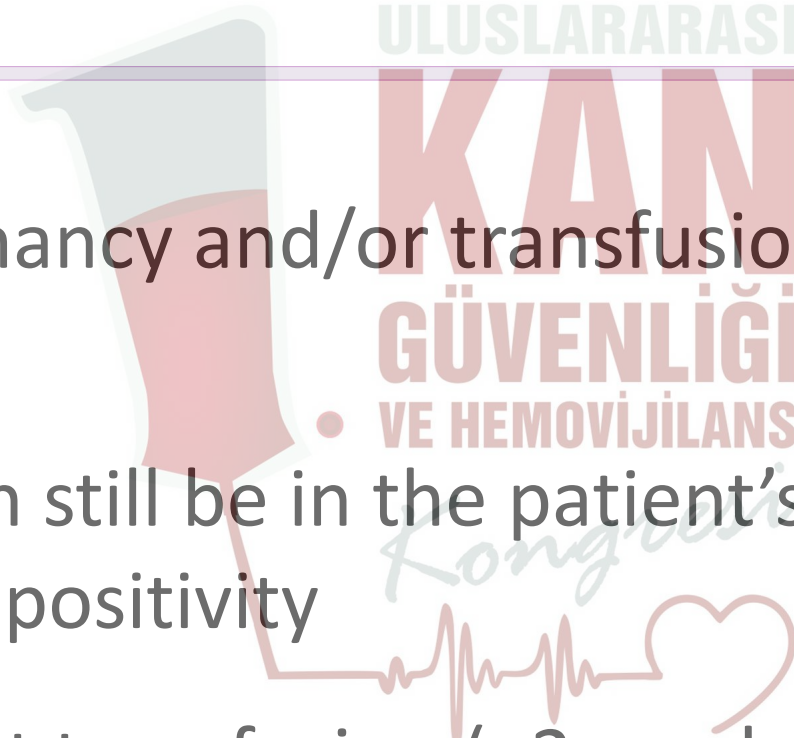
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# Is there a risk of + allo-ab?

- If there is pregnancy and/or transfusion in the past 3 months;
- Foreign RBC can still be in the patient's circulation and may cause DAT positivity
- If there is recent transfusion ( $\approx 2$  weeks); late hemolytic transfusion reaction must be considered



# If there is a risk of + allo-ab

- Try to define the accompanying allo-ab
- Then find the antigen negative RCC to the corresponding antibody
- This antigen negative RCC will still be incompatible



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# If there is a risk of + allo-ab

- If antibody can not be defined
- If there is a theoretical risk of allo-ab but there is no sign of allo-ab in the antibody panel (pan-reactive panel)
- If auto-ab is very strong (4+) and there is a risk that it may hide an allo-ab

# If there is a risk of + allo-ab

- Phenotype matched RCC (as much as possible) can be transfused
- Auto-adsorption:
  - Adsorb all autoantibodies in the patients plasma to patients own RBC
  - Perform antibody panel by the adsorbed plasma



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# If there is a risk of + allo-ab

- Alloadsorbtion
- Elution
  - To define the antibody causing DAT positivity
  - Separate the antibody from RBC: prepare eluate
  - Perform antibody panel from eluate
- Titration of antibodies in the panreactive panel



# Case 3

- 56 years old multiple myeloma patient
- 1 unit of RCC is ordered
- CM incompatible +1
- DAT polyspecific +1
- Ab screen panreactive +1



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- **History:** Ivlg infusion 3 days ago

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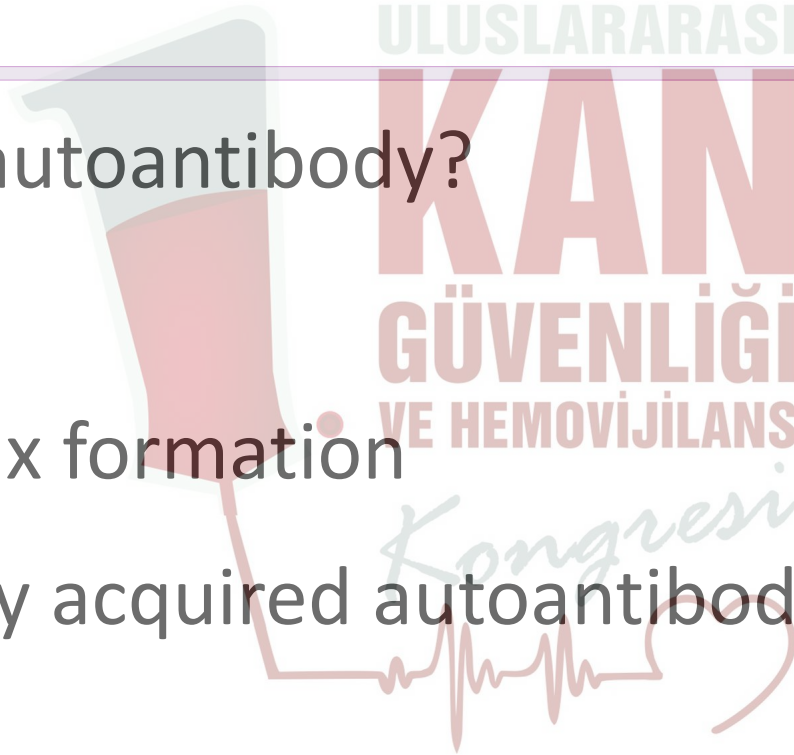
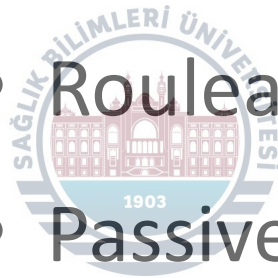
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# Case 3

- Is it an autoantibody?
- Rouleaux formation
- Passively acquired autoantibody (Ivlg)

- Washing usually dissolves the reaction



# Case 4

- 35 years old patient has diabetic foot ;
- Under parenteral antibiotics for 1 week
- Hgb decreased from 11 to 9 gr/dl
- LDH and Rtc elevated
- DAT Ig G +2, C3 –
- Ab screen is negative



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# Drugs

- Drugs can cause DAT positivity  $\pm$  hemolysis via various mechanisms
- If CM is compatible blood can safely be transfused
- Positive DAT and negative eluate is typical



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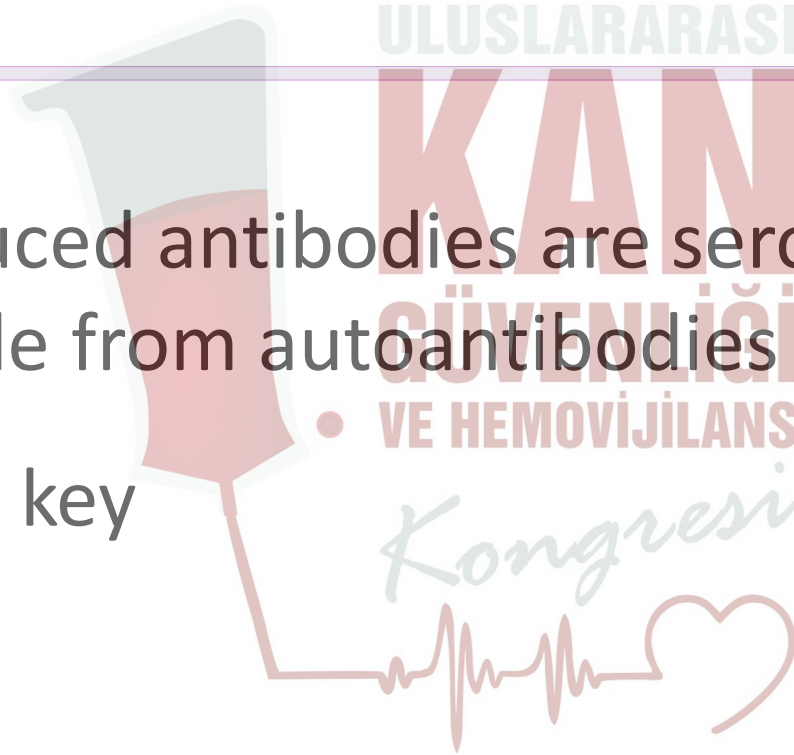


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# Drugs

- Some drug induced antibodies are serologically indistinguishable from autoantibodies
- Suspicion is the key



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# Problems

- Most clinicians don't have sufficient knowledge about transfusion immunology
- Number of certified/educated blood bank personnel are not enough
- Many blood bank laboratories are inadequate to solve antibody problems



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# Solutions

- Open –honest communication between blood bank and clinician
- Education of both doctors and blood bankers
- Transfusion medicine specialists
- A reference laboratory where blood samples can be send
- Widely phenotyped donor pool



# Main References

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