珍しい: Anti-K11 Antibodies

Juan Vitelio Rodriguez, M.D., PGY-4

Transfusion Medicine

Disclosures

- I do not have financial/other relationships with the manufacturer(s) of commercial product(s) or provider(s) of commercial service(s) that would affect my views discussed in this educational activity.

Learning Objectives

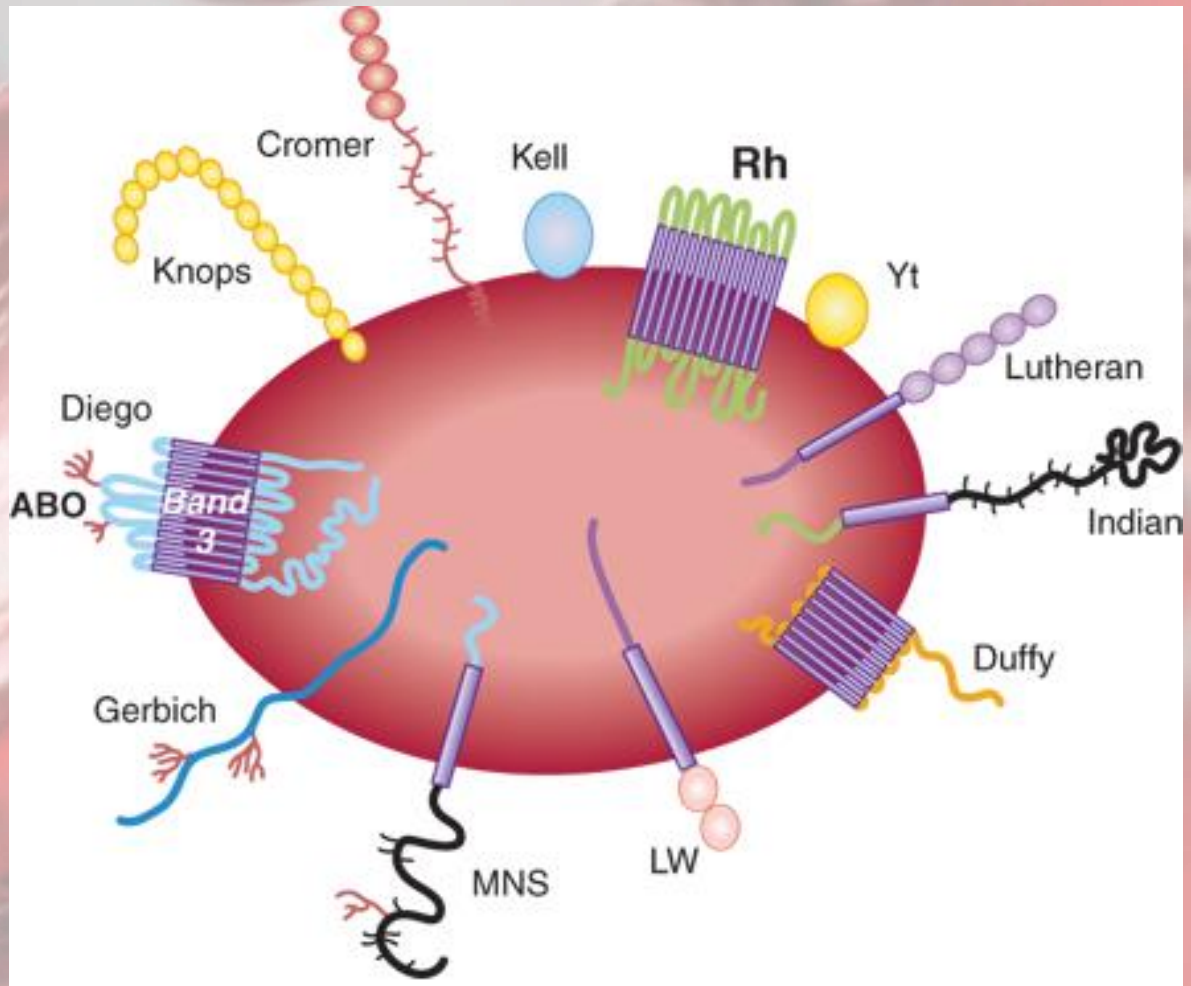
1. Define the structure and clinical significance of the Kell antigen system
2. Describe existing literature regarding anti-K11 antibodies
3. Discuss the process and challenges of executing an international rare donor search

Red Blood Cell Antigens

- Before the 1900s, it was thought that all blood was the same, a misunderstanding that led to frequently fatal transfusions of animal blood into humans and hazardous transfusions of blood between people.
- Human blood is not the same—people belong to different blood groups, depending upon the surface markers found on the red blood cell.
- The cells that make up the body's tissues and organs are covered with surface markers, or antigens. Red blood cells are no different.

Blood Group Systems

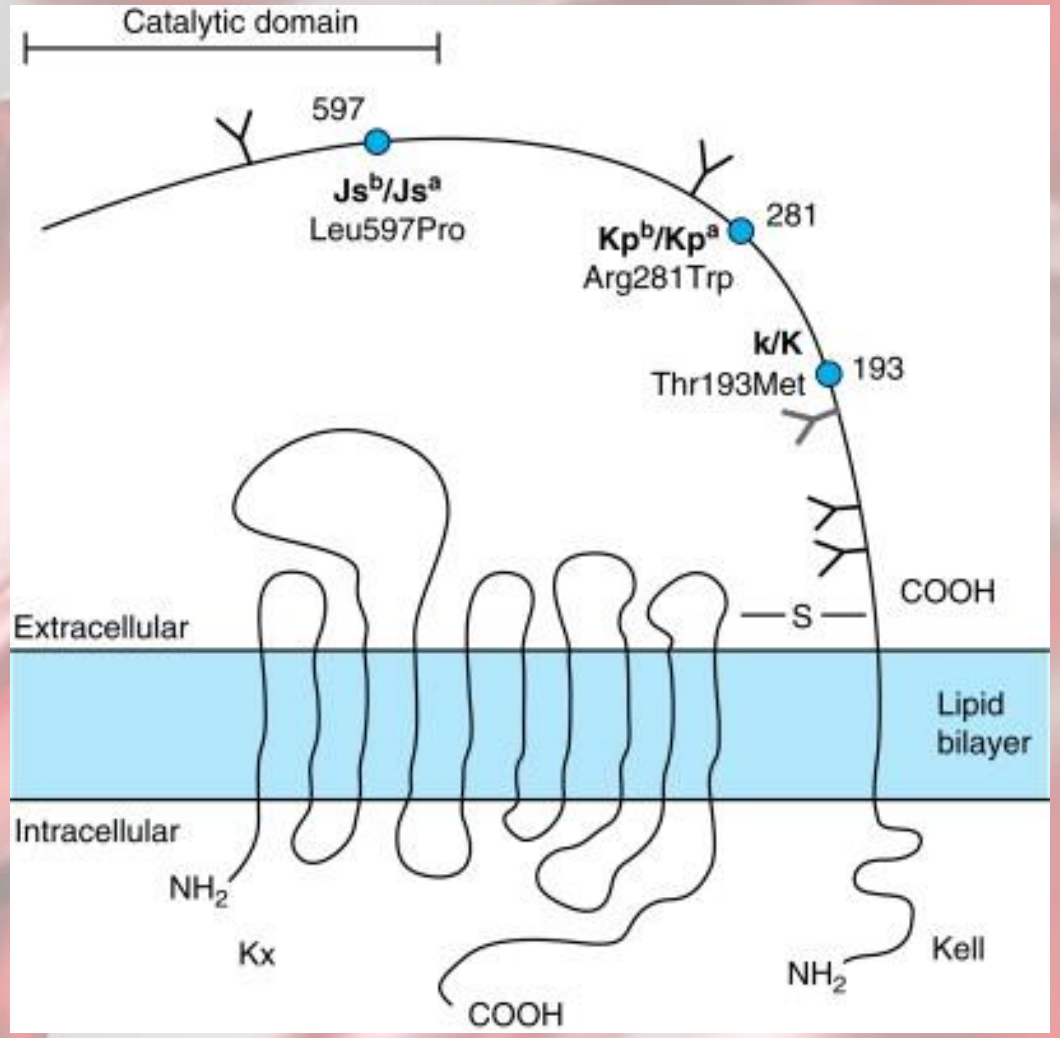
Major	Minor
ABO	MNS
Rh (Rhesus)	P
D	Lewis
C/c	Duffy
E/e	Kidd
	Kell
	Ii
	Lutheran



Source: H. Franklin Bunn, Jon C. Aster: Pathophysiology of Blood Disorders
www.accessmedicine.com
Copyright © McGraw-Hill Education. All rights reserved.

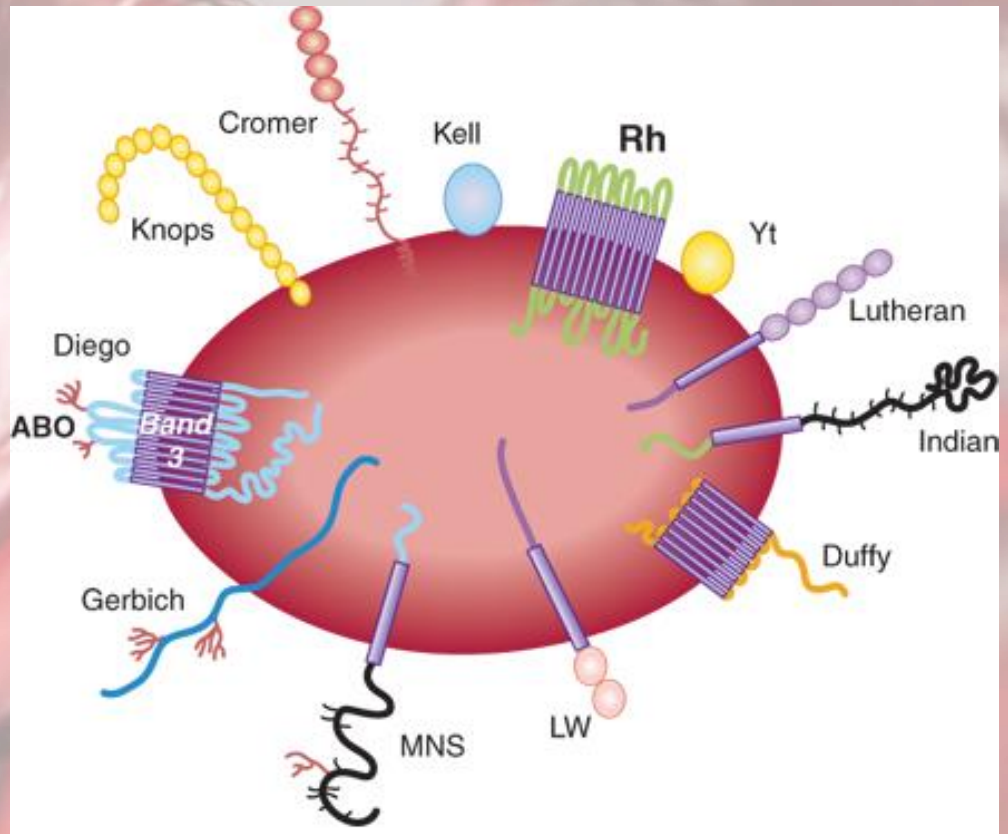
Kell antigen system

- Consists of over 32 high-prevalence and low-prevalence antigens.
- First described in 1946 in the serum of Mrs. Kelleher.
  - The antibody reacted with the RBCs of her newborn infant, her older daughter, her husband, and about 7% of the random population.
- First blood group system discovered after introduction of antiglobulin testing.
- In 1949, anti-k, the high prevalence antithetical partner to K, was described.
- Kell remained a two-antigen system until the antithetical antigens Kp^a and Kp^b were described in 1957 and 1958, respectively.



Kell antigen expression

- Kell blood group antigens are only found on RBCs and not on platelets, lymphocytes, granulocytes, or monocytes.
- The K antigen can be detected on fetal RBCs as early as 10 weeks and is well developed at birth.
- The k antigen has been detected at 7 weeks.
- The total number of K antigen sites per RBC is quite low: only 3,500 and up to 18,000 sites per RBC. Despite its low quantity, K is very immunogenic.



Source: H. Franklin Bunn, Jon C. Aster: Pathophysiology of Blood Disorders
www.accessmedicine.com
Copyright © McGraw-Hill Education. All rights reserved.

Clinical significance

- Excluding ABO, K is rated second only to D in immunogenicity.
- Most anti-K appear to be induced by pregnancy and transfusion.

- Fortunately, the prevalence of K antigen is low (9% in Caucasians, 2% in African Americans) and the chance of receiving a K+ unit is small.
- If an anti-K develops, compatible units are easy to find.

Learning Objectives

1. Define the structure and clinical significance of the Kell antigen system
2. Describe existing literature regarding anti-K11 antibodies
3. Discuss the process and challenges of executing an international rare donor search

K-11

- K-11 (Côté) is a high frequency antigen occurring in >99.9% of Caucasians.
- Initially described in the serum of a multiparous French-Canadian woman, Mrs. Côté in 1971 as part of a preoperative evaluation.
  - The patient had no previous transfusions.
- The clinical significance of transfusion of K-11 erythrocytes into a patient with an anti-K11 antibody is not known.

K-11 in the literature

- A 27 year old G0P0 adopted Caucasian patient on chronic hemodialysis who received multiple transfusions in the setting of four renal transplants and chronic anemia.
- Several years into her transfusions, anti-K antibodies were identified.
- Years later, pan-reactive antibodies were detected and reference labs identified them as anti-K11 antibodies.
- In addition to receiving K_0 units from the ARDP, she was challenged with K11+ cells without adverse effect.

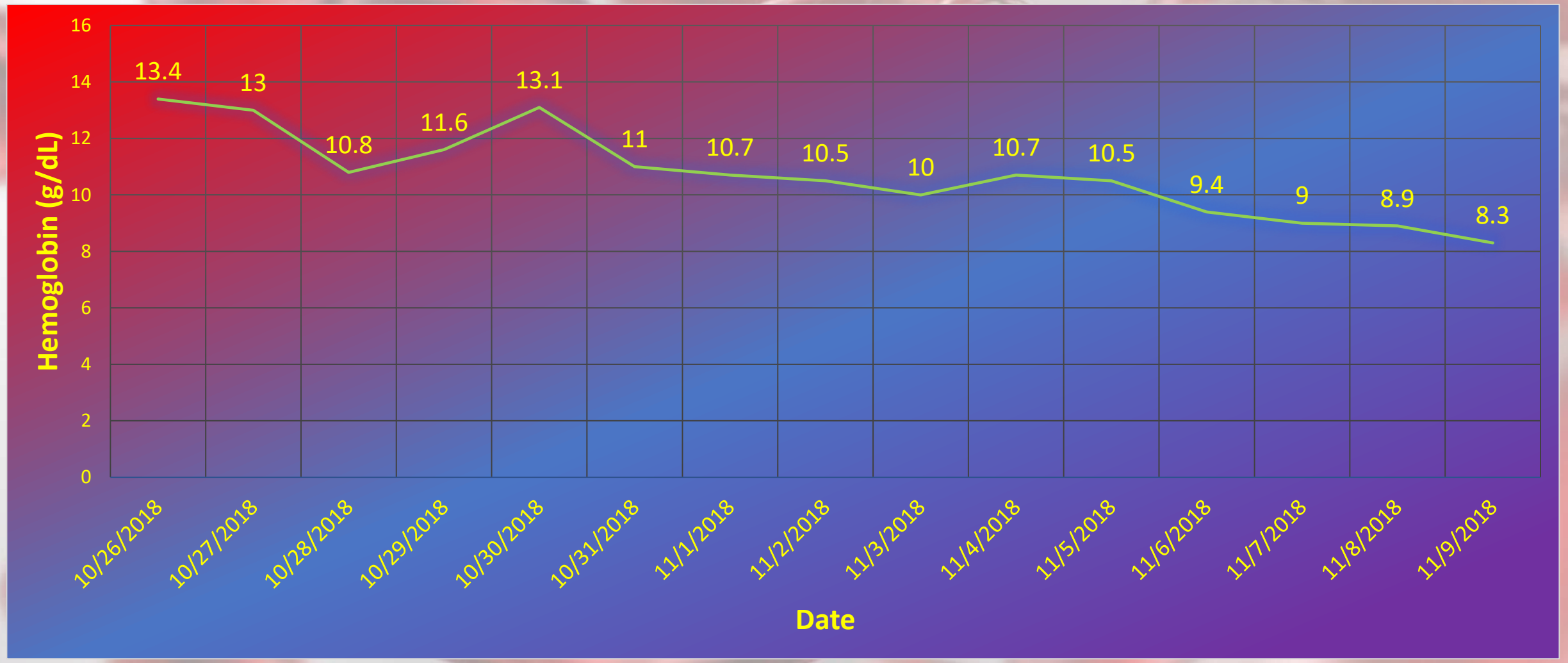
K-11 in the literature

- Red cell survival study and monocyte monolayer assay (MMA) were within normal limits.
- Despite significant antigenic challenge with transfusions on two separate occasions, the patient had no change in antibody response.
- **While a single patient experience cannot be widely generalized, these findings suggest that K-11 red blood cells may be given cautiously in urgent situations to patients with anti K-11 antibodies especially when rare K_0 units are not available.**

Case presentation

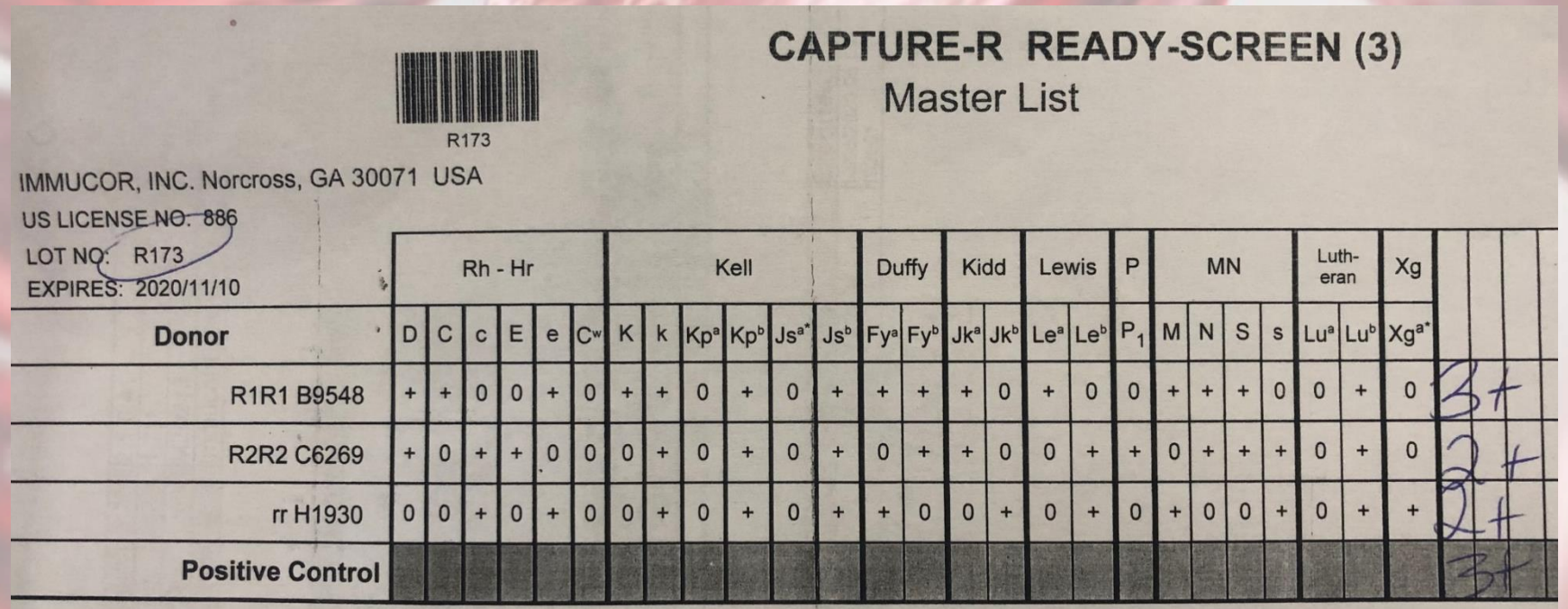
- The patient is a 39-year-old female who is wheelchair-bound and with a history of spina bifida, scoliosis, neurogenic bladder, depression, iron deficiency anemia, right below the knee amputation (2015), and on chronic narcotics.
- The patient presented to the BUMC-T Emergency Department on October 2018 following an accidental knife injury secondary to syncope due to suspected hypovolemia as a result of vomiting and poor oral intake.
- The patient's hemoglobin at presentation: 13.4 g/dL (Oct. 26, 2018).

Hemoglobin trend during first presentation



Second hospitalization (November 2018)

- On November 23, 2018, the home health nurse noticed extensive, spontaneous bleeding from the left lower extremity wound VAC and the patient returned to the ED for further care.
- Antibody screen was done for the first time and was positive.



CAPTURE-R READY-SCREEN (3)

Master List

R173

IMMUCOR, INC. Norcross, GA 30071 USA

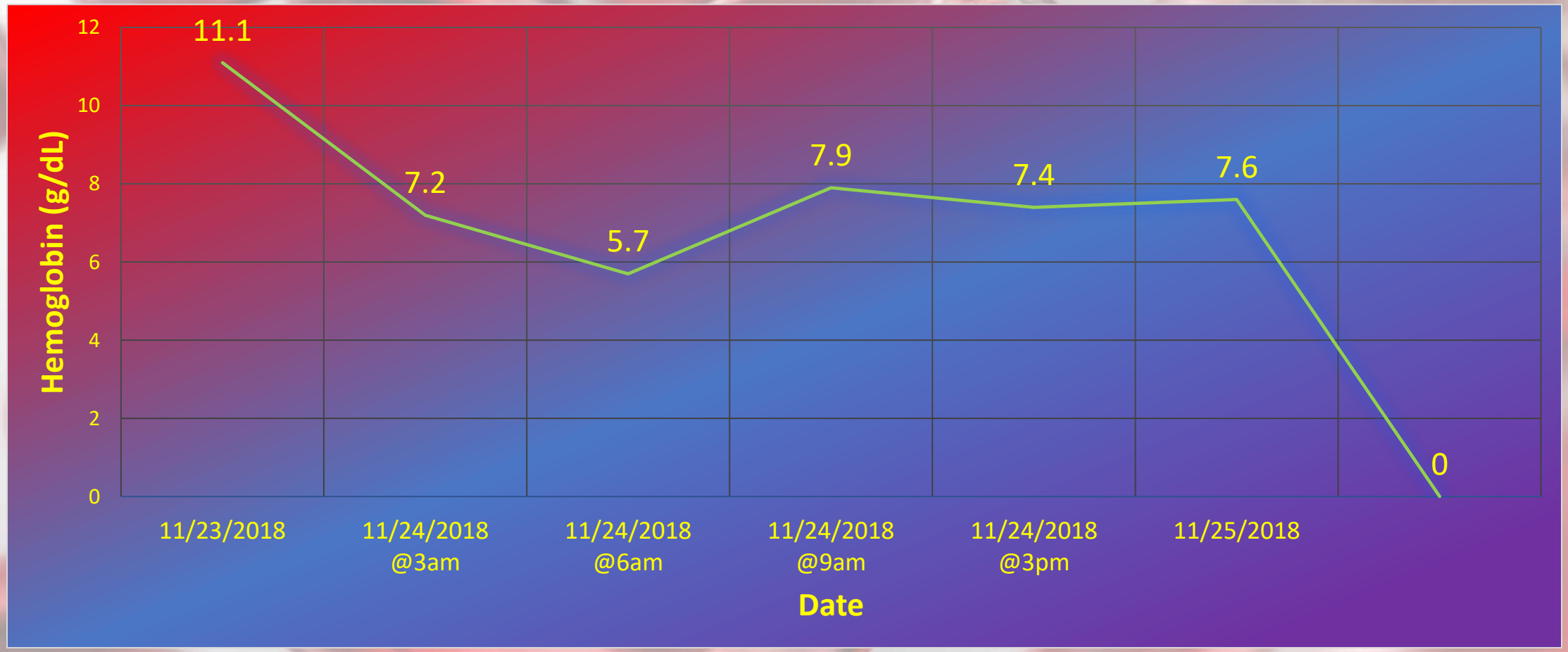
US LICENSE NO: 886

LOT NO: R173

EXPIRES: 2020/11/10

	Rh - Hr						Kell						Duffy		Kidd		Lewis		P	MN				Luth-eran		Xg				
Donor	D	C	c	E	e	C^w	K	k	Kp^a	Kp^b	Js^{a*}	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P_1	M	N	S	s	Lu^a	Lu^b	Xg^{a*}				
R1R1 B9548	+	+	0	0	+	0	+	+	0	+	0	+	+	+	+	0	+	0	0	+	+	+	0	0	+	0	3+			
R2R2 C6269	+	0	+	+	0	0	0	+	0	+	0	+	0	+	+	0	0	+	+	0	+	+	+	0	+	0	2+			
rr H1930	0	0	+	0	+	0	0	+	0	+	0	+	+	0	0	+	0	+	0	+	0	0	+	0	+	+	2+			
Positive Control																											3+			

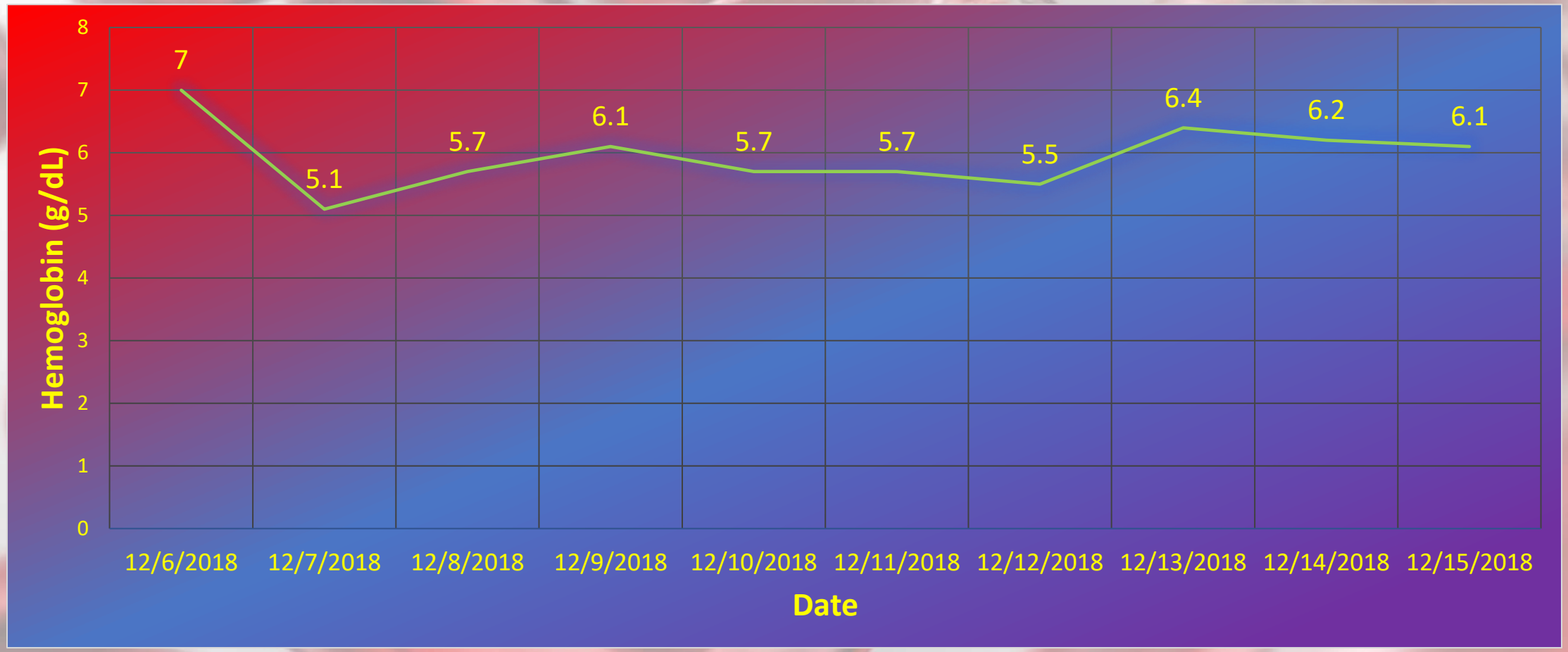
Hemoglobin trend during second hospitalization



3rd hospitalization (December 2018)

- On December 6, 2018, the patient re-presented to the Emergency Department with a 5 day history of increased swelling, severe 10/10 pain, and bleeding of her surgical wound as well as fevers, chills, nausea, and vomiting.

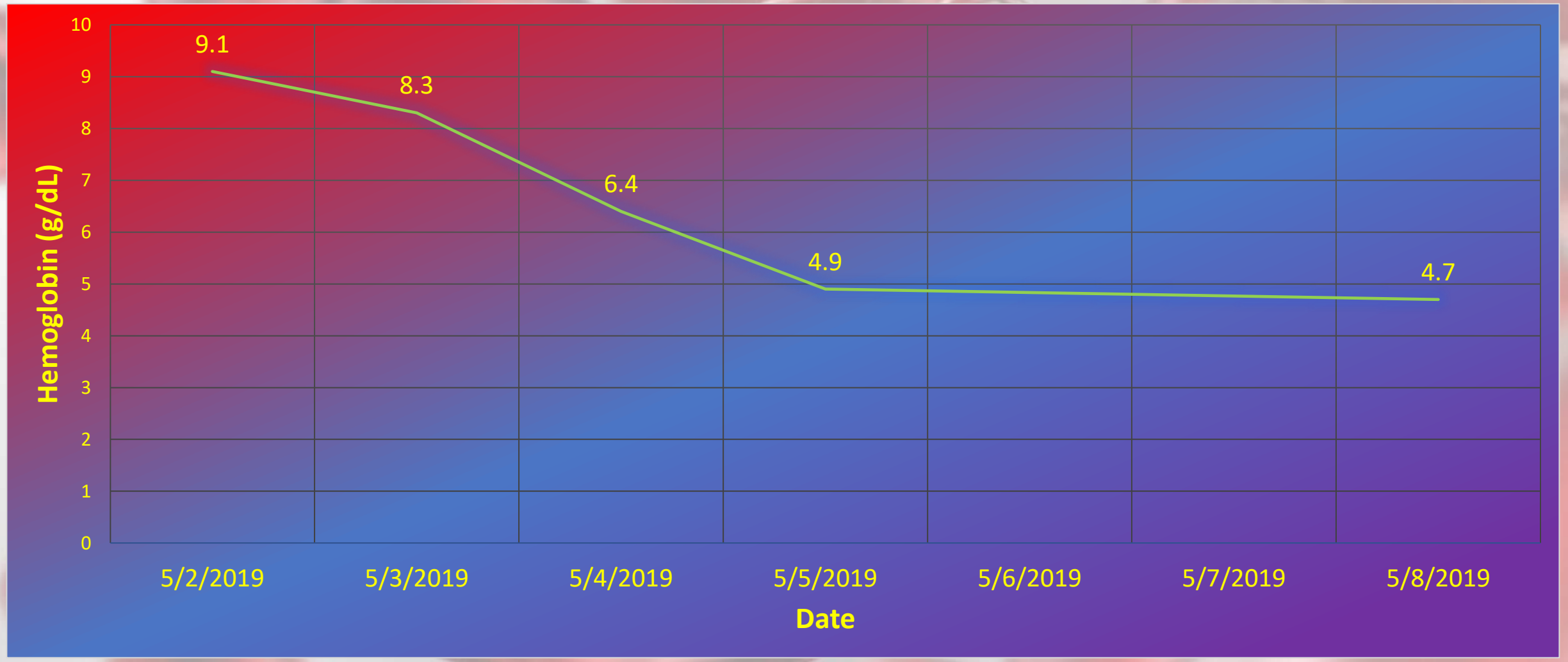
Hemoglobin trend during third hospitalization



April and May 2019

- The patient presented with 10 days of progressively worsening nausea, non-bloody non-biliary emesis, and foul-smelling, loose, watery bowel movements in association with epigastric & left lower quadrant abdominal pain.
  - Found to have complicated cystitis with concern for pyelonephritis due to MDR E. Coli likely related to self-catheterization technique.
- Despite adequate podiatric care and daily dressing changes, there was continuous bloody oozing.

Hemoglobin trend



Learning Objectives

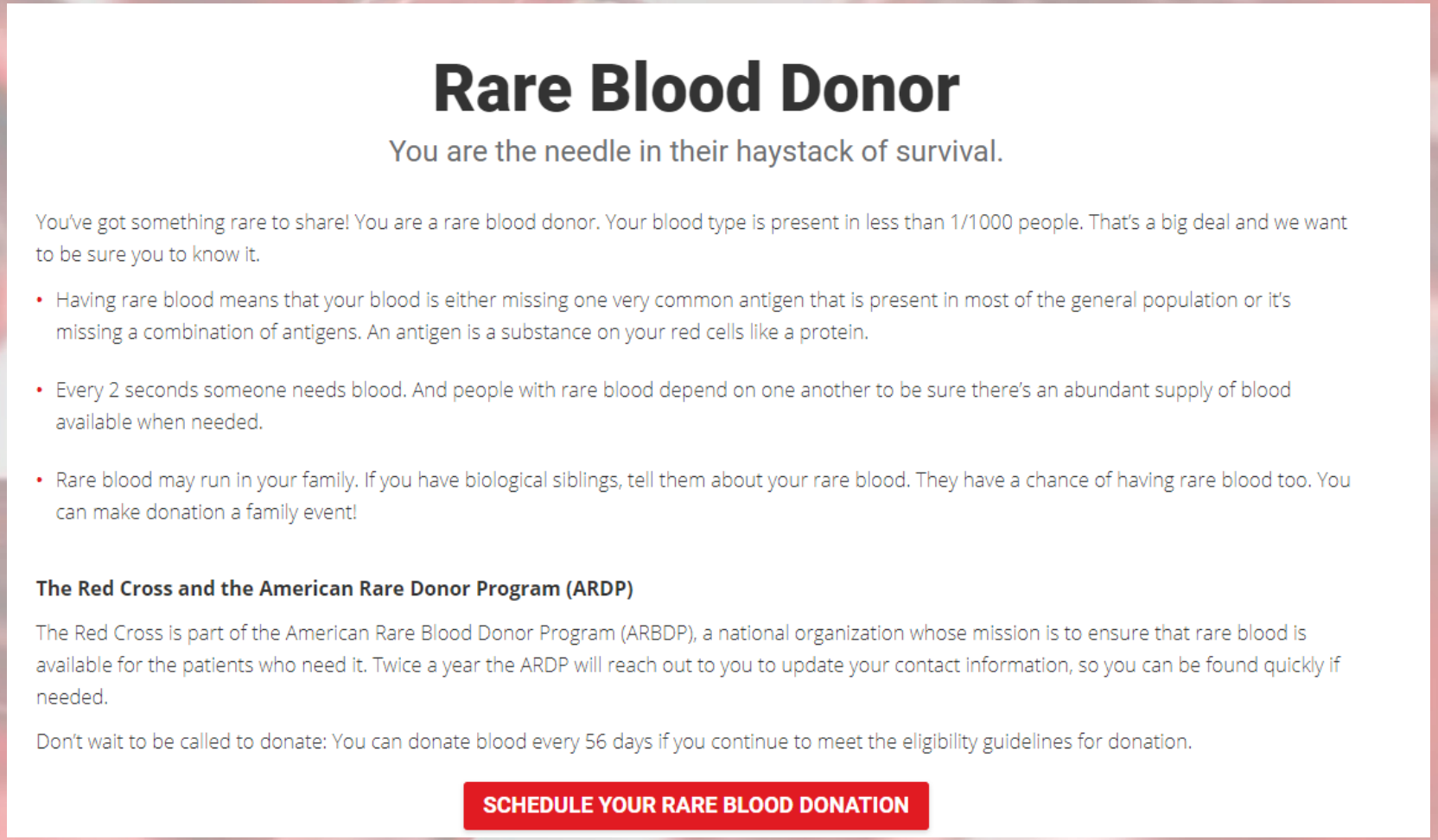
1. Define the structure and clinical significance of the Kell antigen system
2. Describe existing literature regarding anti-K11 antibodies
3. Discuss the process and challenges of executing an international rare donor search

What does it mean by a rare blood type?

- High-prevalence antigen negative
- Multiple common antigen negative
  - One example of a donor in this category is a donor who is group O and Rh(D)−, K−, Fy (a−b−), Jk(a)−, and S−
- Immunoglobulin A (IgA) deficient

American Rare Donor Program (ARDP)

- The ARDP was formed in 1998 as a collaborative effort between the AABB and the American Red Cross to provide rare blood for patients in need.
- Members of the program identify rare donors and submit donor information for entrance into a database, REGGI.
- What options are available if rare blood cannot be located in the United States?



Rare Blood Donor

You are the needle in their haystack of survival.

You've got something rare to share! You are a rare blood donor. Your blood type is present in less than 1/1000 people. That's a big deal and we want to be sure you to know it.

- Having rare blood means that your blood is either missing one very common antigen that is present in most of the general population or it's missing a combination of antigens. An antigen is a substance on your red cells like a protein.
- Every 2 seconds someone needs blood. And people with rare blood depend on one another to be sure there's an abundant supply of blood available when needed.
- Rare blood may run in your family. If you have biological siblings, tell them about your rare blood. They have a chance of having rare blood too. You can make donation a family event!

The Red Cross and the American Rare Donor Program (ARDP)

The Red Cross is part of the American Rare Blood Donor Program (ARBDP), a national organization whose mission is to ensure that rare blood is available for the patients who need it. Twice a year the ARDP will reach out to you to update your contact information, so you can be found quickly if needed.

Don't wait to be called to donate: You can donate blood every 56 days if you continue to meet the eligibility guidelines for donation.

SCHEDULE YOUR RARE BLOOD DONATION

International search

- An international search can be initiated to locate units.
- If units cannot be located in the United States, international registries can be contacted by the ARDP regarding the availability of units.
- The transfusing physician must understand the limitations imposed by regulatory agencies when rare units are imported into the United States.
- If the units are not used, the units cannot be placed into routine inventory for transfusion to other patients and will have to be discarded.

The cost of blood

- The ARDP members are charged a membership fee to obtain search services.
- The mean cost of a leukocyte-reduced RBC in the United States is $200-300.
- The cost of a rare unit of blood obtained in the United States ranges from approximately $1148 to $1373.

May 20, 2019

- An international search executed by the American Rare Donor Program identified two irradiated, group O, K_{null}, Jk(a)-negative units that were predicted to be crossmatch-compatible with the patient's plasma.

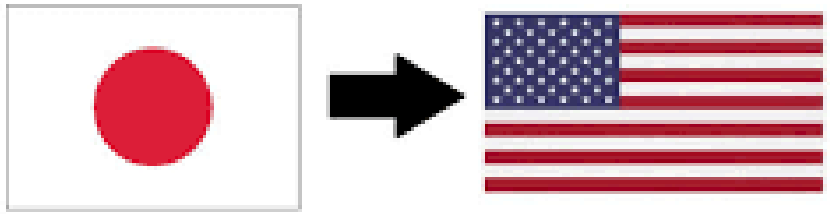
日本赤十字社

日本赤十字社
Japanese Red Cross Society


献血
O
Ir-FTRC-LR-2
O型21-0525-8541


Japanese
Red Cross Society
日本赤十字社
JAPANESE RED CROSS SOCIETY
輸血の安全性を高めるため
求められています！
400mL献血
広島県赤十字血液センター

和英訳
Japanese-English translation



照射年月日 Irradiation date ’16.10.19
照射線量 Irradiation dose 15 Gy

本剤１袋中に、血液４００mLに由来する量のヒト赤血球を含有する。
This single unit contains 400 mL of human red blood cells.

本剤は、交差適合試験用血液（セグメントチューブ）を付属する。
This medical product comes with a segment tube that passes cross-match compatibility testing.

貯法：２～６℃で貯蔵する。

Storage condition: Store at 2-6 degrees Celsius.

注意ー医師等の処方箋により使用すること。

Attention - Use under doctors’ orders.

生物学的製剤基準ー通則４４に規定する輸血用器具を使用すること。

Biological products standards - Under common rule 44, use in accordance to blood transfusion.

外観上異常を認めた場合は使用しないこと。

If you recognize an abnormality in its appearance, do not use it.

- 製造販売元　日本赤十字社

The production sales agency　Japan Red Cross Society

- 所在地: 東京都港区芝公園１丁目２番１号

Address: 1-2-1, Shibakoen, Minato-ku, Tokyo

- 解凍人赤血球液）照射　解凍赤血球液ーLR「日赤」静　点滴

(Thawed red blood cell liquid) Irradiated thawed red blood cell liquid-LR 「Red Cross」Venous Intravenous drip injection

- 🅃　献血　　特生物　採血国：日本　　O 型　D（Rho) 陽性

Blood donation an inherited characteristic [quality]

Country where blood was drawn: Japan　Type O　D (Rho) positive

- 採血 Blood drawn
- 年月日 10/18/2016

- 凍結 Frozen
- 年月日 10/22/2016

- 解凍 Defrosted
- 年月日 5/26/2019 at 3pm

- 最終有効 Expiration date
- 年月日 5/29/2019

Result type:	BB Pathologist Interpretation
Date/Time of Service:	May 28, 2019 10:40 MST
Result status:	Auth (Verified)
Contributed By:	STEPHENS MD, LAURA DILLY on June 04, 2019 8:42 MST
Verified by:	STEPHENS MD, LAURA DILLY on June 04, 2019 8:42 MST
Encounter info:	53310231, BUMCT, Inpatient, 04/23/2019 - 06/18/2019

* Final Report *

Antibody Results

The patient is blood type O, RhD-positive. She has received prior transfusions at an outside institution and has a history of anti-Jk(a) and anti-K11 antibodies.

The current antibody screen is positive, and the patient's serum reacts strongly with all reagent test cells, consistent with pan-reactive anti-K11 antibodies. Because no clinically significant alloantibodies can be ruled out in the current specimen, the patient has been assigned an "unidentified" antibody.

Assessment

The patient's anti-K11 antibodies are significant. K11 is an antigen in the Kell blood group system and is expressed on virtually all individuals' red blood cells. Anti-K11 antibodies would, therefore, react with nearly all donor units and may cause transfusion reactions or hemolysis.

An international search executed by the American Rare Donor Program identified two irradiated, group O, Knull, Jk(a)-negative units that were crossmatch-compatible with the patient's plasma. These units were successfully transfused on 5/29/2019 without evidence of adverse reactions.

Recommendations

It is imperative that the patient considers autologous donation for long-term cryopreservation once her hemoglobin reaches the FDA-stipulated minimum of 11 g/dL. Should the patient ever require transfusion therapy in the future, it is likely no allogeneic units would be compatible—domestically or internationally.

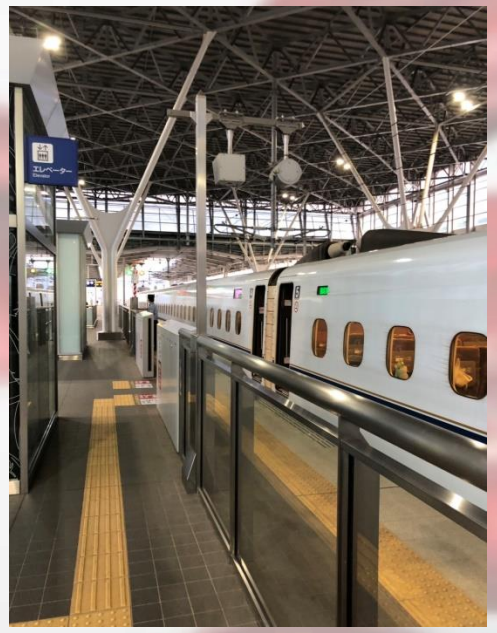
Please consult the Blood Bank with questions/updates/requests.

Laura Stephens, MD (Attending Clinical Pathologist)
Location Performed: Banner- UniversityMedical Center Tucson, 1501 N. Campbell Ave. Tucson AZ 85724

I reviewed the patient's clinical history and pertinent data and/or test results, and I performed the critical elements required for professional review, consultation, diagnosis, and billing for this case.
06/04/2019 08:40:48 MST


博愛ナル大日本赤十字衛生隊
白露戰闘中負傷者救護之畫

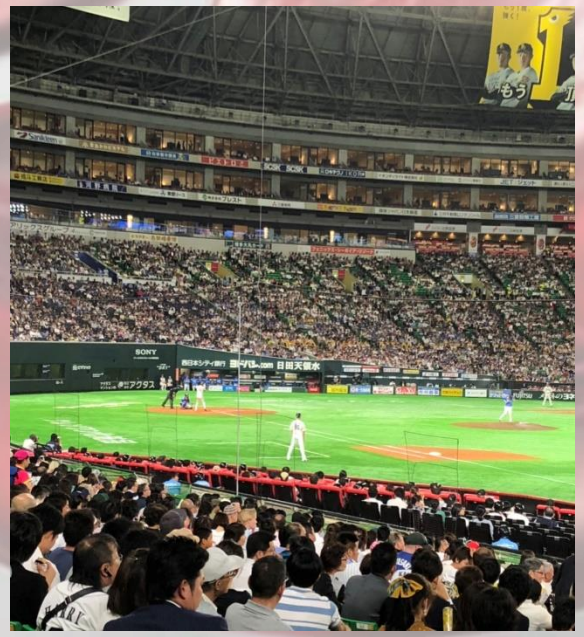
日本の旅行




献血
ご協力お願いします。
みなさんの
善意の献血が、
尊い命を救います。
月日 6月7日（木）
時間 10:00～16:00
会場 中央区保健福祉センター（中央保健所）「あいれふ」5階
主催：舞鶴校区献血推進協力会


Okinawa
Hokkaido
Miyagi
Kanazawa
Kyoto
Tokyo
Fukuoka
Osaka
Nagoya
Nara
Kagawa


清陽軒
とんこつラーメン誕生80周年記念
とんこつ風呂
#とんこつ風呂
seiyo-ken.jp



References

1. Hillyer CD, et al. 2007. *Blood Banking and Transfusion Medicine: Basic Principles and Practice, 2nd edition*. San Diego, CA: Elsevier Academic Press.
2. Guévin R. M., et al. *The Côté Serum (Anti-K11), an Antibody Defining a New Variant in the Kell System*. Vox Sang. 1976;31(1 SUPPL):96-100.
3. Kelley, C.M., et al. *Outcome of Transfusion of K:11 Erythrocytes in a Patient with Anti-K11 Antibody*. Vox Sang. Volume 74, Issue 3. April 1998. Pages 205-208
4. Harmening, D.M. *Modern Blood Banking & Transfusion Practices* Philadelphia, 2018. 7th Edition.
5. Flickinger, C. “REGGI and the American Rare Donor Program.” *Transfusion medicine and hemotherapy : offizielles Organ der Deutschen Gesellschaft fur Transfusionsmedizin und Immunhamatologie* vol. 41,5 (2014): 342-5. doi:10.1159/000366149.
6. Flickinger C. *Miracles do happen: meeting the challenges of providing rare blood through the American Rare Donor Program*. Immunohematology. 2016 Jun;32(2):75-77. PMID: 27901574.
7. Meny, GM., et al. "The American Rare Donor Program." *Journal of Critical Care* 28.1 (2013): 110.e9-10.e18. Web.
8. Janis R. Hamilton, Connie M. Westhoff, Chapter 27 - Kell, Kx and Kidd Blood Group Systems, Editor(s): Beth H. Shaz, Christopher D. Hillyer, Morayma Reyes Gil, Transfusion Medicine and Hemostasis (Third Edition), Elsevier, 2019, Pages 157-161.

ありがとうございました！

- Dr. Laura Stephens
- Dr. Erika Bracamonte
- Blood Bank Technologists