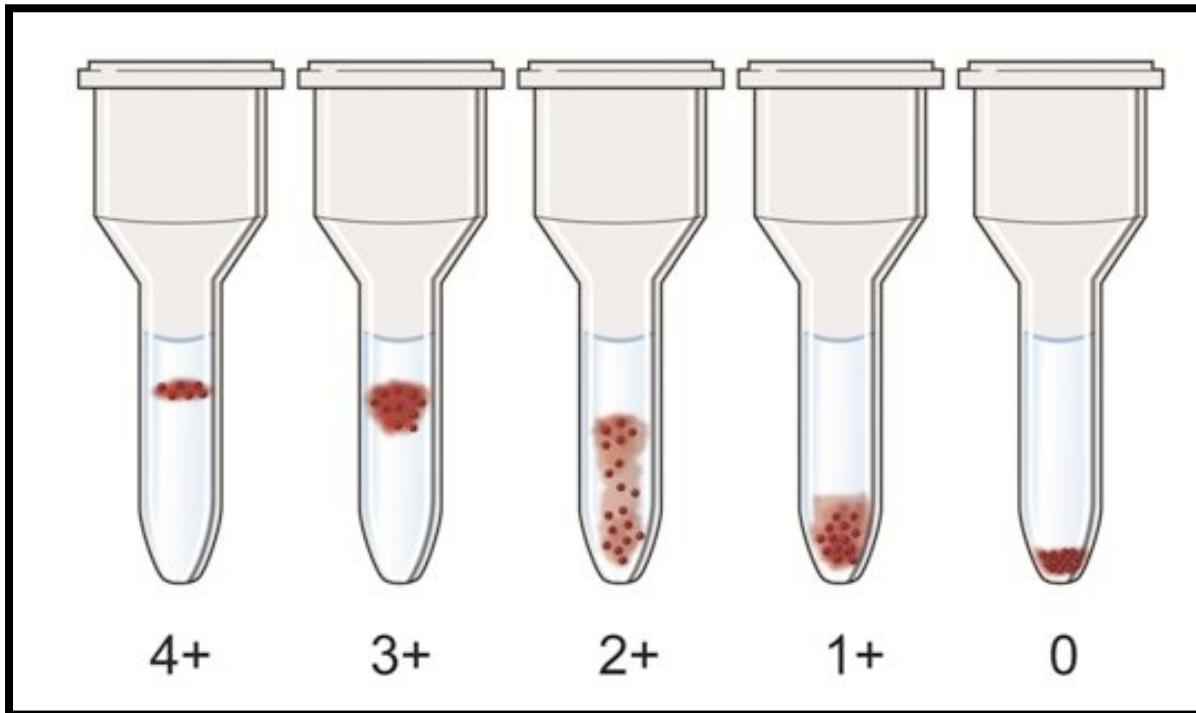


Red Service Survival Guide

2022-2023



**Washington University School of Medicine
Department of Pathology & Immunology
Division of Laboratory and Genomic Medicine**

Important numbers

Location	Number
BJC central page	362-1242
BJC IT help desk	362-4700
BJH Lab Medicine central page (phone tree)	747-1320
Transfusion Medicine:	X 1
Chemistry:	X 2
Microbiology:	X 3
Molecular pathology:	X 4
Hematology/Coagulation:	X 5
BJH Labs Customer Service	362-1470
BJH Apheresis Charge desk	454-8445/362-1449
BJH Blood bank	362-3884
Chemistry Supervisor on call	801-3118
Core lab sendouts	362-1127
Copath IT help desk	362-2347
Fax number for LGM	362-1461
Flow cytometry lab	362-4628
GPS lab	747-7337
HLA Lab	362-5322
Mayo Clinic Laboratories	800-533-1710
Chemistry sendouts client code	7014435
Microbiology Lab	362-3898
Microbiology supervisor on call	801-3122
Molecular Diagnostics Lab (MDL)	454-8685
Outpatient lab draw (CAM 3rd flr)	286-1797
Paraffin FISH lab	362-7851
SLCH Central page	454-6000
SLCH Core lab	454-4628
SLCH Blood bank	454-6204
Surgical Pathology Clerical	362-0101
Wash U IT Help desk	933-3333
AP Chief Resident	701-3107
CP Chief Resident	394-1567

Trainees

Trainee	Role	Track	BJH Cell
Agboola, Tomilola	PGY1	AP/CP	459-4988
Burk, Justin	PGY1	AP/CP	642-2719
Goodman, Kyle	PGY1	AP/CP	699-2960
Hubler, Zita	PGY1	CP	459-1958
Li, Jiannan	PGY1	AP/CP	699-2986
Marolt, Clayton	PGY1	AP/CP	699-2984
Rowe, Jackson	PGY1	AP/CP	574-6213
Snyder, Christopher	PGY1	CP	699-2998
Stark, Lauren	PGY1	AP/CP	459-1972
Tichenor, Madison	PGY1	AP/CP	459-1124
Weli, Homayemen	PGY1	CP	642-2723
Chapagain, Udita	PGY2	AP/CP	503-3621
Crumley, Brenndan	PGY2	AP/CP	503-3791
Frick, Robert	PGY2	CP	283-1203
Hernandez, Patricia (CP Chief resident)	PGY2	CP	283-1296
Limia, Melissa	PGY2	AP/CP	503-3961
Russler-Germain, Mimi	PGY2	AP	503-6339
Sadegh, David	PGY2	AP/CP	503-7342
Spies, Nicholas	PGY2	CP	283-1415
Vacca, Francesca	PGY2	AP/CP	503-8969
Wallace, Lisa	PGY2	AP/CP	503-9201
Ahmed, Safee	PGY3	AP/CP	574-1373
Almeida, Guilherme	PGY3	AP/CP	267-6491
Azimi, Vahid	PGY3	CP	280-7455
Borcherding, Nicholas	PGY3	CP	536-5233
Khonde, Pooja	PGY3	AP/CP	565-7649
Kreutz, Kasey	PGY3	AP	393-6476
Morse, Patrick	PGY3	AP/CP	574-0597
Raju, Saravanan	PGY3	CP	280-1605
Roberts, Kaleigh	PGY3	AP/NP	565-2588
Wein, Alexander	PGY3	AP	393-0602
Wong, Amanda	PGY3	AP	565-3163
Castro, Eleanor	PGY4	AP/CP	482-1351
Cheema, Hassam	PGY4	AP/CP	482-1360
Jabbari, Shiva	PGY4	AP/CP	482-1366
Sina, Jason	PGY4	AP/CP	482-1391
Shenoy, Krithika (AP Chief Resident)	PGY4	AP/CP	482-1394
Upchurch, G. Michael	PGY4	AP/CP	482-1413
Wu, Ariel (WE Chief Resident)	PGY4	AP/CP	482-1419
Bailey, Cedric (AP Chief Resident)	PGY5	AP/CP	480-0043
McLamb, Nathan	BB/TM Fellow		801-3103
Brown, Hannah	Jr Clin Chem fellow		
Omosule, Cate	Sr Clin Chem fellow		747-4972
Bosserman, Rachel	Jr Clin Micro fellow		294-3689
Tarlton, Nicole	Sr Clin Micro fellow		273-1811
Ghasemi, Reza	LGG fellow		
Mojarad, Bahareh	LGG fellow		
Hughes, Andrew	MGP fellow		
Khan, Fahd	MGP fellow		
Zazueta, Fernando	MGP fellow		

Note: fill in blank spaces as that information becomes available

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Contact Information

NOTE: MUST DIAL ALL 10 DIGITS (WITH AREA CODE 314) FOR ALL HOSPITAL NUMBERS

Transfusion Medicine Attending Physicians

- Ask your attending how they prefer to be contacted
- If not otherwise specified, try cell or office number, then home number
- Last resort: call a different attending, TM fellow, or CP chief resident
- Attending on-call changes at 7AM on Monday morning

Attending	Office	Cell (314- unless noted)	Home
George Despotis	362-6586	791-5519 (day)	984-9715 (night)
Chuck Eby	362-1302	954-1242	863-3850
Brenda Grossman	362-6032	458-4582	721-2125
Ron Jackups	362-8413	578-3940	N/A
Chang Liu	747-5773	503-709-1055	N/A
Mei San Tang			
Suzie Thibodeaux	273-1465	504-577-7897	N/A

Laboratory Medicine Administrative Staff

Role	Name	Office
LGM Faculty Coordinators	Julie Shafferkoetter	362-3186
	Dionne Brierton	362-2207
Fellowship Program Coordinator	Ashley Edwards	273-5476
Residency Program Coordinator	Sharon Aubuschon	747-0687

BJH Apheresis Center: General phone numbers by location

FAX	454-8002
Front Desk	362-1489
Charge Desk	454-8445 / 362-1449
Photopheresis Desk	362-1254
Conference Room	747-4012

BJH Apheresis Leadership

Clinical Manager	Office	Work Cell	Personal Cell
Lisa Brown	362-3233	305-1510	954-7602
Assistant Clinical Managers			
Kelly Lloyd	362-1950	801-3123	724-8990
Donna Mansfield	362-1531	574-5431	680-0693
Resource Nurses			
Tricia Frazier	747-1395	220-1397	308-8999
Connie Hamilton	747-4011	220-4267	565-2041

BJH Apheresis Nurse Practitioners

Name	Office	Work cell	Personal cell
Jessica File	747-6987	283-4508	636-219-0636
Christine Nicola	747-3674	801-3126	537-0089
Meaghan Keeven	747-6987	283-4508	306-4227

BJH Apheresis Nurses

Name	Work Cell	Personal Cell	Home Phone
Barks, Kristen	749-4480	403-3752	N/A
Butler, Shannon	574-5526	417-483-8182	N/A
Gunther, Christina	574-5563	618-444-3447	618-656-4847
Hammond, Miranda	599-3359	309-645-1054	N/A
Hillyer, Lisa	574-5466	825-8989	636-349-8989
Johnson, Angela	305-2737	556-5545	N/A
King, Nikki	319-7501	618-954-0911	N/A
Lyons, Tam	319-7452	680-8986	N/A
Mathenia, Sandy	574-3865	618-670-2187	N/A
Mattingly, Julie	574-5556	618-531-5165	636-226-4300
Pearman, Debbie	261-6516	920-8791	636-285-6057
Phillips, Kelley	220-9522	618-792-8423	618-792-8423
Smith, Megan	769-5321	618-567-4545	618-452-0192
Shelley, Lydia	280-3128	481-7523	N/A
Voelkel, Kelly	574-5480	618-401-2668	618-633-2165

BJH Blood Bank

Manager	Office	Work Cell
Cindy Ingold	362-1447	540-9471

Supervisors

Fairfax Altheimer	362-3891	801-3145
Linda Huckelberry	747-1819	801-3144
Ron Rojas	362-5379	912-8767
Uvancha Colebrook	362-1492	801-3142

Quality Coordinators

Karlyn Rensing (CTL, Aph)	454-8414	801-3141
Marcella Hermann (BB)	273-7775	540-9264

BJH Cell Therapy Lab

	Office	Work Cell
CTL front	454-7673	N/A
CTL back	454-7808	N/A
Diane Sempek, Technical Supervisor	362-3890	801-3147

SLCH Blood Bank

	Phone
SLCH Blood Bank Main	454-6204
David Baker, SLCH BB Supervisor	454-6083

BJH Laboratory

Laboratory	Phone	Fax	Location
Administration	362-1782	362-2097	4 IOH
Blood Bank / Transfusion	362-3384	362-1261	4IOH
Core Lab - Chemistry	362-5257	362-3061	4 IOH
Cryopreservation	454-7673	454-7806	4 IOH
Customer Service	362-1470	362-5735	4 IOH - Rm 4501
Cytology	362-0123	362-6036	3 IOH
Express Testing	-----	747-9528	3 CAM
Core Lab - Hematology	362-5203	362-5850	4 IOH
Flow Cytometry Lab	362-4628		4 IOH
Highlands – Lab	747-2411	647-0663	1110 Highlands Plaza - Suite 325
Histology	362-0138	-----	3 IOH
HLA	362-5322	362-4647	5 IOH
Immunology/Serology	362-3215	362-5850	5 IOH
LIS	-----	286-0198	Meridian Building
Microbiology	362-3898	362-4710	5 IOH
MDL	454-8685	454-7616	5 IOH
Pheresis	362-1254	362-1466	CAM - 4E
Point of Care	454-7180	747-2119	4 IOH
South County Lab - CAM	286-1200	286-1201	5201 MidAmerica Plaza, Suite 1200
South County Lab - Siteman Bldg	286-2652	286-1997	5225 MidAmerica Plaza, Suite A100
Supervisor (On Call)	801-3122 (cell)		
Surgical Pathology	362-0101	362-8950	3 IOH

Blood Centers

Versiti Wisconsin (formerly Blood Centers of WI)	800-245-3117
Versiti Immunology lab extension	X 6250
American Red Cross STL (Distribution)	658-2136
American Red Cross STL (Reference Lab)	658-2084
American Red Cross STL (donor)	658-5847
American Red Cross - Philadelphia Lab	215-451-4901
Versiti Wisconsin (formerly Blood Centers of WI)	800-245-3117

BMT Contacts (updated as of 4/1/22)

To contact BMT: Inpatient – contact floor, and ask for fellow

Outpatient – call/page nurse coordinator

Cancer Care Clinic (aka 24/7 clinic): 747-7796

DR. CAMILLE ABOUD	314-747-7951	Mon-CAM/Wed-SNC/Fri-SIL	PAGER 585-943-6977	DIRECT #	iPhone DEVICE
Stephanie Vollmer - Nurse Practitioner				314-454-8407	314-536-7723
Paul Freeman - Transplant Coordinator	(Clinic: Mon CAM & Wed SNC)			314-454-8604	314-536-7729
Jessica Litteken - Nurse Coordinator (IL)	(Clinic: Fri SIL)			618-607-1429	618-291-0528
DR. RAMZI ABOUD	314-747-8173	Fri-CAM	PAGER 314-508-8964	DIRECT #	iPhone DEVICE
Melissa Edwards - Nurse Practitioner				314-747-7979	314-536-7728
Marnie Agne - Transplant Coordinator				314-747-1835	314-368-8781
DR. NANCY BARTLETT	314-362-9505	Mon AM-SWC/Wed-Thur-CAM	PAGER 314-836-8618	DIRECT #	iPhone DEVICE
Mandy Piela - Nurse Practitioner				314-747-7556	314-827-2556
Katrina (Rakers) Sopiars - Nurse Coordinator (Wednesday Bartlett/Fellow 1, Bartlett Thursday)				314-747-8392	314-536-7744
Lisa Millay - Nurse Coordinator (CAM Wednesday/Monday Bartlett/Fellow 2)				314-747-8462	314-280-8970
Susanna O'Rando - Nurse Coordinator (Bartlett only, Wednesday & Thursday)				314-747-2043	314-536-7771
DR. AMANDA CASHEN	314-362-3515	Wed-CAM	PAGER 314-508-0623	DIRECT #	iPhone DEVICE
Holly Comer - Nurse Practitioner				314-454-2718	314-536-7730
Becky Eisele - Transplant Coordinator			M-Z	314-454-7924	314-536-7699
Robin Schultz - Transplant Coordinator			A - L	314-362-0765	314-261-6406
DR. MATTHEW CHRISTOPHER	314-273-0286	Tue-SSP	PAGER 314-508-5887	DIRECT #	iPhone DEVICE
Carmen (Kari) Wilson - Physician Assistant				636-916-9975	314-297-6422
Sarah Geear - Transplant Coordinator			A - L	314-273-3074	314-324-4791
Colleen Brady - Transplant Coordinator			M-Z	314-273-2415	314-495-4317
DR. JOHN DIPERSON	314-454-8310	Mon/Thur-AM CAM	PAGER 314-836-8617	DIRECT #	iPhone DEVICE
Stephanie Bauer - Nurse Practitioner, APP Supervisor				314-454-7127	314-827-2555
Jordan Shockley -Transplant Coordinator			A - K	314-454-8507	314-283-8224
Elizabeth Salanik - Transplant Coordinator			L - Z		314-536-7601
DR. TODD FEHNIGER	314-747-1385	Thur AM-CAM	PAGER 314-510-2397	DIRECT #	iPhone DEVICE
Sarah Geear - Transplant Coordinator			A-K	314-273-3074	314-324-4791
Colleen Brady - Transplant Coordinator			L-Z	314-362-0765	314-261-6406
DR. ARMIN GHOBADI	314-747-2743	Mon-SSC/Wed-CAM	PAGER 314-508-9792	DIRECT #	iPhone DEVICE
Melissa Edwards - Nurse Practitioner				314-747-7979	314-536-7728
Allison Eshelman - Transplant Coordinator			A-K	314-273-4710	314-518-0347
Andrea Smith - Transplant Coordinator			L-Z	314-454-8458	314-536-7714
DR. MEAGAN JACOBY	314-747-7949	Tue-CAM	PAGER 314-509-3406	DIRECT #	iPhone DEVICE
Stephanie Vollmer - Nurse Practitioner				314-454-8407	314-536-7723
Megan Ottermann - Transplant Coordinator				314-273-2414	314-536-7718
DR. BRAD KAHL	314-747-6250	Mon-SSC/Wed-CAM	PAGER 314-508-6819	DIRECT #	iPhone DEVICE
Ashleigh Wesselschmidt - Nurse Practitioner				314-286-2154	314-536-7716
Laura Verstreeter - Nurse Coordinator			J - Z	314-273-6077	314-536-7751
Nicki McFerren-Wells - Nurse Coordinator			A - I	314-747-8469	314-536-7739
DR. NEHA MEHTA-SHAH	314-273-1070	Wed AM-SWC/Thur-CAM	PAGER 314-508-8270	DIRECT #	iPhone DEVICE
Nina Fragale - Nurse Practitioner				314-273-0238	314-305-0410
Colleen Wagner - Nurse Coordinator			M-Z	314-747-1366	314-536-7702
Jason Clark - Nurse Coordinator			A-L	314-747-8135	314-536-7687
DR. ISKRA PUSIC	314-286-2508	Fri-CAM	PAGER 314-508-4220	DIRECT #	iPhone DEVICE
Brooke Ramsey - Nurse Practitioner				314-454-8194	314-536-7740
Kathryn O'Brien - Transplant Coordinator			(Wed-Fri)	314-747-0830	314-536-7733
DR. MARK SCHROEDER	314-286-2726	Thur/Fri-CAM	PAGER 314-510-8472	DIRECT #	iPhone DEVICE
Carmen (Kari) Wilson - Physician Assistant				636-916-9975	314-297-6422
Rebecca Thompson - Transplant Coordinator				314-286-2542	314-536-7701
DR. KEITH STOCKERL-GOLDSTEIN	314-747-7859	Tue-CAM/Fri-SSC	PAGER 314-508-9744	DIRECT #	iPhone DEVICE
Maggie Kavanaugh - Nurse Practitioner				314-454-8644	314-218-5345
Beth Duisen - Transplant Coordinator			M - Z	314-747-2733	314-536-7600
Jarrod Williams - Transplant Coordinator			A - L	314-747-8374	314-536-7766
DR. GEOFFREY UY	314-747-7867	Mon-CAM	PAGER 314-508-0642	DIRECT #	iPhone DEVICE
Brooke Ramsey - Nurse Practitioner				314-454-8194	314-536-7740
Nicole Knebel - Transplant Coordinator				314-747-1832	314-536-7601
DR. RAVI VUJ	314-454-8346	Mon/Tue/Fri-CAM	PAGER 314-508-0235	DIRECT #	iPhone DEVICE
Angela Vickroy - Nurse Practitioner				314-454-7923	314-536-7606
Abbie Johnessee - Transplant Coordinator			A - L		314-901-3687
Lindsay Hobbs - Transplant Coordinator			M - Z	314-454-8385	314-504-1964
DR. MATTHEW WALTER	314-362-9409	Fri-CAM	PAGER 314-841-0466	DIRECT #	iPhone DEVICE
Megan Ottermann - Transplant Coordinator				314-273-2414	314-536-7718
DR. PETER WESTERVELT	314-454-8365	Tues-CAM/Fri-SWC	PAGER 314-663-8709	DIRECT #	iPhone DEVICE
Katy Thomas - Nurse Practitioner				314-454-7948	314-536-7695
Michele Hill - Transplant Coordinator			A - K	314-747-8890	314-536-7604
Rachel Wagoner - Transplant Coordinator			L - Z	314-273-2512	314-280-5375

BMT inpatient team

INPATIENT TEAM	FAX 314-747-0232	DIRECT #	iPhone DEVICE
Meaghan Ryan - Lead Inpatient Nurse Practitioner		314-747-1145	314-536-7743
Daniel Swinger - Nurse Practitioner		314-747-5315	314-218-5428
Emily Kemp - Nurse Practitioner		314-747-4475	314-218-5415
Lanita Hawkins-Fisher - Nurse Practitioner		314-747-1260	314-536-7708
Rebecca Petersen - Nurse Practitioner		314-859-0964	314-657-8185
Savannah Cincoski - Nurse Practitioner		314-454-7917	314-495-2985
Taryn LeGette - Nurse Practitioner		314-859-1057	314-536-7724
Jamie Bugg - Nurse Coordinator (Team C/10800)		314-747-0903	314-297-9319
Kimberly Carter - Nurse Coordinator (Team A/8800)		314-454-7925	314-536-7685
Nicole Rudiger - Nurse Coordinator (Team B/9800)		314-859-1296	314-267-9746
Leanne Scott - Nurse Coordinator (Auto/CAR-T Cell Patients & Telephone Triage)		314-454-8654	314-536-7713
Susan Young - Nurse Coordinator		314-454-7030	314-891-5641

Hematology Contacts (updated as of 1/6/2022)

To contact Hematology/Oncology/BMT: Fellow On-call: 747-3536 (follow prompts)
 Attending Physician On-call cell phone: 584-0378

Hematology Clinical Practice Contact List

Team		Role	Phone	Pager/Cell
Inpatient NPs				
	Kim French	Nurse Practitioner	454-8532	584-0374 (cell) / pgr 419-6613
	Adella Mujkanovic	Nurse Practitioner	273-1364	574-0838 (cell)
Morey BLINDER		Attending physician	362-8857	960-4254 (cell)
Team	Catherine (Kate) Rogers	Nurse Practitioner	362-8900	419-3499
	Lauren Brewer	Nurse Practitioner	273-1366	419-2857
Elaine MAJERUS		Attending physician	362-8866	419-8588
	Lynn Golec	Nurse Practitioner	747-7470	419-6438
Stephen OH		Attending physician	362-8846	
	Catherine (Kate) Rogers	Nurse Practitioner	362-8900	419-3499
Kristen SANFILIPPO		Attending physician	362-0233	419-7384
	Lynn Golec	Nurse Practitioner	747-7470	419-6438
Amy ZHOU		Attending physician	747-7735	419-3491
	Holly Wiesehan	Nurse Practitioner	273-0565	419-8708
Sana SAIF Ur Rehman		Attending physician	273-1290	419-6614
Amber AFZAL		Attending physician	273-0564	216-856-1722
Allison KING		Attending physician		360-4823
DIVISION OF HEMATOLOGY FAX 314-696-1391				

Lung Transplant

To contact lung transplant: Lung Transplantation Office: 362-5378, option 2
Inpatient: call floor, ask for fellow
Outpatient: call/page nurse-coordinator

Name	Role	Phone
Beth Albertin	Pre Lung Coordinator	747-5618
Laura Ebel	Post Lung Coordinator	362-5327
Jan Fassler	Post Lung Coordinator	362-5409
Tracey Francescon	Post Lung Coordinator	362-4747
Emily DeTienne	Pre Lung Coordinator	273-6189
Erin Laney	Post Lung Coordinator	747-1841
Carol Miller	Post Lung Coordinator	362-4572
Wanda Panus	Pre Lung Coordinator	362-7333
Amanda Heinzmann	Post Lung Coordinator	273-2647
Stacie Rupp	Post Lung Coordinator	362-5328
Masina Scavuzzo	Pre Lung Coordinator	362-5062
Rebecca Mathews	Post Lung Coordinator	273-8603

Name	Role	Phone
Madeleine Roberts	Pre Lung Program Assistant	454-7701
Sacha Jackson	Post Lung Program Assistant	273-4394
Esther Perez	Post Lung Program Assistant	362-4031
Lori Rogers	Pre Lung Program Assistant	362-5406
Tanaya Amerson	Post Lung Program Assistant	362-5416

Neurology

General Neurology on call phone 574-0722
Stroke on call 393-8952
Stroke fellow 419-1552

Operative Services (quick reference for blood product triage)

On-call Anesthesiology attending phone: 749-6200
OR coordinator: 362-4000

Miscellaneous

BJH Occupational Health: Daytime: 454-7002
After hours: 503-2695

BJH IT iPhone repairs, issues, or lost/stolen: 362-4700, option #5; report problem to TFC

Cerner Bridge Access for card swipe on inpatient computers: 362-4700

General hospital numbers (updated June 2022)

Location	Phone	Location	Phone
Cardiovascular		Operative services	
56ICU (CT ICU)	362-4026	OR24/7 Phone Number	362-4000
6300 Adv. Hrt Failure Unit	273-5026	Recovery Room CNM South PACU	362-4020
7200 (cardiac surgery)	362-4032	Trauma Service	362-9175
7300 (cardiothoracic)	362-5286	Ambulatory Recovery (North)	454-7855
7400 (thoracic surgery)	362-4054	Pod 1: Pelvic Pod (2 EPOR)	362-5447
7500 (cardiovascular)	362-5394	Pod 2:ACCS/Ortho/Plastics/Trauma (2 SWT)	362-4000
8200 ICU - COVID	273-6785	Pod 3:CTOR / HPB / Vas/Transp (3SWT)	362-1831
83CTICU	362-5171	POD 4 CAM OR (4CAM)	454-7965
9200 (cardiology)	362-5274	Pod 4: CAM Pre/Post PVT PACU	747-4965
10200	362-5279	Pod 5:Neuro/ENT	362-3382
104I (CICU)	362-5096	Pod 6: Orthopedic Center (OC)	514-3509
11200	362-5280	OC PrePost	514-3614
12200	362-6620	CPAP (1 Shoenberg)	454-8134
Cardiac Diagnostic Lab	362-5441	Module E (Phase 1 Recvry/PCCA, 3rd fl RJ)	362-4011
Medicine		Module B (Phase 1 Recvry, 2nd fl RJ)	362-4020
5200 COVID	273-1798	Module C (Holding 2EP)	362-4050
5300	362-5141	Module D (Holding 3 RJ)	362-1188
5400	362-5090	Module A (Holding; 2nd floor RJ)	362-4560
5500	362-5272	Module F (Outpatient Recovery 3 FL RJ)	362-3393
6200	362-4250	Anesthesia Support (CAM/S. OR)	362-2089
6300 PPCU	362-5134	OR Off Shift Mgr	362-4000
79100 (med 1)	362-5276	CSPD-Lead Phone 24/7	362-1059
79200 (med 2)	362-5088	Electrophysiology	747-2583
8300 ICU	362-5360	Periop Scheduling	747-7444
8400 ICU	747-8850	Surgical Reception	362-1164
8900 (pulmonary)	362-1380	Surgery	
Neurology/Medicine		2800 Dialysis PVT	859-0210
3500 Observation Unit	273-4336	4900 Short stay surgery	454-8680
9400 Neuro ICU	273-3194	6900 (colorectal)	454-8690
10400 Neuro ICU	362-5138	16300PCU	747-1161/747-5588
10500	362-5136	16400 Transplant	362-4048
11300	747-3005	17300	362-4075
11400	362-5130	17400 Spine	747-7240
11500	362-3828	17500 Ortho	362-4059
14300 Acute Dialysis	362-5350	Trauma	
14300/Schukar(S)	747-6700	44ICU (SICU)	362-4060
14400	747-9120	6400	362-5161
14500	362-0499	6500	362-4052
Oncology		Women and Infants	
5900 (Gyn Onc)	362-4040	5800 L&D	362-5178
7800 Oncology ICU	454-7300	5800 Antepartum	362-2475
8800 Oncology	454-8637	5800 Women's Assess Cntr (WAC)	362-5157
9800 Oncology	454-8590	6800 Newborn Asses Cntr	362-5170
10800 Oncology	454-8580	6800 Mother/Baby (Post Partum)	362-5164
11800 Oncology	454-8282	OB / GYN In Vitro	286-2400
12800 Oncology	747-4901	OB / GYN Ultrasound	454-8181
Barnard Cancer Information Center	362-7844	Ambulatory Services	
Breast Health Center	454-7635	Billiary/GI/Endo (10 CAM)	454-7921
Mammography Van	454-7812	DDCC	362-5676
Cancer Care Clinic	747-7796	Interventional Pulmonology	362-9366
Chemo Ctr Cam 13th fl Suite	747-5218	Med /Foot Clinic	362-7741
Patient Care Coordination Center	747-3046	OB-GYN Clinic	454-7882
Siteman Clinic	362-7179	Outpatient Infusion Center	362-0814
Specialty mAb Therapy Clinic	859-0176	Pain Management Ctr:	362-8840
Anesthesia		Psychiatry Clinic	362-5065
Anesthesia trauma resident pager	490-1541	Specialty Care Clinic (COH Suite 420)	362-9100
Anesthesia trauma attending	749-6200	Surgical and Wound Care Clinic	362-1300
Anesthesia CRNA BJH (L&D)	280-2558	SLCH	
Anesthesia resident (L&D)	267-8738	SLCH operator	454-6000
Anesthesia attending inhouse BJH L&D	659-0112	SLCH PICU	454-4466
Anesthesia NP1 (BJH)	280-0716	SLCH hematology clinic	454-6018
Anesthesia NP2 (BJH)	280-0717	SLCH admit	454-6021
Anesthesia on call (BJH)	305-4049	Miscellaneous	
Anesthesiology pager (BJH)	424-8433	Emergency Department	362-9123
Anesthesia in-house call (SLCH)	305-4049	Emergency department doctor's line	362-9104
Psychiatry		Int rad (north)	454-8964
15300 Adult Psych	362-5125	Int rads after hours	362-8085
15400 Geriatric	362-4074	Int rad (main)	362-6681
15500 Psych ICU	362-4070	Pharmacy inpatient	362-5339

Learning Objectives on Transfusion Medicine and Hematology Services

Transfusion Medicine/Apheresis

- Discuss the causes and lengths of deferrals for prospective blood donors
- List and interpret required testing for blood donors
- Describe the manufacturing and shelf lives of blood components and coagulation factors
- Discuss the evidence-based uses of blood components and coagulation factors
- Manage blood product shortages in the hospital setting
- Describe the regulatory and quality assurance activities as it relates to transfusion medicine
- Diagnose transfusion reactions and develop appropriate treatment and avoidance recommendations
- Describe and interpret commonly used blood bank tests
- Discuss the major RBC antigen groups and their clinical correlations
- Identify RBC auto-, alloantibodies and interferences from blood bank serologic workups
- Discuss the clinical significance and management of RBC alloantibodies
- Identify autoimmune hemolytic anemias and recommend appropriate management
- Diagnose hemolytic disease of the fetus and newborn and recommend appropriate management
- Diagnose neonatal autoimmune thrombocytopenia and recommend appropriate management
- Discuss differences in transfusion practices and blood bank procedures between adult and pediatric patient populations
- Diagnose platelet refractoriness, list the differential diagnosis, and recommend appropriate workup and management
- Discuss the theoretical and technical aspects of apheresis
- Describe the indications for and clinical risks of therapeutic apheresis
- Perform medical assessment for prospective therapeutic apheresis and cellular therapy
- Develop treatment plans for therapeutic apheresis, including timing of procedures and necessary laboratory monitoring
- Manage the proximal clinical issues of patients before, during, and after apheresis, and modify procedures and testing accordingly
- Recognize common cellular therapy product infusion reactions
- Contribute to the service team (residents, fellows, attendings, nurses, and techs) regarding both clinical management and education

Hematology/Coagulation

- Interpret the tests performed in the hematology/coagulation laboratory
- Diagnose coagulation and platelet disorders and recommend appropriate management
- Discuss hereditary and acquired factors that predispose patients to bleeding and thrombotic risks in the inpatient and perioperative setting
- Diagnose benign and malignant hematologic disorders on peripheral blood smears
- Diagnose hemoglobinopathies/thalassemias from hemoglobin electrophoresis

Duty Hours and Responsibilities

Transfusion Medicine Service Call Schedule

The Transfusion Medicine service is run by the on-call (primary) LMR (trainee - resident or fellow) and supported by a backup (secondary) LMR. The service phone is active 24 hours per day, including weekends and holidays. The primary LMR handles issues concerning inpatients, the outpatient apheresis center, the blood bank, and laboratories. Communication between the LMR and clinical counterparts should start with the clinical resident and evolve with discussion if needed. Both trainees (primary and secondary) must be immediately available during their assigned call.

Primary LMR service schedule: Friday 9:30 am to Friday 9:30 am. The general daily schedule is described below, see On-Call Daily Checklist for more details.

Monday – Friday

- 8:00 AM to 5:00 PM (or until the last procedure of the day is completed, whichever is later): be physically on campus and immediately available to apheresis, blood bank, and cell therapy services
- Before 9:30 AM: pre-round at bedside on all patients undergoing apheresis that day
- 9:30 AM to noon: TM service rounds
- Noon-1pm: transfusion-related and/or LGM conferences
- 24/7 while primary trainee on service - Answer phone calls to the TM service phone

Weekends

- By 7:30 AM: Pre-round on all patients undergoing apheresis that day
- 7:30 AM: Discuss cases with apheresis attending and call on-call apheresis nurse with patient updates
 - The on-call Apheresis nurse will NOT come to campus until the LMR has confirmed that the procedure can proceed
- Be immediately available as procedures occur:
 - Trainee must be on campus for all new consults, procedures on ICU patients, and as individual circumstances necessitate
 - If not on campus, the trainee must be immediately available by phone
 - Update attending on procedure status

Emergent procedures after hours (during weekdays) and during weekends/holidays

- Gather all information as you would for any new consult
- Notify the attending to review/discuss/approve the consult
- Notify the apheresis nurse about the procedure
 - The on-call nurse should only come to campus when vascular access has been and confirmed
- Keep attending informed of the status of the procedure including any unexpected events
- Remain on campus until the procedure is complete

Handoff/signout in the event of after hour procedures (i.e. procedure ends after midnight)

- Primary LMR signs out at 7:00 AM by phone to the secondary LMR
 - Give sufficient information for secondary LMR to take over with no need to contact you for additional information
 - Remain at home to rest and not attend rounds or conferences
- Secondary LMR covers all duties from 7:00 AM to 6:00 PM
 - The secondary LMR must be sufficiently prepared to act as primary LMR on service at any given time
- Secondary LMR signs out to Primary LMR at 6:00 PM by phone

On-Call Duties

- Be immediately available to BJH apheresis, blood bank, and cell therapy services
- Provide oversight for all inpatient apheresis procedures (except GVHD extracorporeal photopheresis in north campus inpatient locations which is staffed by apheresis NPs)
- Provide medical direction of blood bank, including blood product approvals and serving as the interface between the blood bank and clinicians
- Provide interpretation of transfusion reactions and stem cell infusion reactions
- Write up transfusion reaction interpretive reports in EPIC from previous 24 hours
- Assess platelet refractoriness and coordinate HLA-compatible platelets requests
- Assess and coordinate granulocyte requests and ordering
- Field SLCH blood bank calls: these should always be discussed with Ron Jackups (SLCH BB Medical Director) unless directed otherwise
- Manage therapeutic phlebotomy patient evaluations
- Provide coverage to the apheresis NPs as needed
- Approval of send out testing (such as RBC genotyping, platelet antibodies, ADAMTS13, etc.)

Secondary LMR Duties

- Write up blood bank interpretive reports in EPIC for those that result before 3pm

TM Service Rounds

TM Service rounds start promptly at 9:30 AM on weekdays. The trainees, attending, one of the nurse managers, apheresis charge nurse, and any other rotating students or trainees meet in the Apheresis Center to review and discuss all apheresis patients and blood bank calls occurring since the last rounds. The primary LMR presents all current inpatient therapeutic apheresis patients who will be receiving treatment that day and all blood bank issues from overnight. The secondary LMR may also present any blood bank interpretive reports that might be of interest or relevant to patient care inquiries. Attendings will often provide case-based or other planned teaching during this time. All patients receiving apheresis that day are then seen on walking rounds, led by the primary LMR. Finally, the team will visit the BJH blood bank reference bench to see if there are interesting cases or ones requiring LMR follow up. Altogether, rounds may last until noon conference.

Transfusion Medicine Service Conference Schedule

Conferences you are expected to attend:

There are several regularly occurring conferences related to transfusion medicine topics that are of high educational value. As some of these meetings occur quarterly (i.e. this could be the only opportunity to see it during your residency experience in transfusion medicine), you are expected to prioritize those meetings. If there is a potential conflict, please discuss with the rotation director before the meeting occurs for guidance.

- Hematology Case Conference (weekly)
- Transfusion Medicine Journal Club (approximately once per month)
- Transfusion Medicine Attending Meeting (every other month; TM attendings discuss pertinent issues)
- BJH Transfusion Committee Meeting (quarterly; meeting of blood bank and clinical services dealing with hospital transfusion policies and compliance, blood wastage, etc.)
- Coagulation Beeper Report (quarterly)
- LGM-wide weekly conferences (Case Conference, Grand Rounds)
- Pathology department-wide conferences (RFM, Management Series)

Conferences at which you are expected to present

- TM Journal club: once (LMR), once per block (TM fellow) - Trainees will be assigned date
- LGM Case Conference (TM topic): once (LMR), twice (TM fellow) - Trainees must identify faculty mentor
- BJH Transfusion Committee: once, as applicable
 - If a fatality is reported to the FDA as potentially related to transfusion, the trainee is expected to attend the next BJH Transfusion Committee and present the case
 - Hematology case conference – as needed, Hematology may seek TM input on a case to be formally presented

Transfusion Medicine Service Weekly Schedule

	Monday	Tuesday	Wednesday	Thursday	Friday
09:30 AM	Rounds	Rounds	Rounds (HLA plt update)	Rounds	Rounds
12:00 PM	Heme Case Conference	LGM Case Conference	Transfusion Committee, RFM/ Management Series	LGM Grand Rounds	Coag Beeper Report

On-Call Daily Checklist

Primary LMR Daily Checklist

7:30 AM - 9:30 AM: Pre-rounds

- Review clinical data
 - Vital signs, labs, overnight events, clinical team communication, upcoming plans for the patient such as other procedures for which coordination might be needed
- **Visit all inpatients at bedside**
- Develop a plan for the patient's apheresis procedure
 - Discuss any questions or substantial changes to the lab with attending before finalizing

- Call apheresis charge nurse at 7:30 AM with patient and procedure details
- Update all EPIC patient lists
- Update apheresis inpatient log on Pathology Intranet with interval history and plan
- Update granulocyte requests daily
 - Review patient status (alive, ANC, infection) with chart review and with the clinical team and notify Linda Huckelberry about extended/cancelled orders
- Update HLA platelet requests (Wednesdays)
- Pick up transfusion reaction and cell therapy infusion forms from LMR inboxes in BB and CTL

9:30 AM -Noon: Rounds

- Lead table rounds:
 - Assume rounds start promptly at 9:30 am unless informed otherwise
 - Gather all attendees (RN manager, charge RN) to be ready to start at 9:30 am
 - Present:
 - All inpatients undergoing procedures that day
 - All transfusion and stem cell infusion reactions occurring since last rounds
 - Forms should be completed before presentation if possible
 - All blood bank calls occurring since last rounds
- Lead walking rounds:
 - See all inpatients undergoing apheresis that day
 - Visit blood bank reference bench

Noon-1 pm: Lunch/conferences

1 pm-5 pm or when last procedure is finished (whichever is later): follow ups and continued care

- Complete notes in EPIC for all patients undergoing procedures **before** leaving for the day
- Work up transfusion/infusion reactions
 - A differential list/instruction are provided later in this book
 - Present to attending (these should still be discussed at rounds the next day)
 - Call blood bank back and clinical team with recommendations
- Take care of any other pending business (clinical questions, platelet refractory, sendouts, etc.)
- Update apheresis log on the Path Web-portal to include procedures and plan
- Place orders for following day

Handoff at time of scheduled primary LMR change:

- Trainee going off service:
 - Stops handling all new calls at 9:30 am Friday
 - Leads rounds Friday morning (including pre-rounds, table rounds and walking rounds)
 - Follows up on any outstanding issues that arose while being primary trainee on service
- Trainee coming on service:
 - Starts handling all new calls at 9:30 am Friday
 - Writes notes on patients with procedures on Friday

Outpatient Daily Checklist (LMR/Fellow covering for NPs)

7:30am-9:30am: Pre-rounds

- **Be in outpatient center by 7:30 AM**
- Visit each outpatient, review vital signs, and inquire about changes since last visit

9:30am-Noon: Rounds

- Schedule with attending to work around inpatient rounds
- Present outpatients to attending
- Follow attending on walking rounds on outpatients

Noon-1pm: Lunch/conferences

1pm-5pm: Afternoon issues

- May require second rounds with attending for afternoon procedures
- Write procedure notes (start notes before patients are checked out)
- Write orders for the next day
- Complete medical assessments scheduled throughout afternoon
- Take care of any other pending business
- **REMAIN in outpatient center until the last patient leaves**

Additional Responsibilities on the Transfusion Medicine Rotation

- **Transfusion medicine laboratory checklists** (at the back of this book)
 - Checklists include:
 - Blood bank/serology
 - Blood Product Inventory Management
 - Product Preparation and Issue
 - Product Manufacturing
 - Apheresis
 - Laboratory Management
 - Cell therapy lab
 - During weeks not on call, you should schedule time to observe each technique/procedure listed in the back
 - Contact Linda Huckleberry in the blood bank to schedule
- **Transfusion audits – twice during rotation**
 - Follow a unit of blood from the blood bank through the first 15 minutes of transfusion
 - Arrange during an off-call week with Marcie Hermann, the Blood bank Quality Coordinator

APHERESIS

Handling Apheresis Requests: Overview

Apheresis is requested by clinicians by contacting the LMR for inpatients or nurse practitioner (NP) for outpatients. Gather pertinent clinical information, evaluate the case under attending supervision, and complete and coordinate the following events:

1. Evaluate the consult.

Review the patient's chart, including history, vital signs, labs, imaging, medications, if the patient has or will need venous access, pending clinical care that might affect procedure timing, and reason for consult. Determine if there is a previous history of therapeutic apheresis (by reviewing chart, procedure records in apheresis center and/or the Pathology log archive); if so, review previous procedure notes for response to therapy and any adverse events. Evaluate the urgency/acute of the clinical situation and clinical status of the patient to determine if the request is considered emergent (i.e. must happen as soon as possible versus starting the next day). Review medications to evaluate for potential considerations such as: ACE inhibitors (may lower BP in certain circumstances), therapeutic anticoagulation (including patients on ECMO), immunoglobulins (e.g. IVIG, rituximab, etc.), medications that are highly protein bound (removed by during procedure), and continuous medication drips that might require adjustment. Review pertinent patient labs to determine if parameters are met to safely proceed with procedure. Determine any potential clinical care that might affect the timing of performing apheresis (such as dialysis, blood product transfusion, imaging studies, etc.). Develop a plan to include procedure type, duration and frequency of requested procedure, goal of procedure (i.e. when to stop and/or reassess), amount of patient's volume to be exchanged/processed and replacement fluids. To estimate replacement fluid volume, calculate plasma volume (PV), with adjusted weight if BMI ≥ 30 : **PV = weight (kg) x 70mL/kg x (1-Hct)**.

2. Discuss the case with your attending.

All procedures **must** be discussed with and approved by the attending. Present the case to the attending with the information that you have gathered, discuss and collect any additional data.

3. IV Access.

Adequate intravenous access, which can be peripheral or central, is critical to a successful apheresis procedure. Peripheral venous access may be appropriate for procedures occurring once in stable patients who can participate in the procedure (e.g. regular hand squeezing). During daytime hours, the apheresis nurses can perform a vein assessment to determine if peripheral access is possible. Most emergent procedures require placement of an apheresis-compatible central venous catheter (CVC). The primary team requesting apheresis should arrange for placement of an apheresis/dialysis compatible CVC (see chart). Vascular interventional radiology (VIR) is the primary service that places CVCs. If the procedure is emergent and the patient is in an amenable location (such as the ICU or ED), venous access can be established at bedside by the primary team. CVCs may be placed either in the neck (IJ or SC) or the groin (femoral). **CVC placement in the neck requires documentation that the line is correctly placed and ready for use (required by BJH nursing policy before the procedure can begin).** Sufficient documentation includes the VIR procedure note (if placed by VIR), a chest x-ray and radiology report documenting correct placement (if placed at the patient's bedside), or a nursing communication that the line is ready to use (if X ray

interpreted by a floor doctor). Femoral lines require patients to have restricted mobility and are an infection risk, so judicious use and timely removal is important. Some patients undergoing chronic red blood cell exchange or extracorporeal photopheresis may have an apheresis-compatible port (see chart below). **Ports should be implanted 2 weeks before use to allow for sufficient healing unless there are extenuating circumstances. In that case, its use must be approved by a TM attending .**

Types of access for apheresis

Peripheral	
Requirements	Adequate peripheral veins as determined by an apheresis nurse Patient must have free mobility and ability to squeeze hand grips
Central Venous Catheters – can be double or triple lumen, can be tunneled or non-tunneled	
Type	Trifusion, Duraflow, Trialysis, Hemocath, Neostar
Anatomic Location	Neck (IJ or SC vein) – documentation of ready for use required Groin (femoral vein) – requires patient mobility restrictions, risk for infection
Ports – for long term use, Access can be single, single with peripheral, or dual	
Types, indications and access	Vortex - Red cell exchange: dual, single with peripheral ECP: dual (preferred) or single
	Powerflow - Red cell exchange: single with peripheral, two singles (dual powerflow does not exist yet) ECP: single

4. Discuss the case with apheresis nurse.

Contact the charge nurse during regular business hours; contact the nurse on call after hours and on weekends. Inform the nurse of patient's name, medical record number, date of birth, procedure (indication and type), and replacement fluid (volume and type). Discuss timing of the procedure and clarify any questions that arise.

5. Obtain informed consent for the procedure.

Informed consent **must** be obtained prior to starting the procedure. If informed consent cannot be obtained from the patient (sedated, altered mental status, etc.), informed consent must be obtained by the legal guardian, power of attorney, or patient's next of kin (in the following order: spouse, adult child, parent, sibling). Informed consent may be obtained from the appropriate surrogate by phone, but a witness to the conversation is required (such as apheresis nurse, floor nurse or co-resident). All documentation must be done on the appropriate pre-printed form, affixed with the patient's printed label (hand-written identifiers in the chart are not allowed) on both sides of the form. Apheresis consent forms are accessible via the "Forms on Demand" link found under "Clinical Web Portals" in EPIC. To ensure you have the most current consent form and for document control, do not print more than needed ahead of time.

Informed consent includes review of the procedure, discussion of risks and benefits, and opportunity for questions to be answered. The informed consent provides guidance as to the apheresis risks; common risks to discuss include infection, symptoms of hypocalcemia (paresthesias, nausea/vomiting) and treatment (oral, IV calcium), and the potential for platelet and/or blood loss.

Informed consent is valid during a single hospital admission for the duration of the procedure series determined at initiation of apheresis. After reaching the agreed upon endpoint for apheresis, any

subsequent procedures will require new informed consent, even if it is the same hospital admission. A new informed consent form is required if a regular outpatient receives procedures as an inpatient.

6. Obtain blood product transfusion consent if applicable.

A separate informed consent for blood product transfusion is required for procedures if plasma or red blood cells (RBCs) are used as the replacement fluid (in Forms on Demand). If consent has already been obtained, additional consent is not needed (“Chart Review”, “Media” tab in EPIC), but discussion in the context of the procedure is still warranted. Blood product consent is not required if albumin is the only replacement fluid.

Note: If blood products will be used as replacement fluid, there must be an ABO/Rh type on file for the patient. A current (\leq 3 days old) type and screen from the current admission is required to transfuse RBCs. If a patient has known RBC alloantibodies, inform the blood bank as soon as possible and provide an estimate of the amount of blood needed. The blood bank cannot begin crossmatching RBC units until a prepare order is received (important for planning overnight and weekend procedures), but calling the blood bank to let them know may still be useful in order to supplement inventory as needed.

7. Make sure the primary team requesting the procedure orders a “Request for Apheresis” in EPIC.

“Request for apheresis” documents the consult in EPIC and **must** be done by the primary requesting team. Confirm this has been placed before the apheresis procedure has begun (use the “Search” function or look under the “Consults & Referrals” section of “Active Orders”).

If the physician needs guidance putting the request provide instructions on how to do it:

1. In the “Orders” search window type “Apheresis”; a new window will appear.
2. Under the “Procedure” section double click on “Request for apheresis”
3. Type in the indication for apheresis (diagnosis)
4. Choose the type of procedure
5. Leave call back number
6. Click “Accept”

8. Place apheresis orders and labs in EPIC.

We utilize order sets for apheresis procedures. It may be necessary to order specific tests outside of the order set to be drawn by the floor nurse prior to starting the procedure (e.g. CBC, PT/INR, fibrinogen, type and screen). Occasionally, you may need to call the floor nurse or add comments to the order to ensure the necessary labs are drawn. When placing orders, do not change anything in the phase of care section.

9. Attend/oversee the procedure.

For a new patient’s first therapeutic procedure, you are **required** to be at the bedside for the first 15 minutes and in-house for the remainder of the procedure. For ICU or unstable patients requiring subsequent procedures, you are required to be in-house for the procedure. You must be immediately accessible by phone at all times. For patients undergoing chronic scheduled procedures (such as routine inpatient RBC exchange and extracorporeal photopheresis) the LMR is not required to be at the bedside for the first 15 minutes, unless circumstances necessitate (such as patient’s clinical condition).

10. Document the procedure.

A procedure note in the patient's chart written by the trainee and cosigned or attested by the attending serves as physician documentation. Document the service/attending requesting the procedure and construct a brief clinical note, including the indication for the procedure (provide the ICD10 codes specific for the diagnostic indication and procedure), the procedure parameters, complications, and plan going forward. When finished, sign the note to send it to the attending for cosignature/attestation. This must be done prior to leaving the hospital for the day, unless note completion will cause you to stay past midnight (ONLY in that event can the note be written the following morning). Update the Apheresis Inpatient log on the Pathology Intranet with the patient information, procedure parameters, complications, and plan.

Summary Checklist—Before Starting Apheresis Procedure:

- Obtain relevant medical history
- Attending approval
- The primary physician's request for apheresis (EPIC order)
- Notify charge/on-call nurse
- Documentation of correct line placement
- Informed consent for therapeutic apheresis
- Informed consent for blood products (if applicable)
- EPIC procedure orders

Common Apheresis Procedures

Therapeutic apheresis

Therapeutic apheresis is a general term for a procedure in which a patient's blood is passed through an extracorporeal medical device which separates components of blood to treat a disease.

Therapeutic plasma exchange (TPE): Blood is passed through an apheresis device that separates out plasma from the other blood components. The plasma is then replaced with plasma or albumin. Many indications for TPE involve removal of antibodies in the patient's blood.

Red blood cell exchange: Red blood cells are separated from the other blood components and replaced with donor red blood cells. Red cell exchange is most commonly performed for acute and chronic complications of sickle cell disease.

Erythrocytapheresis (red blood cell depletion): Red blood cells are separated and removed; the other blood components are returned to the patients. Red cell depletion is typically requested for patients with polycythemia and inability to tolerate therapeutic phlebotomy.

Leukocytapheresis (leukapheresis, leukoreduction): White blood cells are separated and removed, and the other blood components are returned. Leukocytapheresis may be requested when a patient has acute leukemia with hyperleukocytosis and is exhibiting symptoms or signs of leukostasis.

Extracorporeal Photopheresis (ECP): White blood cells (buffy coat) are separated, treated with a psoralen compound with subsequent activation by UV light exposure to induce DNA damage in lymphocytes (specifically targeting T cells), and then returned back to the patient. ECP is typically a long-term treatment and is performed for cutaneous T cell lymphoma, graft-versus-host disease and cellular mediated solid organ transplant rejection.

Thrombocytapheresis (plateletpheresis): Platelets are separated and removed; the other blood components are returned to the patient. Thrombocytapheresis is typically requested for patients with essential thrombocythemia (ET) and thrombotic complications.

Therapeutic Phlebotomy: Collection of whole blood from a peripheral vein (resembling whole blood donation) for therapeutic purposes, typically for patients with polycythemia vera (PV), porphyria cutanea tarda, and iron overload due to hemochromatosis.

Donor apheresis

Peripheral Blood Mononuclear Cell collections: White blood cells are collected from the peripheral blood by apheresis for a variety of therapeutic purposes, including for hematopoietic stem cell transplantation (autologous and allogeneic), donor lymphocyte infusions, and collection for manufacturing (for example, chimeric antigen receptor, or CAR, T cells).

Common Adverse Reactions

Although generally considered safe, apheresis procedures are not without risk. Below highlight some commonly encountered adverse events and strategies to mitigate them.

Hypocalcemia: Hypocalcemia can occur during apheresis due to use of anticoagulant citrate dextrose (ACD)-A. Symptoms initially include parasthesias (peripheral, perioral), followed by muscle spasm, nausea/vomiting, and/or hypotension; if untreated, cardiac arrhythmias or seizures can develop. Severe hypocalcemia can develop with large processing volumes or blood product replacement (also contain ACD-A). Calcium replacement can be oral (calcium carbonate) or IV (calcium gluconate).

If symptoms of hypocalcemia develop, pause the procedure (to temporarily stop ACD-A flow into patient), order a STAT ionized calcium level (iCa), and administer IV calcium gluconate following general guidelines outlined below:

- Administer Calcium gluconate IV based on iCa level:
 - iCa <4.5 mg/dL: 1 gram calcium gluconate IV, rate: 1 gram over 15 minutes
 - iCa level <3.5 mg/dL: 2 grams calcium gluconate IV, rate: 1 gram over 15 minutes
- Re-check the ionized calcium
 - If iCa >4 mg/dL, increase calcium gluconate infusion rate of 1 or 2 grams over the remainder of the procedure
- If symptoms persist, further adjustments may be necessary
- If >10 grams are administered, evaluation of hypomagnesemia might be warranted

Hypotension: Some patients (e.g. those with autonomic instability or negative fluid balance) may become hypotensive during the procedure. Prebolus for prevention or bolus for treatment, of 250mL 5% albumin helps manage hypotension. Prebolus or priming the machine with albumin is needed if the extracorporeal volume is ≥15% of the patient's total blood volume.

ACE inhibitors: Patients generally should not receive ACE inhibitors while undergoing therapeutic apheresis, particularly TPE with albumin replacement, due to risk for adverse reactions from increased bradykinin levels. Symptoms can include hypotension, flushing and GI upset. Waiting 24 hours after the last ACE inhibitor dose prior to initiation of apheresis is preferred, unless emergent. This effect does not apply to angiotensin receptor blockers (ARBs).

Transfusion reactions: In some TPEs and all RBC exchanges, patients receive several blood products in rapid succession, all of which pose a risk for transfusion reaction. Patients may receive premedication with acetaminophen and/or diphenhydramine. If a transfusion reaction occurs, the procedure must be stopped, the patient evaluated and given supportive therapy (IV fluids, acetaminophen, diphenhydramine, call rapid response team if acute hemodynamic instability), and machine lines flushed. Unless a mild allergic reaction, a transfusion reaction investigation should be sent to the blood bank. Regardless of the nature of the reaction, the implicated unit must not be used. If the procedure is restarted, a new unit must be used.

Transient coagulopathy: Coagulation factor levels are transiently lowered during TPE when albumin is the sole replacement fluid (see table). Generally, most patients with adequate liver function maintain sufficient levels, but PT/INR and/or fibrinogen may be monitored on the day of procedures prior to starting. If coagulopathy is suspected, bleeding risk factors are present, TPE is performed perioperatively, the patient has undergone recent operative procedures and/or ECMO (which uses heparin) or ventricular assist devices (VADs - can lower anti-thrombin levels which may precipitate thrombotic complications), use of plasma to varying degrees as replacement fluid is warranted. For partial plasma replacement, the procedure is started with albumin replacement with transition to a defined amount of plasma (by volume, percentage or number of units) replacement. Another mitigation strategy to consider in patients with isolated labs suggestive of transient coagulopathy is delaying the procedure by an additional day if warranted and clinically appropriate.

Estimated alterations in blood constituents after 1 plasma volume TPE with albumin*

Constituent	Percent decrease from baseline	Percent recovery in 48 hours
Clotting Factors	25-50	80-100
Fibrinogen**	25-50	65
Immunoglobulins	63	45
Paraproteins	30-60	Variable
Liver Enzymes	55-60	100
Bilirubin	45	100
C3	63	60-100
Platelets	25-30	75-100

* Replacement fluid consists of 4-5% albumin in 0.9% sodium chloride

**Recovery rate for fibrinogen is quite variable between patients varying from 0.5 -10 mg/hour

At the end of a 1.5 PV TPE:

- All FFP: no anticipated major changes in amount of coagulation factors
- All Albumin: residual patient plasma ~22%, plasma removed ~78%
- Half and half (first half albumin and last half plasma): factor activity about ~75% of pre-TPE
- Last liter plasma: factor activity is about ~50% of pre-exchange

Volume Overload: Patients receiving apheresis can be susceptible to volume overload due to fluids given (albumin prebolus, ACD-A); patients with heart failure or significant renal dysfunction may be particularly susceptible. Knowledge of patient history and fluid status and communication with the clinical team are important considerations. It is our responsibility to manage patients with fluid overload during collections. Strategies may include use of diuretics with or without potassium and/or magnesium supplementation, if necessary, or heparin for anticoagulation to decrease amount of fluid used. Patients undergoing cellular therapy collections may be referred to the BMT clinic for IV magnesium infusion following apheresis. Contact the transplant coordinator and BMT fellow/attending when considering interventions.

Indications for Apheresis

Common Indications for apheresis encountered at BJH (by procedure type) are described below.

Therapeutic Plasma Exchange (TPE)

Thrombotic Thrombocytopenic Purpura (TTP):

TTP is a potentially fatal disease with a rapidly progressive course. TPE is initiated as soon as possible, even pending definitive diagnosis. Ensure a sample is collected for testing ADAMTS-13 activity and inhibitor before starting the first procedure. Patients typically undergo TPE daily, with 1.5 plasma volume exchanged with all plasma replacement fluid (to replace deficient ADAMTS13), until the platelet count is $\geq 150K/cumm$ for 2-3 days, after which TPE is either stopped or tapered as agreed upon with the hematology service. Daily labs to monitor include CBC daily (platelets), with LDH, haptoglobin and creatinine if needed. Ensure there is a current type and screen for plasma.

Myasthenia Gravis (MG):

Urgent/emergent indications for TPE in MG include (1) signs or symptoms of respiratory failure and/or (2) dysphagia with risk of aspiration, in which cases TPE is initiated urgently to prevent intubation or hasten ventilator independence. Less urgent indications include (1) dysphagia (without aspiration risk) (2) muscle weakness (3) diplopia (4) pending thymectomy. Patients typically undergo 5 TPE procedures, with the first 2 on successive days, and then the last 3 every other day, with 1 plasma volume exchanged with albumin. Clinical improvement typically occurs relatively quickly over the duration of TPE; respiratory parameters to follow daily are negative inspiratory force (NIF) and forced vital capacity (FVC). Patients with MG can exhibit autonomic instability and hypotension, so 250mL albumin prebolus is typically given unless the patient is hypertensive or has volume overload.

Guillain-Barre Syndrome (GBS):

GBS is an acute autoimmune inflammatory neuropathy. If respiratory failure is imminent, patients are treated emergently. The standard course is 1.0 plasma volume exchanged with 5% albumin for a total of 5 procedures, performed daily or every other day for the first two procedures, then every other day for the remaining three procedures. Patients with GBS may exhibit autonomic instability and hypotension, and may benefit from an albumin prebolus to minimize procedure-related hypotension.

Solid organ antibody-mediated transplant rejection:

Donor-specific HLA antibodies (DSA) in solid organ (specifically heart, lung and kidney) transplant recipients are strongly associated with antibody-mediated rejection. TPE is performed to decrease DSA levels. Pre-transplant TPE may be considered when the transplant occurs across an immunological barrier (pre-existing DSA or positive crossmatch). Patients typically undergo 1 pre-transplant TPE and post-transplant procedures daily or every other day for 5-7 total procedures. Post-transplant TPE may be based on positive HLA crossmatch, continued DSA detection, or HLA antibody titer increase. Presence of DSA together with organ dysfunction is sufficient for diagnosis. Discuss replacement fluid (albumin vs. FFP) with the primary service as some transplants have lower risks of severe bleeding (i.e. kidney transplant), and moderate coagulation defects may be tolerable. Around post-transplant day 3, if coagulation test results are favorable and no post-operative bleeding, transition to partial FFP replacement may be considered, and patients further out can be considered for albumin replacement.

Hematopoietic stem cell transplant (HSCT) with pre-transplant donor specific antibodies (DSAs):

In patients undergoing HSCT across immunologic barriers (known HLA DSAs), TPE to decrease DSA levels (i.e. desensitization) can be considered. DSA testing should be performed on recent serum specimens. Patients typically undergo 5 TPEs pre-HSCT, every other day, with 1 plasma volume exchanged (and IVIG given by primary team between TPEs), usually starting as outpatient and transitioning to inpatient (LMR responsible) the day before transplant. An HLA antibody screen must be ordered on the recipient before initiation of the final procedure to determine need for post-HSCT TPE. If the HLA DSA mean fluorescent intensity (MFI) is >2,000 before TPE #5, 2 more TPEs are performed days 1 and 2 post-HSCT. If the HLA DSA MFI <2,000, no additional post-HSCT procedures are required.

Red Cell Exchange

Acute complications of sickle cell disease:

RBC exchange has been best established for evolving stroke and acute chest syndrome, both of which are considered emergent indications. Target hematocrit and %HbS goals are decided with the Hematology service (see below). Review history of recent transfusions, transfusion reactions, and RBC alloantibodies (could increase search time for blood products). If the patient is unknown to the BJH blood bank but has a known or reported history of transfusion, it is important to attempt to obtain a transfusion history from other blood banks so the most appropriate blood can be ordered. Contact the BJH blood bank before the procedure to determine how best to approach obtaining this history. Sickle-dex negative donor RBCs matched or antigen negative for C, E, and K RBC antigens are used. Ensure a pre- and post-procedure Hb analysis and a post-procedure CBC are collected. Premedication with diphenhydramine and acetaminophen may reduce incidence and/or severity of allergic or febrile transfusion reactions, respectively.

Diphenhydramine administration should be considered in the context of concurrent sedatives or pain medication and/or acute respiratory distress, due to potential for exacerbation.

Chronic complications of sickle cell disease:

Chronic RBC exchange is usually performed for previous history of stroke as an outpatient or inpatient, depending on individual circumstance. The typical exchange interval 4-6 weeks, with the goal to maintain pre-procedure HbS <50%.

Red cell exchange parameters: *Review previous procedures*

Pre-procedure (starting) hemoglobin HbS%

- | | |
|---------|---|
| Acute | • If no/unknown recent transfusions, assume HbS is 100% |
| Chronic | • Estimate by averaging last 5 pre-procedure HbS% |
- If a HbS% from <7 days is available, use that value as starting HbS%
 - If known recent transfusion, multiply HbS% by (pre-transfusion Hgb / post-transfusion Hgb)
 - For HbSC, add HbS and HbC for total abnormal Hb (30% HbS + 30% HbC = 60% abnormal Hb)

Post-procedure (target) Hb S%

- | | |
|---------|---|
| Acute | • 30% |
| Chronic | • 20%, if no history of stroke <2 years ago
• 10%, if history of stroke <2 years ago |

Fraction Cells Remaining (FCR) = post-procedure HbS / pre-procedure HbS

- Ex. starting HbS = 45%, and target HbS = 20%, FCR is 20/45 = 44%

Post-procedure (target) hematocrit (hct)

If starting hct is:	Then the target hct is:
≤30%	30%
30-35%	same as starting hematocrit
>35%	35% *

*High end hematocrits are generally avoided due to the potential for higher blood viscosity.

Determining Volume of red blood cells for red cell exchange: Use the Terumo RBCX Calculation Tool (app on service phones). Enter the following info: height, weight (adjusted if BMI >30), hematocrit, blood warmer volume of 100 mL, exchange type: exchange, exchange fluid hematocrit (61%), target hematocrit and FCR. Add an extra 100-200 mL to the final volume to ensure enough blood is ordered. Report the volume to the charge nurse and blood bank.

Erythrocytapheresis (red blood cell depletion)

RBC depletion is used to rapidly decrease hemoglobin while maintaining overall blood volume. The Terumo RBCX Calculation Tool can be used to calculate amount of replacement fluid for RBC depletion. Enter the following info: height, weight (adjusted if BMI >30), hematocrit, blood warmer volume of 100 mL, exchange type: depletion, exchange fluid type (plasma/albumin).

Leukocytapheresis

Patients with acute leukemia and hyperleukocytosis may present with symptoms of leukostasis in the cerebral (altered mental status) or pulmonary (respiratory distress) vascular beds, especially with blast counts $>100,000/\mu\text{L}$. Debulking circulating blasts before chemotherapy initiation may reduce risk of tumor lysis syndrome. Review the peripheral blood smear in Cellavision to verify the differential and rule out acute promyelocytic leukemia (fragile cells could lyse in the machine); confirm hematology has done the same and is in agreement with indication and goal (usually blast count $<50,000/\mu\text{L}$). Specify target layer – mononuclear (MNC, most common, removes blasts, lymphocytes, immature/maturing myeloid cells) or polymorphonuclear (PMN, uncommon, removes mature myeloid cells and requires hespan (hetastarch) to separate PMNs from RBCs). RBC transfusion should be delayed if possible to reduce potential decreases in capillary flow. 2 blood volumes are usually processed and should be isovolemic. Check CBC pre-, mid- and post-procedure; expected WBC count reduction is $\sim 50\%$.

Thrombocytapheresis (plateletpheresis)

A platelet count $>1,000\text{K}/\mu\text{L}$ can pose risk of thrombosis, despite platelet dysfunction associated with essential thrombocythemia (ET). Processing 2 blood volumes is expected to reduced platelet count by $\sim 50\%$ and should be isovolemic. Check CBC pre-, mid- and post-procedure for platelets.

Extracorporeal Photopheresis (ECP)

ECP is only performed during normal business hours Mon-Fri and never emergently. The NPs manage inpatients receiving ECP for GVHD on North Campus; trainees manage inpatients receiving ECP for all other indications and locations. The Cellex ECP machine can be used in patients $>45\text{kg}$, high triglycerides, high bilirubin, and/or anemia (with TM attending approval). Several procedures (weeks to months) are usually needed for ECP benefits to become apparent. Indications include cutaneous T cell lymphoma (CTCL)/Sezary syndrome (FDA and CMS approved), graft-versus-host disease (GVHD, CMS approved), and cardiac transplant rejection (FDA approved), and lung allograft rejection (under study). For transplant rejection, patients typically receive 24 ECP procedures (12 cycles, 2 ECP/cycle) over 6 months: 1 cycle/week for 4 weeks, 1 cycle every other week for 10 weeks, then 1 cycle/month for 3 months. For CTCL or GVHD, patients receive 1 cycle/week (severe acute GVHD) or 1 cycle every other week (CTCL, non-severe GVHD) with reassessment and adjustment based on clinical response.

Therapeutic phlebotomy

Phlebotomy of one unit (450 mL) of whole blood is performed for polycythemia and iron overload due to hemochromatosis, and requests are handled differently depending on timing. During regular business hours an Apheresis RN performs the procedure at bedside for inpatients or in the Apheresis Center for outpatients. The LMR is not directly involved in procedure oversight but obtains informed consent, orders the therapy plan and writes a procedure note (see “outpatient apheresis”). During non-business hours, the primary requesting team performs the procedure. Supplies (phlebotomy kit and scale) and instructions are in the Blood Bank. If efforts by the primary requesting team to perform the phlebotomy are unsuccessful, options include the apheresis RN performing the procedure during business hours or emergent automated erythrocytapheresis (may require central line placement).

Donor Collections

Mononuclear cell collections for cellular therapies:

Some patients undergo autologous collection for cellular therapies that require manufacturing. Chimeric antigen receptor (CAR) T cells are a common indication for MNC collection. Patients are not mobilized since the target population is lymphocytes, and in most cases one collection is usually sufficient.

HPC collections for stem cell transplant:

Most hematopoietic progenitor cell (HPC) collections are by apheresis from autologous (donor is the recipient) or allogeneic (donor is not the recipient) donors. HPC collections are performed during regular business hours, usually as outpatient. Inpatient collections are done for patients with amyloidosis or major comorbidities (managed by LMR). Information to obtain (from chart review, clinical team and patient) includes: diagnosis, previous treatments (especially chemotherapy), medications (including diuretics and ACE inhibitors), allergies, review of systems relevant to collection (heart disease, diabetes, kidney disease, blood pressure issues, bleeding issues, parasthesias or neuropathies), electrolyte abnormalities (K, Mg), access type needed, mobilization, collection goal (Oncology tab in EPIC). Obtain informed consent and a storage agreement for autologous donations. For allogeneic PBSC collection, a storage agreement is not needed. HPCs are mobilized into peripheral blood with G-CSF (starting ~4 days prior) +/- plerixafor daily. Usually 20 liters is processed, for collections goals of ≥ 2.0 (allo), ≥ 2.5 (auto) or ≥ 5.0 (auto for myeloma) $\times 10^6$ CD34 $^{+}$ cells/kg recipient body weight. Number of collections vary, from 1 day (for most healthy allogeneic) to several days (for autologous donors with previous chemotherapy); donors who do not meet goal may be remobilized later. Donors on research protocols may have different collection parameters (BV processed, collection goals, anticoagulant used, etc.).

Donor Lymphocyte Infusions (DLI):

Allogeneic donors may donate lymphocytes as an outpatient for previously transplanted patients with relapse to promote graft vs. tumor effect. Donors are not mobilized unless concurrent collection for HPCs occurs. Usual DLI collection goal is 9×10^7 CD3 $^{+}$ cells, and cells are frozen into three aliquots (with 1, 3 and 5×10^7 CD3 $^{+}$ cells).

ASFA Clinical Guidelines on Therapeutic Apheresis Indications

The American Society for Apheresis (ASFA) provides recommendations regarding indications for therapeutic apheresis. Each indication is assigned a category and grade based on the strength of available evidence following GRADE criteria. This is not an exhaustive list, but it provides guidelines and references when weighing the risks and benefits of apheresis. Apheresis *always* carries risks and the TM service reserves the right to refuse apheresis treatment (under the direction/potential direct involvement of attending). See reference for individual fact sheets.

Padmanabhan, et al. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice – Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Eighth Special Issue Journal of Clinical Apheresis. 2019;34:171–354.

Table. Category definitions for therapeutic apheresis as defined by ASFA

Category	Description
I	Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.
II	Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum role of apheresis therapy is not established. Decision making should be individualized.
IV	Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken in these circumstances.

Table. Grading Recommendations, Strength and Quality of Evidence as defined by ASFA

Recommendation	Description	Methodological Quality of Supporting Evidence	Implications
Grade 1A	Strong recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Grade 1B	Strong recommendation, moderate quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Grade 1C	Strong recommendation, low-quality or very low-quality evidence	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
Grade 2A	Weak recommendation, high quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2B	Weak recommendation, moderate-quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2C	Weak recommendation, low-quality or very low-quality evidence	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

Table 1. Category and Grade Recommendations for Therapeutic Apheresis

Disease	TA modality	Indication	Category	Grade	Page
Acute disseminated encephalomyelitis (ADEM)	TPE	Steroid Refractory	II	2C	187
Acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barré syndrome)	TPE IA	Primary Treatment Primary Treatment	I I	1A 1B	189
Acute liver failure	TPE-HV TPE		I III	1A 2B	191
Age related macular degeneration, dry	Rheopheresis	High-risk	II	2B	193
Amyloidosis, systemic	β 2-microglobulin column TPE	Dialysis-related amyloidosis Other causes	II IV	2B 2C	195
Anti-glomerular basement membrane disease (Goodpasture syndrome)	TPE TPE TPE	Diffuse alveolar hemorrhage (DAH) Dialysis- independence Dialysis-dependence, no DAH	I I III	1C 1B 2B	197
Atopic (neuro-) dermatitis (atopic eczema), recalcitrant	ECP IA TPE/DFPP		III III III	2A 2C 2C	199
Autoimmune hemolytic anemia, severe	TPE TPE	Severe cold agglutinin disease Severe warm autoimmune	II III	2C 2C	201
Babesiosis	RBC exchange	Severe	II	2C	203
Burn shock resuscitation	TPE		III	2B	205
Cardiac neonatal lupus	TPE		III	2C	207
Catastrophic antiphospholipid syndrome (CAPS)	TPE		I	2C	209
Chronic focal encephalitis (Rasmussen Encephalitis)	TPE		III	2C	211
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	TPE/IA		I	1B	213
Coagulation factor inhibitors	TPE IA		III III	2C 2B	215
Complex regional pain syndrome	TPE	Chronic	III	2C	217
Cryoglobulinemia	TPE IA	Severe/symptomatic Severe/symptomatic	II II	2A 2B	219
Cutaneous T cell lymphoma (CTCL); Mycosis fungoides; Sézary syndrome	ECP ECP	Erythrodermic Non-erythrodermic	I III	1B 2C	221
Dilated cardiomyopathy, idiopathic	IA TPE	NYHA II-IV NYHA II-IV	II III	1B 2C	223
Erythropoietic protoporphyrina, liver disease	TPE RBC Exchange		III III	2C 2C	225

Disease	TA modality	Indication	Category	Grade	Page
Familial hypercholesterolemia	LA	Homozygotes	I	1A	227
	LA	Heterozygotes	II	1A	
	TPE	Homozygotes/ Heterozygotes	II	1B	
Focal segmental glomerulosclerosis (FSGS)	TPE/IA	Recurrent in kidney transplant	I	1B	229
	LA	Recurrent in kidney transplant/ Steroid resistant in native kidney	II	2C	
	TPE	Steroid resistant in native kidney	III	2C	
Graft-versus-host disease (GVHD)	ECP	Acute	II	1C	231
	ECP	Chronic	II	1B	
Hemolysis, elevated liver enzymes, and low platelets syndrome (HELLP Syndrome)	TPE	Postpartum	III	2C	233
	TPE	Antepartum	IV	2C	
Hemophagocytic lymphohistiocytosis (HLH); Hemophagocytic syndrome; Macrophage activating syndrome	TPE		III	2C	235
Heparin-induced thrombocytopenia and thrombosis (HIT/HITT)	TPE	Pre-cardiopulmonary bypass	III	2C	237
	TPE	Thrombosis	III	2C	
Hereditary hemochromatosis	Erythrocytapheresis		I	1B	239
Hyperleukocytosis	Leukocytapheresis	Symptomatic	II	2B	241
	Leukocytapheresis	Prophylactic or secondary	III	2C	
Hypertriglyceridemic pancreatitis	TPE/LA	Severe	III	1C	243
	TPE/LA	Prevention of relapse	III	2C	
Hyperviscosity in hyper gammaglobulinemia	TPE	Symptomatic	I	1B	245
	TPE	Prophylaxis for rituximab	I	1C	
IgA nephropathy (Berger's Disease)	TPE	Crescentic	III	2B	247
	TPE	Chronic progressive	III	2C	
Immune thrombocytopenia (ITP)	TPE/IA	Refractory	III	2C	249
Inflammatory bowel disease	Adsorptive cytapheresis	Ulcerative colitis/Crohn's disease	III	1B	251
	ECP	Crohn's disease	III	2C	
Lambert-Eaton myasthenic syndrome	TPE		II	2C	253
Lipoprotein(a) hyperlipoproteinemia	LA	Progressive atherosclerotic cardiovascular disease	II	1B	255
Malaria	RBC Exchange	Severe	III	2B	257
Multiple sclerosis	TPE	Acute attack/relapse	II	1A	259
	IA	Acute attack/relapse	II	1B	
	TPE	Chronic	III	2B	
	IA	Chronic	III	2B	

Disease	TA modality	Indication	Category	Grade	Page
Myasthenia gravis	TPE/IA	Acute, short-term treatment	I	1B	261
	TPE/IA	Long-term treatment	II	2B	
Myeloma cast nephropathy	TPE		II	2B	263
Nephrogenic systemic fibrosis	ECP/TPE		III	2C	265
Neuromyelitis optica spectrum disorders (NMOSD)	TPE	Acute attack/relapse	II	1B	267
	IA	Acute attack/relapse	II	1C	
	TPE	Maintenance	III	2C	
<i>N</i> -methyl-D-aspartate receptor antibody encephalitis	TPE/IA		I	1C	269
Overdose, envenomation, and poisoning	TPE	Mushroom poisoning	II	2C	271
	TPE	Envenomation	III	2C	
	TPE	Drug overdose/poisoning	III	2C	
Paraneoplastic neurological syndromes	TPE/IA		III	2C	273
Paraproteinemic demyelinating neuropathies; Chronic acquired demyelinating polyneuropathies	TPE	IgG/IgA/IgM	I	1B	275
	TPE	Anti-MAG neuropathy	III	1C	
	TPE	Multiple myeloma	III	2C	
	TPE	Multifocal motor neuropathy	IV	1C	
Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS); Sydenham's chorea	TPE	PANDAS, exacerbation	II	1B	277
	TPE	Sydenham's chorea, severe	III	2B	
Pemphigus vulgaris	TPE	Severe	III	2B	279
	ECP/IA	Severe	III	2C	
Peripheral vascular diseases	LA		II	1B	281
Phytanic acid storage disease (Refsum's Disease)	TPE/LA		II	2C	283
Polycythemia vera; Erythrocytosis	Erythrocytapheresis	Polycythemia vera	I	1B	285
	Erythrocytapheresis	Secondary erythrocytosis	III	1C	
Post-transfusion purpura (PTP)	TPE		III	2C	287
Progressive multifocal leukoencephalopathy (PML) associated with natalizumab	TPE		III	1C	289
Pruritus due to hepatobiliary diseases	TPE	Treatment resistant	III	1C	291
Psoriasis	ECP	Disseminated pustular	III	2B	293
	Adsortive cytapheresis	Disseminated pustular	III	2C	
	TPE	Disseminated pustular	IV	2C	
Red cell alloimmunization, prevention and treatment	RBC exchange	Exposure to RhD+ RBCs	III	2C	295
	TPE	Pregnancy, GA < 20 wks	III	2C	
Scleroderma (Systemic sclerosis)	TPE		III	2C	297
	ECP		III	2A	

Disease	TA modality	Indication	Category	Grade	Page
Sepsis with multiorgan failure	TPE		III	2B	299
Sickle cell disease, acute	RBC exchange	Acute stroke	I	1C	301
	RBC exchange	Acute chest syndrome, severe	II	1C	
	RBC exchange	Other complications	III	2C	
Sickle cell disease, non-acute	RBC exchange	Stroke prophylaxis	I	1A	303
	RBC exchange	Pregnancy	II	2B	
	RBC exchange	Recurrent vaso-occlusive pain crisis	II	2B	
	RBC exchange	Pre-operative management	III	2A	
Steroid-responsive encephalopathy associated with autoimmune thyroiditis (Hashimoto's encephalopathy)	TPE		II	2C	305
Stiff-person syndrome	TPE		III	2C	307
Sudden sensorineural hearing loss	LA/Rheopheresis/TPE		III	2A	309
Systemic lupus erythematosus (SLE)	TPE	Severe complications	II	2C	311
Thrombocytosis	Thrombocytapheresis	Symptomatic	II	2C	313
	Thrombocytapheresis	Prophylactic or secondary	III	2C	
Thrombotic microangiopathy, coagulation mediated	TPE	<i>THBD</i> , <i>DGKE</i> , and <i>PLG</i> mutations	III	2C	315
Thrombotic microangiopathy, complement mediated	TPE	Factor H autoantibody	I	2C	317
	TPE	Complement factor gene mutations	III	2C	
Thrombotic microangiopathy, drug associated	TPE	Ticlopidine	I	2B	319
	TPE	Clopidogrel	III	2B	
	TPE	Gemcitabine/Quinine	IV	2C	
Thrombotic microangiopathy, infection associated	TPE/IA	STEC-HUS, severe	III	2C	321
	TPE	pHUS	III	2C	
Thrombotic microangiopathy, thrombotic thrombocytopenic purpura (TTP)	TPE		I	1A	323
Thrombotic microangiopathy, transplantation associated	TPE		III	2C	325
Thyroid storm	TPE		II	2C	327
Toxic epidermal necrolysis (TEN)	TPE	Refractory	III	2B	329
Transplantation, cardiac	ECP	Cellular/recurrent rejection	II	1B	331
	ECP	Rejection prophylaxis	II	2A	
	TPE	Desensitization	II	1C	
	TPE	Antibody mediated rejection	III	2C	

Disease	TA modality	Indication	Category	Grade	Page
Transplantation, hematopoietic stem cell, ABO incompatible (ABOi)	TPE	Major ABOi HPC(M)	II	1B	333
	TPE	Major ABOi HPC(A)	II	2B	
	RBC Exchange	Minor ABOi HPC(A)	III	2C	
	TPE	Major/Minor ABOi w/ pure RBC aplasia	III	2C	
Transplantation, hematopoietic stem cell, HLA desensitization	TPE		III	2C	335
Transplantation, liver	TPE	Desensitization, ABOi living donor	I	1C	337
	TPE	Desensitization, ABOi deceased donor/ Antibody mediated rejection	III	2C	
	ECP	Desensitization, ABOi	III	2C	
	ECP	Acute rejection/Immune suppression withdrawal	III	2B	
	ECP	Bronchiolitis obliterans syndrome	II	1C	339
Transplantation, lung	TPE	Antibody mediated rejection/desensitization	III	2C	
Transplantation, renal, ABO compatible	TPE/IA	Antibody mediated rejection	I	1B	341
	TPE/IA	Desensitization, living donor	I	1B	
	TPE/IA	Desensitization, deceased donor	III	2C	
Transplantation, renal, ABO incompatible	TPE/IA	Desensitization, living donor	I	1B	343
	TPE/IA	Antibody mediated rejection	II	1B	
Vasculitis, ANCA-associated (AAV)	TPE	MPA/GPA/RLV: RPGN, Cr ≥ 5.7	I	1A	345
	TPE	MPA/GPA/RLV: RPGN, Cr < 5.7	III	2C	
	TPE	MPA/GPA/RLV: DAH	I	1C	
	TPE	EGPA	III	2C	
	TPE	Crescentic RPGN	III	2C	347
Vasculitis, IgA (Henoch-Schönlein purpura)	TPE	Severe extrarenal manifestations	III	2C	
	TPE				
Vasculitis, other	TPE	Hepatitis B polyarteritis nodosa	II	2C	349
	TPE	Idiopathic polyarteritis nodosa	IV	1B	
	Adsorptive cytapheresis	Behcet's disease	II	1C	
	TPE	Behcet's disease	III	2C	
Voltage-gated potassium channel (VGKC) antibody related diseases	TPE/IA		II	1B	351
Wilson disease, fulminant	TPE		I	1C	353

Placing Orders In Epic For Apheresis

The following orders steps are examples. Each patient is different, and order sets must be customized accordingly. Orders are entered into EPIC under the current encounter (hospital admission) once a patient is registered in Soarian and admitted. Urgent procedures during Soarian downtime require downtime paper requisitions (found in the apheresis center).

Note: Please see WUSTL Box Transfusion-Blood Bank folder for additional guides with screenshots that may be helpful while on service.

Ordering Labs in EPIC separately from Apheresis Order set

For labs (CBC, PT/INR, etc.) needed for apheresis to proceed that day, ordering labs the evening before for collection during early phlebotomy rounds (for collection ~5:00AM the next morning) should result by ~7:30AM. Current relevant labs are critical for setting parameters for the procedure. Although requesting that the primary team order needed labs each morning is acceptable, use caution as procedures could be delayed if they do not place these orders.

Labs collected in preparation for apheresis placed outside of order set:

1. In EPIC, while in a patient chart, click on the “Orders” tab.
2. Free text the lab you want to order (e.g. CBC, PT, PTT, Fibrinogen) in the “orders” window on the right side of the screen and hit “Enter”.
3. Select the desired lab order in the pop-up window with the search results.
4. Click on the selected lab in the order window on the right side of the screen, and specify order details (date, time, etc.) in the pop-up window:
 - For “Frequency” select “In AM-Once”, note date/time generated to verify collection time.
 - a. Ordering as “In AM” in Epic will ensure lab draw at default phlebotomy rounds for the certain floor or unit.
 - b. Note: some floors or units draw “morning labs” around 10 pm the night before. So ideally place morning labs at the end of previous day (5 pm). If set a time outside the usual phlebotomy rounds, a call to the floor nurse or significant monitoring may be necessary to ensure the lab is drawn.
 - Specify collection details in the comment section and/or call and inform the floor nurse about the order and the need for labs to be drawn with early AM labs for apheresis.
 - The floor nurse should always be notified of STAT orders.
5. Repeat with any additional labs you may need to order, and click “Sign”.

Additional orders at bottom of all order sets:

There is a section for additional orders at the bottom of all order sets, see examples below

1. Mid-procedure ionized calcium (iCa):
 - Search for “ionized calcium”
 - Choose “Calcium, ionized, whole blood”

- Click on the order under “during visit orders” to specify details (Frequency - once, date of procedure, specimen - blood). Comments: click, type “For apheresis RN only: Please draw mid-procedure ionized calcium
 - Click “accept”
2. Alteplase (for difficulty establishing port access):
 - Search for “alteplase” and choose the “alteplase (CATHFLO ACTIVASE) injection”.
 - Specify dose: 1 mg, frequency once are defaults (nurse may ask for additional dose).
 - Under “Indications” check “Catheter clearance”.
 - Click “Accept”
 3. Lidocaine (for pain associated with accessing ports):
 - Search for “lidocaine” and choose “lidocaine-prilocaine (EMLA) 2.5-2.5% cream”
 - Specify route: topical
 - Under apply to affected area click other and type “on skin over port”
 - Click “Accept”

Modifying Orders and Dates in EPIC

To modify an order that has been signed but not yet released:

1. Under “Orders” tab open the “Signed & Held” Tab
2. Click “Click Here to Modify Signed and Held Orders”
3. Click on “Modify” at the right of the order and make the desired changes
4. Scroll to bottom and click “Save Changes”, but **DO NOT CLICK RELEASE**.
5. A box appears: “These orders WILL BE SIGNED, but NOT RELEASED”
6. Under “reason for holding: select “RN will release”

To modify an order that has been signed and released:

Changes discussed directly with the RN must be documented in EPIC promptly:

1. For minor changes - “Nursing Communication” order:
 - a. In EPIC, while in a patient chart click on “Orders”.
 - b. Free text “Nursing communication”, “enter”, and then select.
 - c. In the comments section click to add text and type, for example: “For apheresis nurse only: please change AC ratio to 18:1 due to thrombocytopenia.”
2. For major changes - New orders are needed. Examples include number of volumes processed, change in replacement fluid type, volume status change, etc).

To place an order for a future date or change the date of the order set:

1. Click the “Options” drop down button above the orders window.
2. Choose “Edit Multiple” from the list.
3. A pop-up window will open. In the upper left of the window, click the “Select All” button.
4. On the right half of the pop-up box, specify the “start date.”
5. Click “Accept”.

Therapeutic Plasma Exchange (TPE)

Therapeutic Plasma Exchange: Overview

- Morning Labs: CBC, PT/INR +/- PTT, +/- fibrinogen
- Plasma volume (PV) exchanged: 1 PV for most (e.g. MG, GBS, AMR), 1 to 1.5 PV for TTP
- Replacement fluid: **Confirm replacement fluid with attending**
 - Albumin: for most indications with no bleeding risks
 - Plasma: for TTP, bleeding risks, recent high-risk surgery, etc.
 - **Note:** The blood bank does not see plasma orders until released by RN. If plasma is needed emergently (ie TTP) call the blood bank to thaw plasma AFTER the line is in and the RN has been called to come in to facilitate the process and minimize delay.
 - Partial plasma replacement - Albumin then transition to plasma
- Prepriming: ACD-A & normal saline
 - Standard anticoagulant: ACD-A (ratio usually 10:1)
 - Note: for patients on ECMO (which involves heparin) ratio should be 15:1
- Prebolus (250 mL albumin): neuro patients, hypotension
- Volume status after TPE: isovolemic if no prebolus, hypervolemic if prebolus
- Vital signs (VS): pre-, during and post-TPE
 - during TPE Q30 min if albumin and stable (**Q15 min if blood products or in ICU**)
- Premedications if blood product replacement (none if albumin replacement)
 - plasma: 25 mg diphenhydramine IV Push
 - RBCs: acetaminophen 650 mg oral & diphenhydramine 25 mg IV
- Hypocalcemia monitoring and intervention
 - Calcium upfront: none for albumin replacement; 2 gm Calcium for plasma replacement
 - Medications PRN: calcium carbonate PO and calcium gluconate IVPB
 - Draw ionized calcium (iCa) for symptoms of hypocalcemia, if patient is sedated, unresponsive or has baseline neuropathy or paresthesia
 - Nursing interventions: 1g calcium if iCa 3.5 - 4.5; 2g calcium and pause TPE if iCa <3.5

Therapeutic Plasma Exchange: step-by-step EPIC ordering

1. In EPIC, while in a patient chart click on “Orders”.
2. Click “Order sets” and type “Apheresis” in the window on the right side of the screen.
3. Double click on “Apheresis Therapeutic Plasma Exchange” and go through each section.
4. Perform Therapeutic Plasma Exchange: click on text:
 - a. Procedure Priority: "Routine"; never "STAT" or "Urgent" regardless of urgency.
 - b. Frequency: "Once" - do not change.
 - c. Date: current date/time is default. Change if needed, as the date must be the date of the procedure. If orders are placed the night before, the date must be changed to the following day or nursing cannot use this order. Use “Edit Multiple” to change date for all orders to future date just before signing (see previous section).
 - d. Diagnosis: choose diagnosis. The most common indications appear as buttons.
 - i. If diagnosis not listed, choose “Other (specify)” and text (use ASFA guidelines)
 - e. Select plasma volume to be exchanged (1PV, 1.5 PV)

- f. Replacement Fluids: select "Albumin 5%", "Plasma" or "5% Albumin and then Plasma".
 - g. BMI: default instructions for adjusted body weight if BMI ≥ 30 or more – do not change
 - h. Final fluid Balance: check the appropriate box
 - i. Isovolemic (most patients)
 - ii. Hypervolemic: type "250 mL albumin prebolus" into the comment box.
 - iii. Hypovolemic (rare) Click "Other", type "Leave patient __ mL negative fluid balance."
 - i. Comments: specify albumin and plasma volumes if using both (e.g. "last 1 liter plasma").
 - j. Click "accept".
5. Access type: select central or peripheral access type.
- a. "Central Venous Catheter" is the default and most common. Everything is pre-selected for the "Apheresis Catheter Maintenance Panel with IV Flushes". Leave everything as is unless patient cannot receive heparin (e.g. history of HIT).
 - i. To discontinue heparin: in "heparin OR sodium citrate for intracatheter dwell" "select radio button "Sodium Citrate 4% flushes" (will unselect heparin flushes)
 - b. "Peripheral venous" if peripheral access
6. Activity: "strict bed rest" is default, do not change.
7. Nursing:
- a. VS: pre-, during and post-TPE are pre-checked.
 - i. During procedure: default is Q30 min. **If blood products or in ICU choose Q15 min.**
 - ii. Weight: choose weight determination based on inpatient or outpatient status
 - b. Nursing Interventions:
 - i. VS: pre-determined VS range outside of which you will be contacted
 - ii. Calcium gluconate (1 gm or 2 gm) for low iCa level
8. Medications:
- a. Anticoagulant-Device Prime: default is ACD-A and saline.
 - b. Replacement Fluids: Check "albumin 5%" if applicable
 - c. Prebolus fluid: If used, check "albumin 5%", default is 12.5g (250mL) over 20 minutes.
 - d. Premedications: for administration of acetaminophen and/or diphenhydramine (if receiving blood products). Collapsed by default; click to add.
 - i. Do not change if albumin is the only replacement fluid (most cases).
 - ii. For plasma, check "Diphenhydramine 25 mg IV (for plasma replacement only)."
 - e. Hypocalcemia prevention:
 - i. For all albumin replacement, leave blank (calcium is usually not needed).
 - ii. If plasma used, select "calcium gluconate in sodium chloride 0.9% 100 mL IVPB":
 - Dose "2gm"; route "intravenous"; frequency "once"; date "date of procedure"; administer "over 60 minutes"; priority "routine", click "accept".
 - If higher doses needed adjust accordingly - generally amount of calcium equal to what was given during the previous TPE (e.g. if a patient required 1g during the last TPE, order 1g calcium up front for next TPE).
 - f. Medications PRN: allows calcium administration if needed. Calcium carbonate (PO) and calcium gluconate 1 gm/50mL (IV) are default checked; do not change.
9. Labs:
- a. "Lab-Panels": Options are "Comprehensive metabolic panel" or "Basic metabolic panel" if needed but are collapsed by default (usually ordered by primary team daily).

- b. "Chemistry-Other": PRN ionized calcium is default checked, leave checked.
- c. "Labs - Pheresis": PT/INR, fibrinogen if needed, aPTT if needed, LDH if needed
- d. "Labs - Hematology": CBC without differential is default checked, other options are CBC with differential, type and screen if needed

10. Blood Product Administration – full unit dosing:

- a. "Pre-prime": allows for RBCs pre-prime of machine (rare)
- b. "Plasma Prepare and Transfuse":
 - i. Check "Blood Administration – Plasma mL" (a new window pops up)
 - ii. "Prepare plasma (in mL)": default checked, fill in details by section
 - Priority: "routine" is default checked
 - Prepare: fill in amount of plasma in first box and units (mL) in second box
 - Yellow box below: "Copy this value to the Transfuse plasma (in mL) order?" click "copy"
 - Date required: pre-filled with current date
 - Transfusion indications: "plasma exchange procedure" is default – don't change
 - Comment: prefilled with "For transfusion by pheresis RN only"
 - Click "accept"
 - iii. "Nursing to update "date required" field in prepare blood product order PRN": default checked, allows nurse to update date for blood products
 - iv. "Transfuse plasma (in mL)" – make sure this is checked
 - v. Click "Accept"

11. Additional orders: put additional orders here (see placing orders section for examples)

12. Review the order set, including the date.

13. Click "Sign" to finalize now or "Save work" if finalizing later

- a. Several alerts may appear, acknowledge and select appropriate override reason
 - i. calcium alerts if calcium ordered
 - ii. heparin alerts if patient is on anticoagulation

Special considerations in TPE for Cryoglobulinemia/Cold Agglutinins: Specimens must be transported on warm packs. The room must be warmed to $\geq 85^{\circ}\text{F}$. Replacement fluid is kept on a warmer. Topical warming devices (Bair Hugger) around apheresis machine may minimize blood cooling and are kept on the floors (coordinate ahead of time with apheresis nurses).

Leukocytapheresis (Leukapheresis/leukoreduction)

Leukocytapheresis: overview

- Define fraction to be targeted, which influences collection parameters:
 - MNC (mononuclear cell fraction) if blasts or immature/maturing cells
 - 2 blood volumes (BV) processed with ACD-A and Normal Saline.
 - PMN (polymorphonuclear fraction) if mature cells (e.g. CML), not commonly used
 - 2 BV processed with Hetastarch/NS + Trisodium Citrate and Normal Saline.
- Volume status: isovolemic
- Vitals pre-, during (Q15 minutes – patients sicker and usually in ICU), and post-procedure

- Labs:

Pre-procedure:	CBC Express
Mid-procedure:	CBC Express, ionized calcium (if indicated)
Post-procedure:	CBC
	Waste bag: WBC with differential (called “blood product”)
- Hypocalcemia monitoring and intervention
 - Calcium upfront: 2 gm Calcium
 - Medications PRN: Calcium Carbonate PO, Calcium Gluconate IVPB
 - Draw ionized calcium (iCa) for symptoms of hypocalcemia, if patient is sedated, unresponsive or has baseline neuropathy or paresthesia
 - Nursing Interventions: 1 gm calcium if iCa is between 3.5 - 4.5; 2 gm calcium and pause procedure if ionized calcium is <3.5
- Follow CBC the next day for sustained reduction of WBC and patient response

Leukocytapheresis: step-by-step EPIC ordering

- 1) In EPIC, while in a patient chart click on “Orders”.
- 2) Click “Order sets” and type “Apheresis” in the window on the right side of the screen.
- 3) Double click on “Apheresis White Blood Cell Depletion” and go through each section.
- 4) Therapeutic apheresis for white blood cells - click on text:
 - a. Procedure priority: "Routine"; never "STAT" or "Urgent" regardless of urgency.
 - b. Frequency: "Once" - do not change.
 - c. Date: current date/time is default. Change if needed, as the date must be the date of the procedure. If orders are placed the night before, the date must be changed to the following day or nursing cannot use this order. Use “Edit Multiple” to change date for all orders to future date just before signing (see previous section).
 - d. Diagnosis: choose diagnosis (default is hyperleukocytosis).
 - e. Collect fraction: select the cell fraction and volume of blood to be processed
 - i. MNC fraction (common) - process whole blood “2 volumes”
 - ii. PMN fraction (uncommon) – process whole blood “2 volumes” whole blood
 - f. BMI: default instructions for adjusted body weight if BMI ≥ 30 or more – do not change
 - g. Final fluid balance: isovolemic
 - h. Click “Accept”
- 5) Access type: select central or peripheral access type.
 - a. “Central Venous Catheter” is the default and most common. Everything is pre-selected for the “Apheresis Catheter Maintenance Panel with IV Flushes”. Leave everything as is unless patient cannot receive heparin (e.g. HIT).
 - i. To discontinue heparin: in “heparin OR sodium citrate for intracatheter dwell” “select radio button “Sodium Citrate 4% flushes” (will unselect heparin flushes)
 - b. “Peripheral venous access”: if patient doesn’t have central access (rare)
- 6) Activity: "Strict bed rest during procedure" is default.
- 7) Nursing:
 - a. Vital signs (VS): VS pre-, during and post-TPE are pre-checked.
 - i. During procedure: default is Q30 min. **Choose Q15 min if in ICU (most likely)**
 - ii. Weight: choose weight determination based on inpatient or outpatient status

- b. Nursing interventions:
 - i. VS: pre-determined VS range outside of which you will be contacted
 - ii. Calcium gluconate (1 gm or 2 gm) for low iCa level
- 8) Medications:
- a. Preprime: not selected unless extracorporeal volume >10% TBV
 - b. Anticoagulant - device prime:
 - i. ACD-A and normal saline are default selected for MNC depletion
 - ii. Hetastarch with Tricitrasol panel is selected only for PMN depletion
 - c. Replacement fluid: both albumin and sodium chloride default checked
 - i. Saline used if volume deficit <500 mL, albumin used if ≥500 mL
 - d. Prebolus fluid: default unchecked, leave unless otherwise indicated.
 - e. Premedication (only if preprime used): for administration of acetaminophen and/or diphenhydramine (if receiving blood product pre-prime).
 - f. Hypocalcemia prevention: select “calcium gluconate in sodium chloride 0.9% 100 mL IVPB” and specify details in popup window.
 - i. Dose – 2gm, or more if needed; route “intravenous”; frequency “once”; date “date of procedure”; administer “over 60 minutes”; priority “routine”, click “accept”.
 - g. Medications PRN: allows calcium administration if needed. Calcium carbonate (PO) and calcium gluconate 1 gm/50mL (IV) are default checked; do not change.
- 9) Labs:
- a. Chemistry – other: PRN ionized calcium default checked.
 - b. Hematology: CBCs pre-, mid-, post-procedure, and blood product (waste) pre-checked.
- 10) Blood product administration (full unit dosing): pre-prime is default unchecked (rarely used)
- 11) Additional orders: put additional orders here (see placing orders section for examples)
- 12) Review the order set, including the date.
- 13) Click “Sign” to finalize now or “Save work” if finalizing later
- a. Several alerts may appear, acknowledge and select appropriate override reason
 - i. calcium alerts if calcium ordered
 - ii. heparin alerts if patient is on anticoagulation

Thrombocytapheresis (Platelet Depletion)

Thrombocytapheresis targets platelets but is similar to leukocytapheresis in the collection parameters. Follow the above for leukocytapheresis orders, with the following differences:

1. Choose order set "Apheresis Platelet Depletion".
2. Therapeutic apheresis for platelets:
 - a. Diagnosis: choose diagnosis (default is thrombocytosis).
 - b. Process whole blood: “volumes” is default, specify 2 blood volumes in text box below.
 - c. Final fluid balance: “Isovolemic”
3. Labs: No CBC on the blood product (waste bag).

Red Blood Cell Exchange (RCE)

Red blood cell exchange: Overview

- Morning labs: type and screen, CBC, hemoglobin (Hb) analysis. Typically ordered by hematology NP the night before; but if not, order labs so the blood bank can screen units.
- RBC pre-priming (only if indicated, such as markedly anemic): 1 unit RBCs (uncommon)
- End hematocrit (Hct) determined by starting Hct: if Hct \leq 30, target Hct = 30; if Hct >30, target Hct up to but not exceeding target Hct = 35 (see indications section).
- Anticoagulant: ACD-A
- FCR (Fraction of Cells Remaining): calculate (see indications section)
- Final fluid status: isovolemic
- Replacement fluids: calculate RBC volume/#units (see indications section)
- Vitals pre-, during and post-procedure. During procedure Q15 min (since RBCs used)
- Labs: CBC Express, Hb analysis before (if not done) and after procedure.
- Premedications: acetaminophen 650 mg PO, diphenhydramine 25 mg IV if indicated.

Red Cell Exchange: step-by-step EPIC ordering

1. In EPIC, while in a patient chart click on “Orders”.
2. Click “Order sets” and type “Apheresis” in the window on the right side of the screen.
3. Double click on “Apheresis Red Blood Cell Exchange” and go through each section.
4. Therapeutic Apheresis for Red Blood Cells: click on text
 - a. Procedure Priority: "Routine"; never "STAT" or "Urgent" regardless of urgency.
 - b. Frequency: "Once" – don't change
 - c. Date: current date/time is default. Change if needed.
 - i. Note: the date must be the date of the procedure (i.e. if you order the night before, this date must be changed to the following day or nursing cannot use this order). Use “Edit Multiple” to change date for all orders to future date just before signing (see previous section).
 - d. Diagnosis: choose diagnosis
 - e. BMI: default instructions for adjusted body weight if BMI \geq 30 or more – do not change
 - f. Procedure Target Values: “end hematocrit” and “FCR” are selected
 - i. Enter values determined/calculated for each
 - g. Final fluid balance:
 - i. Isovolemic - if no calcium administered before procedure
 - ii. Hypervolemic - If calcium is given prior to procedure start
 - Indicate hypervolemic (50 mL saline administered for each 1g calcium)
 - Comments: “hypervolemic *** mL due to administration of ***g calcium”.
 - For each 1g calcium given, 50 mL saline will be given. Example: “Hypervolemic 100 mL due to 2g calcium”
 - h. Click “Accept”
5. Access type: check the appropriate option
 - a. “Central Venous”: Everything is pre-selected for “Apheresis Catheter Maintenance Panel with IV Flushes”. Leave everything as is unless patient cannot receive heparin (e.g. HIT).

- i. To discontinue heparin: in "heparin OR sodium citrate for intracatheter dwell" "select radio button "Sodium Citrate 4% flushes" (will unselect heparin flushes)
- b. "Implantable Port", "Apheresis Implantable Port Access / Decannulation" options are pre-selected. Leave everything as is unless patient cannot receive heparin (e.g. HIT).
 - i. To discontinue heparin: in "heparin OR sodium citrate for intracatheter dwell" "select radio button "Sodium Citrate 4% flushes" (will unselect heparin flushes)
 - c. "Peripheral venous" if peripheral access
- 6. Activity: "Strict bed rest during procedure" is default.
- 7. Nursing:
 - a. Vital signs (VS): VS pre-, during and post-TPE are pre-checked.
 - i. During procedure: **Q15 min since blood products transfused**
 - ii. Weight: choose weight determination based on inpatient or outpatient status
 - b. Nursing interventions:
 - i. VS: pre-determined VS above and/or below which you will be contacted
 - ii. Calcium gluconate (1 gm or 2 gm) for low iCa level
- 8. Medications:
 - a. Anticoagulant - device prime: ACD-A and normal saline are default selected
 - b. Prebolus: default unchecked, leave unless otherwise indicated.
 - c. Premedication: for acetaminophen and/or diphenhydramine
 - i. "Acetaminophen 650 mg PO"
 - ii. 25 mg "Diphenhydramine IV" or "Diphenhydramine PO"
 - d. Note: Maximum dosing up to 100 mg every 6 hours if IV and up to 50 mg every 4 hours if PO. If patient is requiring more than this talk to your attending.
 - e. Hypocalcemia prevention: leave blank unless indicated by history of hypocalcemia
 - i. Select "calcium gluconate in sodium chloride 0.9% 100 mL IVPB" and
 - ii. Specify details in popup window: Dose - 2gm, or more if needed; route "intravenous"; frequency "once"; date "date of procedure"; administer "over 60 minutes"; priority "routine", click "accept".
 - f. Medications PRN: allows calcium administration if needed. Calcium carbonate (PO) and calcium gluconate (IV) are default checked; do not change.
- 9. Labs:
 - a. Chemistry – other: PRN ionized calcium is default checked.
 - b. Hematology: CBC and hemoglobin analysis for pre- and post-procedure
- 10. Blood Product Administration – full unit dosing: a prompt to order type and screen will appear if not current
 - a. "Pre-prime": default unchecked (rarely used)
 - b. Select "RBCs Prepare and Transfuse (mL)" (commonly used)
 - i. "Prepare RBCs (in mL)": default checked, fill in details by section
 - ii. Priority: "routine" is default checked
 - iii. Prepare: Fill in amount of RBCs in first box and units (mL) in second box
 - Yellow box "Copy this value to the Transfuse RBCs (in mL) order?" - click "copy"
 - iv. Date required: pre-filled with current date
 - v. Transfusion indications: select indication ("sickle cell/congenital anemia")
 - vi. Are Special Requirements needed?: Yes

- Special requirements: select “Hgb S negative” and “CEK compatible”
 - Select others only if clinically indicated
- vii. Comments: add if needed
- viii. “Nursing to update “date required” field in prepare blood product order PRN”: default checked, allows nurse to update date for blood products
- ix. “Transfuse RBCs (in mL)” – make sure this is checked
- x. Click “Accept” once both prepare and transfuse boxes are checked
- c. “RBCs Prepare and Transfuse (units)": follow same steps for mL but specify unit number
11. Additional orders: put additional orders here
12. Review the order set, including the date.
13. Click “Sign” to finalize now or “Save work” if finalizing later
- Several alerts may appear, acknowledge and select appropriate override reason
 - calcium alerts if calcium ordered
 - heparin alerts if patient is on anticoagulation

Erythrocytapheresis (Red Blood Cell Depletion)

Erythrocytapheresis: Overview

- Anticoagulant: ACD-A
- Post-Procedure Target Values:
 - End hematocrit – discuss goal with primary team.
 - Volume status: leave isovolemic.
- Vitals: pre-, during and post-TPE:
 - during TPE Q30 min if albumin and stable (**Q15 min if blood products or in ICU**)
- Labs: CBC Express pre- and post-procedure.
- Hypocalcemia monitoring and intervention
 - Medications PRN: Calcium Carbonate PO, Calcium Gluconate IVPB
 - Draw ionized calcium (iCa) for symptoms of hypocalcemia, if patient is sedated, unresponsive or has baseline neuropathy or paresthesia
 - Nursing interventions: 1g calcium if iCa 3.5-4.5; 2g calcium, pause procedure if iCa <3.5

Erythrocytapheresis: step-by-step EPIC ordering

1. In EPIC, while in a patient chart click on “Orders”.
2. Click “Order sets” and type “Apheresis” in the window on the right side of the screen.
3. Double click on “Apheresis Red Blood Cell Depletion” and go through each section.
4. Therapeutic Apheresis Red Blood Cell Depletion: click on text:
 - a. Procedure Priority: "Routine"; never "STAT" or "Urgent" regardless of urgency.
 - b. Frequency: “Once” – don’t change
 - c. Date: current date/time is default. Change if needed.
 - i. Note: the date must be the date of the procedure (i.e if you order this the night before, change date to the following day). Use “Edit Multiple” to change date for all orders to future date just before signing (see previous section).

- d. Diagnosis: choose diagnosis (polycythemia vera, erythrocytosis, other)
 - e. Procedure Target Value: "end hematocrit" is selected
 - i. End hematocrit (%): enter value discussed with primary team
 - f. Final fluid balance: isovolemic
 - g. BMI: default instructions for adjusted body weight if BMI ≥ 30 or more – do not change
 - h. Click "Accept"
5. Access type: check the appropriate option:
- a. "Central Venous": Everything is pre-selected for "Apheresis Catheter Maintenance Panel with IV Flushes". Leave everything as is unless patient cannot receive heparin (e.g. HIT).
 - i. To discontinue heparin: in "heparin OR sodium citrate for intracatheter dwell" select radio button "Sodium Citrate 4% flushes" (will unselect heparin flushes)
 - b. "Implantable Port", "Apheresis Implantable Port Access / Decannulation" options are pre-selected. Leave everything as is unless patient cannot receive heparin (e.g. HIT).
 - i. To discontinue heparin: in "heparin OR sodium citrate for intracatheter dwell" select radio button "Sodium Citrate 4% flushes" (will unselect heparin flushes)
 - c. "Peripheral venous" if peripheral access
6. Activity: "Strict bed rest during procedure" is default.
7. Nursing:
- a. Vital signs (VS): VS pre-, during and post-TPE are pre-checked.
 - i. During procedure: default is Q30 min. **Choose Q15 min if in ICU or unstable**
 - ii. Weight: choose weight determination based on inpatient or outpatient status
 - b. Nursing interventions:
 - i. VS: pre-determined VS above and/or below which you will be contacted
 - ii. Calcium gluconate (1 gm or 2 gm) for low iCa level
8. Medications:
- a. Anticoagulant - device prime: ACD-A and normal saline are default selected
 - b. Replacement fluid: albumin is default checked, check saline too
 - i. Saline used if volume deficit < 500 mL saline, albumin if ≥ 500 mL
 - c. Pre-bolus: default unchecked, leave unless otherwise indicated.
 - d. Hypocalcemia prevention: select "calcium gluconate in sodium chloride 0.9% 100 mL IVPB" and specify details in popup window.
 - i. Dose – 2gm, or more if needed; route "intravenous"; frequency "once"; date "date of procedure"; administer "over 60 minutes"; priority "routine", click "accept".
 - e. Medications PRN: allows calcium administration if needed. Calcium carbonate (PO) and calcium gluconate (IV) are default checked; do not change.
9. Labs:
- a. Chemistry – other: PRN ionized calcium is default checked.
 - b. Hematology: CBCs for pre-, post-procedure
10. Additional orders: put additional orders here (see placing orders section for examples)
11. Review the order set, including the date.
12. Click "Sign" to finalize now or "Save work" if finalizing later
- a. Several alerts may appear, acknowledge and select appropriate override reason
 - i. calcium alerts if calcium ordered
 - ii. heparin alerts if patient is on anticoagulation

Extracorporeal Photopheresis (ECP)

ECP: Overview

- Morning labs: CBC, minimum Hct $\geq 25\%$, CMS study patients Hct $\geq 28\%$.
- Two different anticoagulation protocols can be used:
 - Heparin protocol: default protocol of Heparin Sodium 10,000U, Normal Saline 500 mL
 - platelets must be $> 80K$, no contraindications to heparin
 - ACDA protocol: ACD-A 500 mL, Normal Saline 500 mL
 - Platelets $< 80K$, patient already receiving anticoagulation
 - Hypocalcemia monitoring and intervention
 - Medications: 1g calcium
 - Medications PRN: Calcium Carbonate PO, Calcium Gluconate IVPB
 - Draw ionized calcium (iCa) for symptoms of hypocalcemia, if patient is sedated, unresponsive or has baseline neuropathy or paresthesia
 - Nursing Interventions: 1g Ca if iCa 3.5-4.5; 2g Ca, pause procedure if iCa < 3.5
- Default AC ratio is 10:1 for central catheters; change to 8:1 for patients with ports.
- Vitals pre-, during, and post-procedure, during procedure Q15 minutes
- Other Medications: 8-Methoxysoralen (brand name is Uvadex).
- Lipid TPN (not non-lipid TPN) must be stopped 6 hours prior to ECP procedure.
- IV Tacrolimus must be stopped during ECP procedure.
- Patients should avoid sunlight or other UV exposure for 24 hours following ECP.

ECP: step-by-step EPIC ordering

1. In EPIC, while in a patient chart click on “Orders”.
2. Click “Order sets” and type “Apheresis” in the window on the right side of the screen.
3. Double click on “Apheresis Photopheresis” and go through each section.
4. Perform Photopheresis: click on text
 - a. Priority: “Routine”; never “STAT” or “Urgent” regardless of urgency.
 - b. Frequency: “Once”; don’t change
 - c. Date: current date/time is default. Change if needed.
 - i. Note: the date must be the date of the procedure (i.e if you order this the night before, this date must be changed to the following day or nursing cannot use this order. Use “Edit Multiple” to change date for all orders to future date just before signing (see previous section).
 - d. Diagnosis: choose diagnosis
 - e. AC ratio: 10:1 is preselected. Change to 8:1 if patient has a port.
 - f. Click “accept”
5. Access type: check the appropriate option
 - a. “Central Venous”: Everything is pre-selected for “Apheresis Catheter Maintenance Panel with IV Flushes”. Leave everything as is unless patient cannot receive heparin (e.g. HIT).
 - i. To discontinue heparin: in “heparin OR sodium citrate for intracatheter dwell” “select radio button “Sodium Citrate 4% flushes” (will unselect heparin flushes)

- b. "Implantable Port", "Apheresis Implantable Port Access / Decannulation" options are pre-selected. Leave everything as is unless patient cannot receive heparin (e.g. HIT).
 - i. To discontinue heparin: in "heparin OR sodium citrate for intracatheter dwell" select radio button "Sodium Citrate 4% flushes" (will unselect heparin flushes)
 - c. "Peripheral venous" is peripheral access
6. Activity: "Bed rest with exceptions" and "bedside commode" is default selected.
7. Nursing:
- a. Vital signs (VS): VS pre-, during and post-TPE are pre-checked.
 - i. VS during procedure: **Q15 min**
 - ii. Patient Weight: default checked
 - b. Nursing interventions:
 - i. VS: pre-determined VS range outside of which you will be contacted
 - ii. Calcium gluconate (1 gm or 2 gm) for low iCa level
8. Respiratory: select "oxygen therapy" if indicated
9. Medications:
- a. Anticoagulant-device prime: select appropriate protocol (heparin is common protocol)
 - i. ACD-A Protocol: ACD-A, normal saline, and PRN calcium (PO and IV) are preselected
 - Select "calcium gluconate 10%IV": click "1g", don't change preselections, "accept"
 - ii. Heparin Protocol: heparin and normal saline are default selected.
 - b. Prebolus fluid: default is unchecked
 - c. Photo Activating agent: "Methoxsalen (UVADEX) Injection" is default checked
 - d. Hypocalcemia prevention: addressed above if ACD-A protocol is used, leave unchecked
 - e. Medications PRN: addressed above if ACD-A protocol is used, uncheck
10. Labs:
- a. Chemistry-Other: select PRN ionized calcium, whole blood
 - b. Hematology: Pre-procedure CBC, with differential is default checked
 - c. Coagulation: pre-procedure PT/INR
11. Additional orders: enter any additional orders in this section
12. Review the order set, including the date.
13. Click "Sign" to finalize now or "Save work" if finalizing later
- a. Several alerts may appear, acknowledge and select appropriate override reason
 - i. calcium alerts if calcium ordered
 - ii. heparin alerts if patient is on anticoagulation

Hematopoietic progenitor cell (HPC) collections

HPC collections: Overview

- Morning labs: CBC before each collection, peripheral blood CD34⁺ cell count before 1st collection (verify order placed by CTL), check collection yield from day(s) prior if applicable
 - Ideally should check previous day CBC and discuss with attending the day before if patient is in the "danger zone" of not meeting the below goal in the morning
 - For autologous donors: Hct >27%, Plt >20K (generally)
 - For allogeneic donors: Hct >30%, Plt >100K (generally)

- Standard anticoagulant: ACD-A (heparin in some situations: fluid overload, liver disease, etc)
- Volumes processed: Usually 20L whole blood on Spectra Optia
 - Potential variations: study protocol (4BV on Bioline protocol), Amicus (15L)
 - Check the “Perform Stem Cell Collection” order to confirm process volume (easiest way to do this is search for the order typing in “Perform Stem Cell Collection”)
- Vitals pre-, during and post-procedure: during Q1hr
- Hypocalcemia monitoring and intervention (ACD-A protocol only):
 - Medications: Calcium gluconate IVPB 4g, 500mg calcium carbonate PO every hour
 - Medications PRN: Calcium Carbonate PO, Calcium Gluconate IVPB
 - Draw ionized calcium (iCa) for symptoms of hypocalcemia, if patient is sedated, unresponsive or has baseline neuropathy or paresthesia
 - Nursing Interventions: 1g calcium if iCa 3.5-4.5; 2g calcium, pause procedure if iCa <3.5
- Labs: CBC Express post-procedure if pre-procedure platelet count <50K
- Forms required: consent and storage agreement (available in Forms on Demand)

Peripheral Blood Stem Cell (HPC): step-by-step EPIC ordering

1. In EPIC, while in a patient chart click on “Orders”.
2. Click “Order sets” and type “Apheresis” in the window on the right side of the screen.
3. Double click on “Apheresis Cellular Therapy Cell Collection” and go through each section.
4. Perform Stem Cell Collection: click on text
 - a. Priority: “Routine”; never “STAT” or “Urgent” regardless of urgency.
 - b. Frequency: “Once”; don’t change
 - c. Date: current date/time is default. Change if needed.
 - i. Note: the date must be the date of the procedure (if you order this the night before, change to the following day. Use “Edit Multiple” to change date for all orders to future date just before signing (see previous section).
 - d. Diagnosis: choose cells to be collected (stem cells, therapeutic cells, other)
 - e. Process volume: specify volume to be processed.
 - f. Click “accept”
5. Access: select access
 - a. “Central Venous”: Everything is pre-selected for “Apheresis Catheter Maintenance Panel with IV Flushes”. Leave everything as is unless patient cannot receive heparin (e.g. HIT).
 - i. To discontinue heparin: in “heparin OR sodium citrate for intracatheter dwell” select radio button “Sodium Citrate 4% flushes” (will unselect heparin flushes)
 - b. “Peripheral venous access”
6. Activity: “Bedrest with exceptions” and “bedside commode” is default checked.
7. Nursing:
 - a. Vital signs (VS): VS pre-, during (**Q1 hour**) and post-TPE are pre-checked.
 - b. Nursing interventions:
 - i. VS: pre-determined VS range outside of which you will be contacted
 - ii. Calcium gluconate (1 gm or 2 gm) for low iCa level
8. Medications:
 - a. Anticoagulant-device prime: select appropriate protocol

- i. ACD-A Protocol: ACD-A, normal saline, and calcium gluconate 4g IV are preselected
 - ii. Heparin Protocol: heparin and normal saline are default selected.
 - b. Hypocalcemia prevention: select calcium carbonate PO 500 mg, every hour
 - c. Medications PRN: Calcium Carbonate PO, Calcium Gluconate IVPB default checked
9. Labs:
- a. Nursing communications: select autologous donor or allogeneic donor
 - b. Chemistry-Other: select PRN ionized calcium, whole blood
 - c. Hematology: Pre-and post-procedure CBC
10. Additional orders: enter any additional orders in this section
11. Review the order set, including the date.
12. Click "Sign" to finalize now or "Save work" if finalizing later
- a. Several alerts may appear, acknowledge and select appropriate override reason
 - i. calcium alerts if calcium ordered, heparin alerts if patient is on anticoagulation

Peripheral Blood Mononuclear (MNC) collections

Mononuclear cell (MNC) collection for CAR-T cell therapy or Donor Lymphocyte Infusions (DLIs) is similar to HPC collections. DLIs do not undergo further manufacturing. Lymphocytes collected for CAR-T cells are sent to a facility to be manufactured into CAR T-cells. CAR T-cell collections can be time sensitive as the product may be scheduled for transport off site after collections.

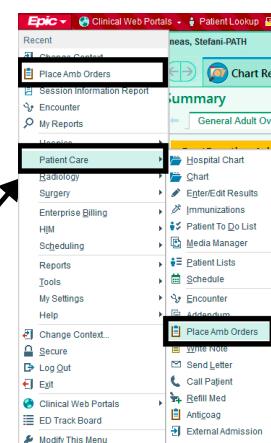
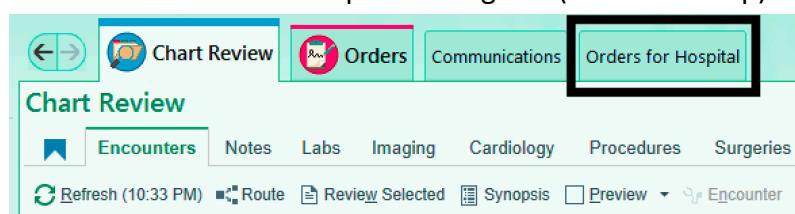
- Note: ensure that the patient's HCT is adequate to proceed with collection the **night before** or discussion with attending may be appropriate as a phone call with the primary team to let them know they need to transfuse blood prior to collection.
- Follow the above for HPC collection orders, with the following differences: Goal collection, volume to be processed, and other aspects may differ depending on protocol. Please look up collection order by searching for "Perform Stem Cell Collection" and look under order comment for specific details for each patient.

Therapeutic Phlebotomy

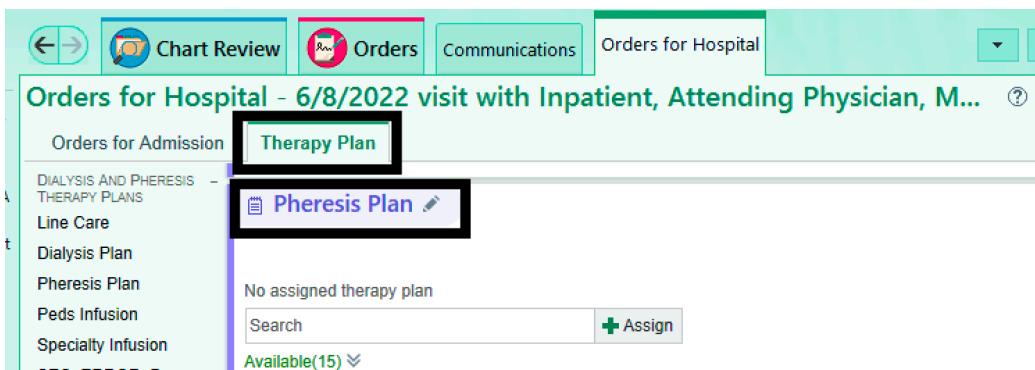
Usually, therapeutic phlebotomy is done as an outpatient in the Apheresis Center, but occasionally there are requests for inpatient therapeutic phlebotomy.

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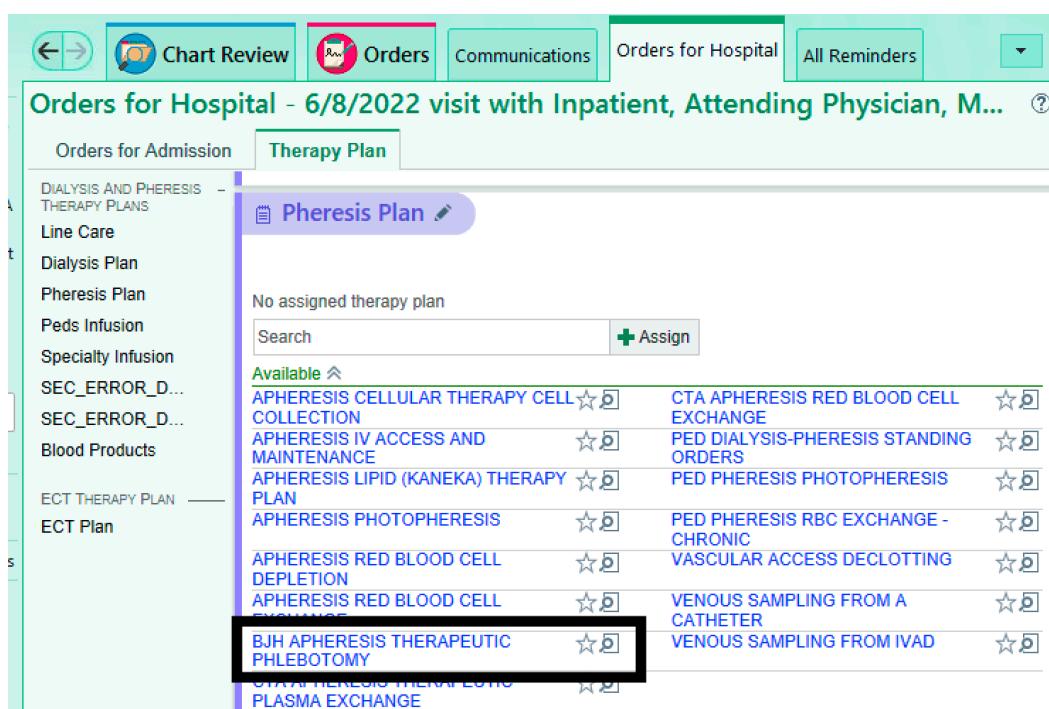
1. Click on the Epic Button on the top right corner
2. Select "Place Amb Orders" either from main menu or under "patient care"
3. Select the "Orders for Hospital" Navigator (left side or top).



4. Choose the Therapy Plan Tab.



5. Go to the Pheresis Plan and choose the **BJH Apheresis Therapeutic Phlebotomy** under the Pheresis Plan. Be sure **NOT** to choose plan under the Specialty Infusion Therapy Plans.



6. Lead provider the referring hematologist, click accept, treatment department **BJH Pheresis**.

Therapy Plan Properties - BJH APHERESIS THERAPEUTIC PHLEBOTOMY	
Plan name:	BJH APHERESIS THERAPEUTIC PHLEBOTOMY
Plan start date:	<input type="button" value=""/>
Lead provider:	Referring hematologist name <input type="text"/>
Treatment department:	BJH PHERESIS <input type="text"/>

- Cancel out the sodium chloride medication order unless there is concern for hypovolemia in the patient. Change the dates to the correct date. "Assign plan" and close.

Therapy Plan Properties - BJH APHERESIS THERAPEUTIC PHLEBOTOMY

Plan name:	BJH APHERESIS THERAPEUTIC PHLEBOTOMY
Plan start date:	6/8/2022 <input type="button" value="Calendar"/>
Lead provider:	Referring Hematologist name <input type="text"/> <input type="button" value="Search"/>
Treatment department:	BJH PHERESIS <input type="text"/> <input type="button" value="Search"/>

[Problems](#) [Preview Plan](#)

BJH APHERESIS THERAPEUTIC PHLEBOTOMY

Apheresis Therapeutic Phlebotomy
No review required for this plan.
Protocol notes: For BJH O/P in their pheresis center. Nov 2018

Orders

	Interval	Defer Until	Duration
Labs			
<input checked="" type="checkbox"/> POCT hemoglobin	On the 1st Sun of every 1 month	Until discontinued	
<input checked="" type="checkbox"/> Ferritin	Day 1 of every 1 month	Until discontinued	
Pheresis Treatment Orders			
<input checked="" type="checkbox"/> Phlebotomy therapeutic	Day 1 of every 1 month	Until discontinued	
Nursing Communication Orders			

Add to favorites

Therapeutic Phlebotomy Therapy Plans

Same instructions as for inpatient procedures.

- Outpatient notes EPIC instructions:** In EPIC, in patient chart click "Notes" (middle row, purple tab, not the same as the "Notes" tab that can be found under "Chart Review").
- In the upper row above the notes click on "New Note". A new window appears on the right.
- Create the note as early as possible and "pend" until procedure is complete/you can finish the note. It is more difficult to write a note when an encounter has been closed (i.e. patient has left the clinic and has been checked out in Epic).
- In the "Type" section type "Procedure".
- The date of service will default to today's date.
- Search for the appropriate attending's name in the "Cosigner" field.
- Type "Apheresis" into "Insert SmartText" section.
- A pop-up window will appear. Choose (double click or "Accept") "BW OUTP PHERESIS ASSESSMENT" for patient assessment or "BW IP PROC NPP PHERESIS" for procedure note.
- The template note will appear. Use F2 to navigate through and fill out the note.
- For the "Physical Exam" portion, include basic information gleaned from interaction with the patient—e.g. General, Head, Extremities, Skin.
- "Sign" the note when finished.

Procedure Notes in EPIC for inpatient procedures

The primary LMR **MUST** write procedure notes at the completion of all procedures they oversee the same day the procedure occurs as soon as possible, before leaving campus for the day on weekdays. **Notes must only be signed after the procedure is complete.** All notes must be signed by the attending on service. Use templates but customize to the patient since all smartphrases may not apply. **Remove/edit parts that are not applicable, inaccurate, or out of date.** **Do not just copy from previous notes.** Use the designated templates to ensure consistent service notes. Carefully review and update all information (attending on service, patient subjective, objective data and procedure details).

Step-By-Step EPIC instructions:

1. In EPIC, while in a patient chart click on “Notes”.
2. Click “Notes” tab.
3. Click on “New Note”, a new window appears on the right.
4. Type: “Procedures”
5. Service: “Pathology”
6. Date of Service: Date/Time procedure performed. Current date/time is prefilled.
7. Cosign required: check box, and select attending on service
8. Choose the appropriate template:
 - a. For therapeutic plasma exchanges: In the note box type “.BJHIPTPE” (BJH inpatient TPE)
 - b. For red cell exchanges: In the note box type “.BJHIPRCE” (BJH inpatient red cell exchange)
 - c. For depletion procedures (leukocytapheresis, thrombocytapheresis, and erythrocytapheresis): In the note box type “.BJHIPDEP” (BJH inpatient depletions)
 - d. For extracorporeal photopheresis: In the note box type “.BJHIPECP” (BJH inpatient ECP)
9. Complete each section of the note template. F2 advances through sections to be filled in. If you need to change a selection, right click on the selection and select “Reselect this Smartlist’s selection”. “***” requires text to replace it.
 - a. Indication for procedure: Select procedure type from drop down list.
 - Select appropriate indication (based on ASFA guidelines if possible)
 - b. Requesting attending: Fill in attending on service whose team requested the procedure
 - c. Summary:
 - Attending selection: Select attending from drop down list.
 - “(Name) is a (age) (gender) who requires...” select appropriate procedure.
 - d. History of present illness: relevant HPI with pertinent details for the apheresis request. Do not copy directly from other services’ notes.
 - Source(s) of info if not directly from patient (for instance, chart review)
 - Example “History obtained from chart review, patient unable to provide”
 - Patient initial presentation (why are they in the hospital)
 - Relevant past medical history (what else do we need to know for the procedure)
 - Summary of clinical course leading to apheresis request, including indication (why do they want apheresis)
 - Any other pertinent details to the patient and patient request

- Informed consent: document that it was obtained along with discussion of risks and benefits and opportunity for questions to be answered.
 - Daily update: Subjective part of a SOAP note – how is the patient doing, how has the patient changed since last procedure. Do not put information about the current procedure here.
- e. Past medical history and Past surgical history: automatically populates
- f. Laboratory and diagnostic data: {Recent labs:21974}, Cntl to select multiple
- Select labs pertinent to apheresis (latest CBC, BMP, Coags)
 - Select labs to display in the note: be specific and include labs reviewed
 - Press control to select multiple
 - Avoid long lists of extraneous information
 - Manually add any other pertinent labs (e.g. fibrinogen, LDH, haptoglobin)
- g. Plan: complete with the procedure performed
- Assessment: One or two sentence summary. Include goal set forth during the initial procedure discussion (include frequency, duration, goal to end or reassessment).
 - Plan: include the following information (look in flowsheet for reference):
 - Procedure details: include volume processed, replacement fluid type, end fluid balance, premedications given, amount of calcium given, any complications:
 - a. For Red cell exchange include the parameters used:
 - i. Starting hemoglobin S%, target hemoglobin S%, target hematocrit, FCR, RBC volume exchanged in mL and number of units transfused
 - b. Complications and management:
 - i. Complications: Include anything you evaluated during the procedure. Examples include vital sign changes, hypocalcemia, etc.
 - ii. To review the nursing procedure in EPIC: “Flowsheets” top tab, “Pheresis treatment” tab (use wrench function to add if needed)
 - iii. Management: include how each complication was managed
 - Next procedure: next planned procedure with dates (with year) if known
 - Mention any considerations relevant to procedure performed. Some examples:
 - If patient on ACE inhibitors: “Avoid ACE inhibitors for duration of treatment”
 - “Transient coagulopathy can occur with therapeutic plasma exchange performed with albumin replacement fluid”
 - “Therapeutic plasma exchange removes highly protein-bound drugs, please plan dosing accordingly”
 - If ECP performed: “Patients should avoid direct ultraviolet (UV) light exposure for 24 hours following extracorporeal photopheresis.”
 - Contact info: “Call Laboratory Medicine with questions 314-747-1320, option 1”
- h. ASFA Category: Enter appropriate ASFA category recommendations
- i. Complete the note: When ready, finalize the note, by clicking “Sign”.
- Pend and save work for later if needed
 - Edit after signing is possible if attending has not yet signed.

Outpatient Apheresis

Apheresis procedures performed in the outpatient apheresis center are usually supervised by nurse practitioners (NP), who are also responsible for inpatients receiving ECP for GVHD on North campus. The NPs stay until the last outpatient procedure is completed each day. LMRs cover the outpatient center if needed when the NPs are not available (should be arranged in advance). When covering the outpatient service, the LMR sees all patients, perform assessments, write notes, and place orders for the next day's procedures. The attending on service needs to sign the notes (exception: apheresis assessments). In addition to ECP, RBC exchange, TPE, and HPC collections there are some additional procedures that you will likely only encounter in the outpatient Apheresis Center.

HPC medical assessments: These are performed by the person covering the outpatient service (NPs or covering LMR). Obtain targeted patient history, explain apheresis and its risks, and obtain informed consent. Important issues for the history for autologous donors include diagnosis, previous treatment, especially a detailed chemotherapy history (often available in prior oncology clinic notes), current medications, including those that affect electrolytes, blood clotting and allergies, and other medical issues which may affect the collection (heart disease, kidney disease, lung disease, bleeding disorder). Patient characteristics to note include: whether the patient has any electrolyte abnormalities (K, Mg) or is taking diuretics, baseline peripheral neuropathies/neuropathic pain, access type, and if relevant, timing of placement, mobilization, collection goal (look under Oncology tab—Pheresis Plan). Write a concise note in the donor's chart. The informed consent provides guidance as to the apheresis risk requiring explanation. Common ones important to discuss include: infection, symptoms of hypocalcemia (paresthesias, N/V), and potential for platelet and/or blood loss necessitating transfusion. Explain hypocalcemia treatment with oral calcium or adjustment of IV infusion rate. The medical assessment schedule for the week can be found on the nurses' clipboard, with most appointments scheduled at 13:00 or later. For autologous PBSC, each donor will need to sign a storage agreement as well to store the cell therapy product frozen until use.

Donor Lymphocyte Infusions (DLI): Sometimes allogeneic donors return for collection of DLI's, which are given to previously transplanted patients who relapse to encourage graft vs. tumor effect. Although the target cells are CD3⁺ lymphocytes (not CD34⁺ HPCs), the apheresis procedure is the same (post-collection processing by the Cellular Therapy Lab is different). The usual DLI collection goal is 9×10^7 CD3⁺ cells. The Cellular Therapy Lab will divide and freeze the product into three aliquots (with 1, 3 and 5×10^7 CD3⁺ cells). If the BMT team also wants to collect CD34⁺ stem cells for a possible re-transplant, they may use mobilization.

Therapeutic phlebotomy: Patients receive this treatment regularly on an outpatient basis. The LMR is not involved in the oversight of the procedure, but will need to consent patients for initial treatment, obtain annual consent thereafter, and order the therapy plan (orders section). This should be done in a similarly other medical assessments (i.e. medical history, reviewing the consent form, and obtaining signature), and does require a note in the patient's chart.

The Blood Bank

The Blood Bank is covered by the primary transfusion medicine LMR. You will be called frequently by the blood bank regarding a variety of issues. In addition, there is a **logbook and LMR review tray** in the blood bank that you must check 2-3 times a day, containing "Attn. LMR" entries that alert things requiring investigation and resolution in the form of documentation in WEISky and the logbook. Most commonly, this will be for blood product transfusion reactions (see transfusion reaction section for more information).

Blood product approvals are a way to ensure transfused patients receive blood products appropriate for their clinical condition. The blood bank will call the LMR if an order falls outside of the blood bank's defined criteria for that patient. Sometimes these unusual requests are legitimate. Contact the clinical service and discuss the case as needed. If a request for a product is not indicated, offer appropriate alternatives (e.g., a bleeding patient with a platelet count of 35,000 and a normal PT/PTT needs platelets, not plasma). Always be diplomatic and professional. Do not refuse blood products without first discussing with your attending; your goal is to educate and provide guidance for appropriate transfusion. **If the clinical service insists on a product that you believe is clearly inappropriate and/or potentially unsafe, contact the attending.**

CMV-seronegative products are collected from donors who are CMV seronegative at time of donation. These products may be in short supply because most of the population (including donors) have been exposed to CMV in their lifetime and are seropositive. CMV seronegative blood products are typically reserved for neonates and CMV-negative transplant recipients. You may be asked to discuss with clinicians who want CMV-negative RBCs or platelets. An acceptable, "CMV-safe", alternative is CMV untested pre-storage leukoreduced (LR) blood products. Although a head-to-head RCT between CMV-negative and LR products has not been performed, available data does not show an increased risk of CMV transmission in LR products compared with CMV-negative blood. BJH now has a universally LR blood supply (PRBCs and SDPs), so the only non-LR products in inventory would potentially occur as a result of blood shortages when we have to accept other products from suppliers. Platelets treated with pathogen reduction technology (PRT) are considered an acceptable substitution for CMV-negative platelets. For this reason, CMV-seronegative products are no longer offered at BJH and SLCH (as well as the other hospitals in the BJC system).

Hemoglobin substitutes are sometimes requested by clinicians caring for patients who refuse blood or blood components. These products are only available for compassionate use, must be obtained by the pharmacy from the manufacturer, and typically require IRB approval. Refer the team to the pharmacy.

Special Product Request Guidelines

Patient population	Irradiated	Sickle-dex negative	Saline washed
Heme/Onc patient or BMT candidate with leukemia, MDS, aplastic anemia	X		
Neonates (<4 mo)	X		
Intrauterine transfusions	X	X	X
Sickle-cell disease		X	
Patients receiving blood from relative	X		
Confirmed IgA Deficient Patient			X

* Washed blood products are only acceptable for patients with a relative Ig A deficiency. Absolute IgA deficient patients (with a IgA level less than 0.05mg/dL and present IgA antibody) will require IgA deficient blood components. **This will require contacting the rare donor registry through the blood center.**

Fresh frozen plasma (FFP)/Plasma frozen within 24 hours after phlebotomy (PF24)

FFP is indicated to correct coagulation factor deficiencies for which no specific factor concentrate is available or emergent reversal of Coumadin (Warfarin) therapy, when 4-factor prothrombin complex concentrate (PCC/Kcentra) is unavailable (see Coagulation Factor Concentrates section).. Most plasma products transfused at BJH are collected as PF24 (interchangeable with FFP).

Guidelines for the prophylactic use of FFP in patients scheduled for surgery generally focus on PT values \geq 1.5 times the reference range midpoint. However, PT or aPTT are crude predictors of surgical bleeding and FFP timing and dose should be carefully considered. **For correction of PT before surgical procedures FFP should be given immediately before the surgery as several coagulation factors have very short half-lives (FVII has a half-life of 3 - 6 hours).**

Dosing: One unit of FFP is ~200 mL and contains all clotting factors at a concentration of ~1 U/mL. A typical dose is 10-15 mL/kg (3 - 4 units in an adult) which should increase coagulation factor ~20-30% immediately after transfusion. Frequently, 2 units FFP are ordered at a time, which is usually insufficient. Monitoring PT is critical to assess response. It is often impossible to completely correct the PT with FFP, due to: (1) the short half-life of Factor VII and (2) limits on tolerable FFP volume.

It takes 30 - 45 minutes to thaw FFP, but the blood bank always has thawed FFP units available for emergencies (\geq 2 type A (or AB) for trauma patients with unknown ABO type). The FDA-licensed product “FFP” outdates 24 hours after thawing when stored at 1-6°C. After thawing, the blood bank converts units to “thawed plasma” (TP), an unlicensed product which can be stored refrigerated for up to 5 days. During thawed storage, TP does begin to lose some labile factor activity, but the change is not usually clinically relevant, so TP is officially allowed as an appropriate substitute for FFP at BJH. So, while a clinician may order “FFP”, they are likely getting “TP”.

Below is the BJH warfarin reversal algorithm:

Reversal of Warfarin (adapted from BJH Tool Book 2016)	
Any INR < 4.5	No Risk Factors for Bleeding: Lower or hold 1 dose of warfarin; monitor
	Rapid Reversal for Surgery: Hold warfarin, give Vitamin K 2.5 mg PO or IV
INR 4.5-9	No Risk Factors for Bleeding: Hold warfarin; monitor
	Risk Factors for Bleeding: Hold warfarin and give Vitamin K 2.5 mg PO
	Rapid Reversal for Surgery: Hold warfarin and give Vitamin K 5 mg PO
INR > 9	Hold warfarin and give Vitamin K 2.5-5 mg PO. INR should be reduced within 24-48 hours. Give additional Vitamin K if necessary.
Serious or life-threatening bleed at any INR	Hold warfarin, give FFP, Prothrombin Complex Concentrate (PCC) Vit. K 5-10 mg slow IV infusion. IV Vitamin K may be repeated every 12 hours. Use 4-factor PCC* if rapid reversal needed for surgery

*Dosing for PCC (Kcentra) based on patient's weight (kg) and INR:

Pretreatment INR	2-<4	4-6	>6
Dose (units FIX/Kg)	25	35	50
Maximum dose	2500	3500	5000

Massive Transfusion Protocol (MTP)

BJH has 2 standardized massive transfusion protocol algorithms. The MTP involves the immediate and continued release of uncrossmatched blood products from the blood bank in a predefined ratio as follows:

Standard MTP:

Box 1: 10 Type O Emergency release RBC + 6 Type A FFP + 1 single donor platelet (SDP)

Box 2: 6 type specific RBC (or type O RBCs) + 6 type compatible FFP + 1 SDP

Box 3+: 6 type specific RBC (or type O RBCs) + 6 type compatible FFP + 1 SDP + 10 Units Cryo

Trauma MTP:

Box 1: 6 Units of whole blood*

Box 2+: same components as Standard MTP box

*blood will be low-[anti-A, anti-B]titer Group O, and may be Rh positive or negative

MTP boxes are prepared every 20 minutes as needed. The protocol must be activated and deactivated by a clinical attending physician. Occasionally, the primary LMR will be contacted to approve additional products with the boxes (e.g. extra SDP, cryo with box 1 or 2), or to contact the clinical team to see if the MTP can be canceled (i.e. they have stopped taking the boxes to the OR/unit).

Blood product wastage

Wastage occurs when a blood product was ordered but neither transfused nor returned in usable form to the blood bank. The blood bank may request follow-up. The blood bank will tell you the patient name, the product in question, and ordering physician name. Verify the listed products were actually wasted, since platelets and FFP are often returned to the blood bank, released into the general supply and then re-issued. Patient chart review should reveal the reason(s) that the product was not used after issue. If the documentation is missing or inadequate, then call the ordering physician to discuss the circumstances surrounding the blood product in question including why the product(s) was ordered and why the decision was made not to transfuse the product(s). Include your findings on the wastage form and let the Compliance Coordinator know the findings.

Platelets

Platelets are requested occasionally for a patient whose platelet count is above the 20,000/ μL threshold. With functional platelets, spontaneous bleeding does not generally occur in patients with platelet counts $>10,000/\mu\text{L}$ (the BMT service uses a platelet count of 10,000/ μL as their “trigger” for prophylactic inpatient platelet transfusion). Requests for platelets in patients with higher platelet counts often come from the CTICU for post-op cardiothoracic patients. The cardiac by-pass instrument causes platelets dysfunction and if there is active bleeding, platelet transfusion is indicated, even if platelet count $>100,000/\mu\text{L}$. The CTOR/CTICU represents a special case, because often patients have been, or will be placed on bypass and their core body temperature is low, resulting in potentially reduced platelet function and substantial quantitative deficiencies in coagulation proteins. Certain perioperative patients therefore may need platelets despite normal platelet counts. Bleeding patients with likely platelet dysfunction whether as a result of longer cardiopulmonary bypass duration, higher risk procedures (repeat or combined procedures), treatment with anti-platelet drugs (e.g. aspirin, irreversible agents like Plavix (Clopidogrel) or GPIIb-IIIa inhibitors) and/or anti-coagulants like direct IIa or Xa inhibitors, are also good candidates for platelet transfusion even with normal platelet counts. You may also encounter such patients on neurosurgery, where intracranial bleeds must be managed quickly, and the drug may still be in circulation.

BJH prophylactic platelet transfusion guidelines

Platelet count	Recommendation
< 10,000 (hospitalized patients)	Transfuse 1 SDP
< 20,000	Transfuse for central venous catheter placement
< 50,000	Transfuse for a moderately invasive procedure (e.g. LP)
<100,000	Transfuse for an invasive procedure (e.g. heart surgery or neurosurgery)

Pathogen Reduction Technology (PRT) Platelets

Our platelet inventory provided by ARC is collected by apheresis, and a significant majority is PRT platelets, specifically INTERCEPT® platelets. These have been incubated with amotosalen and exposed to UV irradiation to cause irreversible nucleic acid damage to most viruses,

bacteria, protozoa, fungi, parasites, and leukocytes. Viable pathogens are reduced by a minimum of 10^4 by this treatment. Notable pathogens not significantly affected are Hepatitis A, Parvovirus B19, and *Bacillus cereus* endospores. At BJH, **PRT platelets substitute for CMV-negative and irradiation, and contain 65% less donor plasma** (made from PAS platelets). The amotosalen-UV treatment does result in slight decreases in unit platelet counts (10-15%) and may result in more frequent platelet transfusions. PRT does not extend unit outdates to 7 days at present. Some HLA-compatible/matched products that are not PRT treated platelets may be sent from other ARC regions, and CMV-matching (if not leukoreduced) and irradiation may be necessary.

Platelet Inventory Management

Due to their short outdate, donor platelets are a relatively scarce resource. One of the most common calls you will receive from the blood bank is to approve the 3rd+ platelet units ordered on a patient within 24 hours. It may be appropriate to transfuse actively bleeding patients with >2 SDPs, but this requires some investigation into the scenario, and possible discussion of other alternatives with the clinical team. Sometimes the clinical team is trying to reach a specific threshold, which may not be realistic (see Platelet Refractoriness). There are many gray areas here; the only “wrong” answers are to approve additional platelets without due diligence, or to deny a transfusion without discussing the case with the transfusion attending (if unable to dissuade the ordering provider).

At certain times of the year our platelet usage can exceed the current supplies. The blood bank should call you if they have less than 15 SDPs available, which will initiate the platelet triaging process. When discussing low platelet inventory with the blood bank, ask:

- How many platelets do we actually have? Are any of those units reserved (HLA-matched)? Some special units may be released to the general pool if needed.
- When is the next expected delivery from the ARC and how many units are expected?
- Is there any unusual utilization of platelets in the hospital?
- Instruct the blood bank to contact the American Red Cross (ARC) and inquire when more platelets can be made available

Gather the above information and determine by midnight if there will be enough platelets available for morning surgeries. Often, additional platelets will be made available from ARC. **If not, talk to the attending on service.** If we cannot get more SDPs to meet the demand of platelet use in the hospital, your attending may potentially need to alert the On-call Anesthesiologist (314-749-6200) or the OR coordinator (314-362-4000), regarding the situation.

You may need to have frank discussions with the Neurosurgery service ordering multiple SDP units until PFA-100 results are completely normal despite large doses of aspirin or NSAIDs that morning. Ducruet AF, et al. (*Neurological Research* 2010;32:706-710) demonstrated no difference in clinical outcomes in using platelets for patients on aspirin with intracranial bleeds. Less published data is available to assess bleeding risk in this setting with the use of preoperative irreversible platelet inhibitors (Plavix, Prasugrel) or direct Xa or IIa inhibitors.

In BMT hospitalized patients (at low risk for trauma), literature supports a 10,000/ μ L threshold for prophylactic platelet transfusion (we usually target 20,000/ μ L for outpatients). There may not be enough SDPs for all the transplant patients <10,000/ μ L. In certain shortage situations, we may have to accept non-PRT platelets, for which donor and recipient CMV status will become relevant. They will need to prioritize based on need and who can accept LR, CMV untested units until inventory is restored.

The arbitrary threshold for most surgeries in non-bleeding patients is 50,000/ μ L platelets. Threshold for central line placement is usually 20,000/ μ L except in cases such as TTP. The 100,000/ μ L desired level for neurosurgery is equally "empiric."

If a bleeding patient's platelet count is >100,000/ μ L, you need to question if platelets are the issue. Consider other factors, such as low fibrinogen (may result in a less than expected coagulation effect from platelets), other lab tests (PT/INR/PTT, PFA-100, D-dimer) and other blood products (FFP or cryoprecipitate) if needed.

If you get a request for multiple SDPs on a patient, call the MD and inquire if there is active bleeding and severity to balance their need against your inventory. **Generally, never release more than two SDPs without requiring a platelet count be checked** again prior to releasing additional units.

One strategy for LMR handling of platelet triage:

1. Call attending to confirm you're starting to triage
2. Call Blood Bank (314) 362-3887 to do the following:
 - a. Instruct to hold all platelets; LMR to release on a case-by-case basis
 - b. Obtain a list of all patients with orders for platelets (full name, MRN, floor, order status) and create a spreadsheet to hold the data.
3. Call the floors and speak to the charge nurse. Explain that platelet inventory is very low and you are triaging until supply is replenished. Ask for their help with 2 things:
 - a. Ask for names/direct numbers for each provider (MD/NP) for the patients on that floor-add to your spreadsheet. Finish getting names and numbers from all floors before you start calling providers- you'll find that the same MD/NP may be covering patients on different floors.
 - b. Ask charge nurse to inform floor staff of low inventory and need for LMR review before platelets will be released for transfusion.
4. Call providers, prioritizing in order of acuity – actively bleeding patients regardless of location, then OR/CTICU/ED , then ICUs/BMT, then general floors
5. Explain the situation and that you are triaging to ensure we don't run out of platelets. Ask for their help determining the situation for their patients:
 - a. Status of each patient? Is transfusion for active bleeding vs prophylaxis?
 - b. Can prophylactic transfusions be delayed until the platelet inventory is replenished?
 - c. If a patient is bleeding and MD wants a unit, approve release of 1 unit and ask MD to reassess post-transfusion.

6. After running the list once, call BB:
 - a. Ask if any updates from ARC
 - b. Confirm current inventory minus released units
 - c. Get list of new platelet orders, and repeat as above
 - d. Call in to BB every 20 min or so to get batches of new orders
7. Once you have contacted all providers and released platelets as necessary, re-confirm platelet inventory and touch base with attending to determine whether you should start releasing platelets for bleeding prophylaxis. If you release a platelet unit that was initially deferred, call the MD to let them know.
8. Once platelet inventory is replenished, call all MDs, as needed to update

Platelet Refractoriness

In general, 1 unit of apheresis platelets should bump the platelet count by 30,000-50,000/ μ L. A more precise way to assess increment is the Corrected Count Increment (CCI):

$$CCI = \frac{(Post-tx \text{ Plt ct} - Pre-tx \text{ Plt ct}) \times BSA}{\text{Platelets transfused} \times 10^{11}}$$

BSA = the square root of the product of the height in cm and weight in kg, divided by 60.

"Normal" BSA is generally taken to be 1.7 m^2 for an adult

1 unit of SDP is assumed to contain 3×10^{11} platelets (denominator = 3)

The causes of platelet refractoriness is usually multifactorial. **A post-transfusion platelet count drawn 10-60 minutes after completion of transfusion is critical** to distinguish immunological from non-immunological causes. An acceptable CCI generally ranges from 5000 to 7500/ μ L. **Immune-mediated platelet refractoriness is defined** as a post-transfusion platelet CCI <5000/ μ L 1 hour after ABO-compatible platelet transfusions of SDP (apheresis platelets) following **two consecutive** transfusions. This is typically the result of alloantibodies binding to surface antigens and causing rapid clearance of donor platelets. Antibodies to class I HLA (HLA-A and B) are the most frequent cause for this while antibodies to human platelet antigens (HPA) are less common. Immune-mediated platelet refractoriness should be differentiated from increased platelet consumption that occurs in DIC, splenomegaly, bleeding or due to drugs, which typically cause a more gradual platelet decline (and may have normal CCIs).

Causes of platelet refractoriness

<u>Immune Causes</u>	<u>Non-immune Causes</u>
ABO antibodies	Massive bleeding
HLA antibodies	Fever/sepsis
Platelet-specific antibodies	Splenic sequestration
Drug-dependent antibodies	Allogeneic transplantation
	TTP
	DIC
	Medications
	Poor storage of platelets

Platelet expression of HLA: Normally only class I HLA molecules encoded by HLA-A and HLA-B genes are present in large amounts. HLA-C molecules are expressed at low levels and not implicated in platelet refractoriness. Antibodies to class II HLA molecules (DP, DQ, DR) are irrelevant to platelet transfusion.

ABO antigens and platelets: A and B antigen expression is variable on platelets. ABO-identical platelets have better survival; however, ABO compatible platelets are typically adequate, and inventory issues make providing ABO identical platelets to every patient impractical.

Relevant non-HLA, non-ABO antibodies:

- Human platelet antigens (HPAs), such as GPIIb/IIIa, GPIb/V/IX, and CD109

Diagnosis of Platelet Alloimmunization

1. Check the 10 minute to one-hour post transfusion platelet count. If a platelet count obtained 2 hours after transfusion may not represent alloimmunization.
2. For practical purposes an increment of <10,000/ μ L each (for a normal sized adult), in the absence of other factors (i.e. splenomegaly, DIC, bleeding or drugs) may be due to alloimmunization. A healthy adult with no additional risk factors should respond with an increase of 30,000-50,000 following a unit of platelets.
3. If no desirable platelet increment is achieved, confirm alloimmunization by having the floor order: **1) HLA Typing (HLA-A and B) and 2) HLA Antibody Screening by single-antigen bead assay (SAB) (Class I).** The turnaround time for these two tests is typically 1-2 business days. Methods for HLA typing and antibody screen are described in a later section.
4. Use the following instructions to help clinicians order appropriate testing for potential HLA refractoriness:
 - a. Under "Orders" search for "HLA".
 - b. A pop-up window will appear. Select "HLA Testing for transfusion support" (change to facility list if necessary).

HLA			Facility List
Order Sets, Panels, & Pathways		User Version Name	Type
	HLA Testing for Disease Association		Order Set
	HLA testing for Non-Renal Transplantation		Order Set
	HLA testing for Renal Transplantation		Order Set
	HLA Testing for transfusion support		Order Set

- c. A brief order set will appear. Expand “Inpatient” by clicking on it, then check the box for “Platelet Refractoriness”.
 - d. Check the boxes for “HLA Typing (HLA-A, HLA-B)” and “HLA Antibody Screen – SAB (Class I)”. Each of these will have 2 pre-checked orders associated with them—leave as is. HLA typing may be omitted if patient has already been typed.
5. If HLA antibodies are negative, and there is still high clinical suspicion of immune refractoriness, testing for HPA1 genotyping (phenotyping not useful for transfused, thrombocytopenic patients) or anti-platelet antibodies may be sent out to Versiti labs in Wisconsin. Note: **ARC will not provide HPA-1A negative platelets without laboratory confirmation** patient is negative for this antigen.

HLA Testing for transfusion support

Outpatient

Inpatient

Platelet refractoriness

HLA Typing (HLA-A, HLA-B)
Once (Routine), today at 2256, For 1 occurrence, Blood
Patient Category: Transfusion Support
Indication: Platelet refractoriness

Collection Task for HLA Typing 1
Once (Routine), today at 2256, For 1 occurrence, Blood

HLA Antibody Screen - SAB (Class I)
Once (Routine), today at 2256, For 1 occurrence, Blood
Patient Category: Transfusion Support
Indication: Platelet refractoriness

Collection Task for HLA Platelet Antibody Screen
Once (Routine), today at 2256, For 1 occurrence, Blood

TRALI Workup (Only Transfusion medicine physician can order)

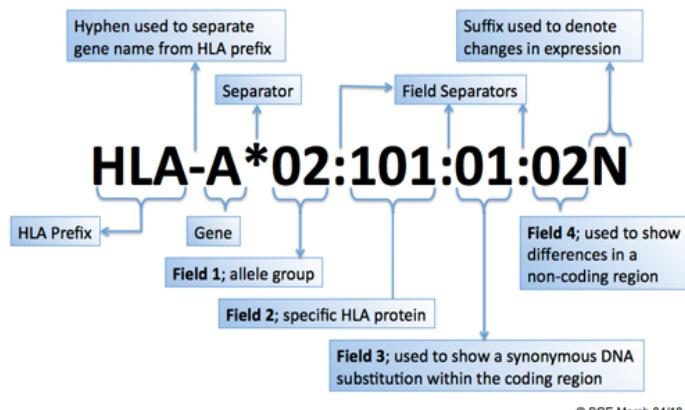
Management of platelet transfusion in the setting of alloimmunization

1. HLA compatible platelets/donors are first identified to avoid antigens to which antibodies are already detected in the patients. This is the minimum requirement. An analogy in red cell transfusion is that we always provide antigen-negative red cells to a recipient who already makes antibodies against that antigen.
2. Among HLA compatible platelet/donors, it is important to prioritize those fully or partially matched for HLA-A and -B antigens. This will theoretically lower the risk of further alloimmunization. However, matched units or donors are not always available.
3. The next best option is to match for CREG (cross-reactive groups) as per the table in the HLA section of this book. Antigens in the same CREG group share one or more public epitopes, and they are considered more similar than antigens in different CREG groups. However, the benefit of CREG matching has not been confirmed.
4. If HLA-matched or CREG-matched platelets are not available, antigen-negative compatible platelets/donors are still acceptable.

Logistics: Once immune-mediated platelet refractoriness and HLA antibodies have been established, talk with the doctor to establish whether or not the patient has any active bleeding or planned procedures which require a certain platelet count, upcoming chemo, etc. **Ask them to provide a specific number of units per week needed.** This number can and should be changed as patient needs change, but we need to provide specific instructions to ARC. You will need to fill out an HLA-matched platelet request form (obtain directly from Linda Huckelberry), submit to Linda Huckelberry or the charge technologist in the blood bank, and update it weekly on Wednesdays. When the order can be canceled, the primary LMR should provide the reason for ending the order and sign the form (at Linda's desk).

HLA Testing

HLA (human leukocyte antigen) molecules are extracellular membrane proteins responsible for antigen presentation to T-lymphocytes. They are the most polymorphic molecules known in humans and the principle barriers to allogeneic transplantation. HLA molecules can be broadly differentiated into two groups, Class I and Class II molecules. They are encoded by a cluster of genes on chromosome 6. HLA-A, -B, and -C encode the heavy chains of class I HLA proteins, and HLA-DRA/DRB1, -DQA/DQB1, and -DPA/DPB1 encode the alpha chains and beta chains of class II HLA proteins. HLA are expressed co-dominantly, so two different proteins are expressed from each heterozygous locus. The molecular nomenclature for HLA alleles is shown in the figure below. Check out this link for detailed explanation: (<http://hla.alleles.org/nomenclature/naming.html>).



HLA typing

HLA typing can be performed at low-intermediate or high resolution by molecular methods using genomic DNA from patients and donors. The BJH HLA lab performs low-intermediate resolution typing by a hybridization-based method on the Luminex platform (LABType). The indications include:

1. Platelet matching
2. TRALI work-up
3. Solid-organ transplantation patients (renal, heart, lung)
4. Some disease-associated studies (e.g. DQ2/DQ8 for celiac disease)

High-resolution typing is performed by next-generation sequencing (NGS) in the HLA lab. The indications include:

- a. Patients with hematologic malignancy being evaluated for allogeneic hematopoietic stem cell transplantation (HSCT)
- b. Related and unrelated allogeneic HSCT donors
- c. Solid-organ donors are typed at high-resolution to facilitate the assignment of donor-specific antibodies.
- d. Some disease-association studies (e.g. HLA-B*57:01 for abacavir hypersensitivity)

Specimen: HLA typing requires 10 mL of blood collected in an EDTA tube (lavender-top tube).

HLA Antibody Detection

Antibodies against HLA are detected by the single-antigen bead (SAB) assay on the Luminex platform. This is a semi-quantitative assay using a cutoff value of 2000 MFI (mean fluorescence intensity) to detect positive antibodies and determine the antibody specificities simultaneously. This cutoff value has an excellent negative predictive value for complement-dependent cytotoxicity (CDC) lymphocyte crossmatch and flow cytometric crossmatch. Positive antibodies detected by the SAB assay carries a higher risk if confirmed by CDC or flow cytometric crossmatches. This section focuses on the SAB assay, and CDC and flow crossmatch techniques will be covered during your HLA rotation.

When do we order SAB assay for a patient?

- a. In the pre-transplant setting, we use SAB assay to determine whether a patient has pre-formed donor-specific antibodies (DSA), hence an increased risk of acute graft rejection. This practice, also called virtual crossmatch, enables efficient allocation of organs from deceased donors to sensitized patients. Virtual crossmatch also allows preliminary evaluation of serological compatibility between a patient and living donor pair. Moreover, the breadth of sensitization in a transplant candidate can be quantified by entering the antibody specificities detected by SAB into an online calculator (<https://optn.transplant.hrsa.gov/resources/allocation-calculators/cpra-calculator/>) to obtain calculated PRA (cPRA, panel reactive antibody). cPRA (e.g. 90%) provides an estimation of the percentage of deceased organ donors that may be incompatible with a candidate. A cPRA of 90% means that 9/10 patients will be incompatible and a cPRA of 20% means that 2/10 patients will be incompatible.
- b. In the post-transplant setting, SAB assay is used to detect DSA for the diagnosis of antibody-mediated rejection (AMR). If the MFI values of DSAs are around 20,000 (approaching the upper limit of the assay) and apheresis is considered to treat the rejection, it is informative to perform a dilution study to determine whether the DSAs turn negative at 1:16 dilution. If not, a prolonged course of plasma exchange and escalation of immune suppression may be warranted.
- c. SAB assay is also used to detect HLA antibodies that may cause platelet refractoriness. Donors with the target antigen specificities are avoided. However, the 2000 cutoff has not been strictly validated for platelet refractoriness and may be too low. To increase the availability of units and donors for highly sensitized patients, it is a reasonable option to prioritize antibodies with MFI above 5000 or even 10,000 as suggested by data from Mayo Clinic (Blood 2016;128(22):1459).

Specimen: HLA antibody detection requires peripheral blood 10 mL serum collected in a clot tube (red-top tube).

In HLA antibody reports low risk antibodies have MFI of 1000 to 2000, moderate risk have MFI 2000-5000, and high risk have MFI greater than 5000.

Please note, in the HLA antibody screens for platelet refractoriness, the reported cPRA takes into account HLA-C antigens. HLA-C antigens as mentioned previously are minimally expressed

on platelets. To find the true cPRA for platelets with multiple HLA-C antibodies plug the moderate and high risk antibodies to HLA-A and –B into the cPRA calculator mentioned above.

HLA-Compatible/HLA-Matched Platelets

****(See corresponding section on Platelet Refractoriness)****

Platelet donors with specific HLA types are recruited when a patient with established platelet refractoriness and a positive HLA antibody screen. Once an **HLA type and HLA antibody screen** have been obtained for the patient, your job is to coordinate getting HLA-compatible/-matched platelet units to the patient. HLA-compatible/matched platelets are requested from the American Red Cross which will identify HLA-compatible or HLA-matched donors for the patient. A **compatible** platelet lacks HLA antigens for which the patient has confirmed antibodies and is often easier to obtain. A **matched** platelet expresses the same HLA antigens as the recipient; the best donor is a perfect match for all four HLA-A and HLA-B antigens (called a grade “A” match, uncommon). Refer to the match grade table below from the AABB Technical Manual.

Match Grade	Description	Examples of Donor Phenotypes for a Recipient Who Is A1, 3; B8, 27
A	4-antigen match	A1, 3; B8, 27
B1U	1 antigen unknown or blank	A1, –; B8, 27
B1X	1 cross-reactive group	A1, 3; B8, 7
B2UX	1 antigen blank and 1 cross-reactive	A1, –; B8, 7
C	1 mismatched antigen present	A1, 3; B8, 35
D	2 or more mismatched antigens present	A1, 32; B8, 35
R	Random	A2, 28; B7, 35

The LMR fills out the “Special Product Request” Form and submits it to the Blood Bank. The form is available directly from Linda Huckelberry in the Blood bank. Determine the number, frequency and selection of donors needed to meet the platelet requirements of the patient and update the form weekly or as soon as there is a change. This involves:

- 1. Estimating the patient’s platelet requirements:** This should be done early, with consultation between you and the team taking care of the patient. There is often no hard and fast answer to this question. Things to consider are whether the patient is actively bleeding, if the patient is headed for surgery, and how long the thrombocytopenia is expected to last. Acutely, it is not a bad idea to have a few extra units of specific platelets in the blood bank for emergencies. Once the patient is stabilized, the number of units ordered can be reduced, reducing the number of donors recruited.
- 2. Monitoring the blood bank HLA-matched platelet supply:** SDPs are good for five days post-collection, although they are unavailable for the first two days pending bacterial testing. Please be aware of the supply and demand for each patient. Each morning check to see if the patient received platelets overnight, how many units remain, and how many donors are scheduled over

the next few days. The special product request form should be updated weekly, or more frequently based on the changing needs of the patient. Platelet demand is monitored by the blood bank. As specific platelet units approach their expiration date, the blood bank should call you about giving them to the intended patient or releasing them into the general supply prior to expiration. If you find yourself releasing multiple units, you need to reevaluate the special product needs of that patient.

3. Evaluating the response to the specific platelet donations: Perhaps your most important role is ensuring that these HLA-compatible/matched platelets are actually benefiting the patient. Check daily platelet counts of the patients receiving these units and see if they respond improve with specific platelet units. Make sure a 10-minute or 1-hour post-transfusion count is obtained. If some units provide a bump in counts when others do not, it may be possible to further specify which HLA types are the most beneficial. Organizing these donations is a major effort for the blood bank personnel. When the transfusion outcome is not improving with the special products, it is important to verify whether the special products are truly antigen-negative (compatible) and what the match grades are.

4. Tracking products is done using the blood bank computer. In the electronic blood bank inventory, the transfusion status and expiration date is available for each blood product.

HLA cross-reacting groups (CREGs)

Antigens in the same CREG group share one or more public epitopes, and they are considered more similar than antigens in different CREG groups (see table below). Antigens may also have non-shared private epitopes that are unique to individual antigens. Each HLA molecule has multiple different epitopes, which causes the CREG groups to overlap sometimes, e.g. A28 appears in both the 10C group and 2C group.

Keep in mind that HLA antibodies are against epitopes not antigens. That means a serum sample with antibodies against the public epitope for a CREG will produce a distinctive reactivity pattern with all or most of the CREG members being reactive. Therefore, having some knowledge about the CREGs allows you to better understand and interpret the HLA antibody testing result. For example, if you see anti-A2, 34, 24, 68, 69, and B57, B58 on the report, this patient did not make 8 different antibodies against 8 different antigens, rather the antibody is probably binding public epitopes shared among antigens in the 2C group (see table below). Similarly, if you see positive antibodies against all/most of the Bw4 group antigens but not the Bw6 group members (see table below), it is almost certain that the patient was sensitized to the public epitope on Bw4 antigens, in which case it is appropriate to avoid exposure to donor antigens in the Bw4 group.

Table: HLA class I serologically defined cross-reactive groups (CREGs) based on the Rodey scheme (Blood. 2007;109:4064-4070)

1C	A1, 3, 9 (23, 24), 11, 29, 30, 31, 36, 80
10C	A10 (25, 26, 34, 66), 11, 28 (68, 69), 32, 33, 43, 74
2C	A2, 9 (23, 24), 28 (68, 69), B17 (57, 58)
5C	B5 (51, 52), 15 (62, 63, 75, 76, 77), 17 (57, 58), 18, 21 (49, 50), 35, 46, 53, 70 (71, 72), 73, 78
7C	B7, 8, 13, 22 (54, 55, 56), 27, 40 (60, 61), 41, 42, 47, 48, 59, 67, 81, 82
8C	B8, 14 (64, 65), 16 (38, 39), 18, 59, 67
12C	B12 (44, 45), 13, 21 (49, 50), 37, 40 (60, 61), 41, 47
Bw4	A23, 24, 25, 32, B13, 27, 37, 38, 44, 47, 49, 51, 52, 53, 57, 58, 59, 63, 77
Bw6	B7, 8, 18, 35, 39, 41, 42, 45, 46, 48, 50, 54, 55, 56, 60, 61, 62, 64, 65, 67, 71, 72, 73, 75, 76, 78, 81, 82

Granulocytes

Granulocytes are used for patients with neutropenic sepsis (i.e. with refractory life-threatening infections and ANC <500/ μ L) in the setting of aplastic anemia and chemotherapy, including patients undergoing bone marrow transplantation.

The LMR discusses the clinical decision to initiate granulocyte transfusions with the BMT team. Granulocyte request forms are submitted to the blood bank and subsequently forwarded to the American Red Cross (ARC). If the LMR receives a request for granulocytes over the weekend, the LMR may fax the request form to 362-1261 (or scan the request form and email it to the blood bank supervisor). **NOTE:** Verbal orders and email orders without the signed request form are **not** accepted. **The granulocyte request form is available directly from Linda Huckelberry.**

Granulocytes must be transfused within 24 hours of collection, but all attempts should be made to infuse within 6 hours of product collection due to the short viability of granulocytes ex vivo.

To avoid unnecessary recruitment of donors and/or wastage of products, the **LMR needs to confirm that granulocytes need to be obtained for a given recipient with daily communication** with the requesting service determining clinical necessity. A decision is required early in the day to enable the ARC to identify a donor for the following day. Ideally, **requests should be made by 7:30 am daily**. The request form needs to be updated daily as the recipient's condition can evolve rapidly. Granulocytes are commonly ordered at BJH for once daily transfusion x5 days.

Daily updates and communication with the clinical team regarding the medical necessity for continued granulocyte infusions are also essential to reduce unnecessary risk of donor exposure to dexamethasone or hespan (hetastarch; RBC sedimenting agent with colloid effects), and unnecessary donation of granulocytes with a reduction in the platelet collection pool. **If there is no longer a need for granulocytes, the LMR immediately contacts the blood bank, who will then notify the American Red Cross.**

Serologic issues related to granulocyte donations:

- Donations must be ABO and Rh compatible (granulocyte product Hct is 5-10%)
- Confirm with the Blood Bank that the patient has **no current or historical alloantibodies**.
- If patient has other Rh alloantibodies (anti-C or anti-E), collect from Rh negative donors.
- Granulocytes from CMV positive donors are acceptable, irrespective of the recipient's status, because the critical issue in these cases is the life-threatening neutropenic sepsis.

Additional regulatory issues:

- AABB requires that granulocyte units contain $\geq 1 \times 10^{10}$ granulocytes in $\geq 75\%$ of units tested.
- Granulocyte units are stored for up to 24 hours at 20-24°C without agitation. This necessitates special release of the product from the blood center before completion of infectious disease testing.
- Granulocyte units must be irradiated to prevent TA-GVHD.
- NO LEUKOREDUCTION FILTERS.

Transfusion Support for Hematopoietic Stem Cell Transplantation (HSCT)

A number of unique medical problems or adverse reactions may arise in the HSCT recipient prior to, during, and after engraftment, all of which need careful monitoring and management. Potential adverse reactions occur in response to: ABO incompatible transplants, red cell antigen alloimmunization, platelet refractoriness, and neutropenia.

Phases of Transplantation from transfusion medicine perspective

1. Pre-transplantation phase (recipient blood type)
2. Peri-transplantation phase – from time of pre-transplant chemotherapy until red blood cell engraftment (and patients have stable blood types)
3. Post-transplantation phase (donor blood type)

ABO incompatible transplants

There are 4 possible ABO combinations between the donor and recipient pair:

1. Compatible
2. Major incompatibility (recipient has antibodies against donor's red cell Ag)
3. Minor incompatibility (donor has antibodies against recipient's red cell Ag)
4. Bidirectional incompatibilities (both Major and Minor incompatibility)

Major incompatibility

- Recipient has antibodies against donor's RBC antigens, e.g. A donor and O recipient.
- To minimize the risk of hemolysis of ABO incompatible RBCs being infused with the graft, incompatible RBCs are removed with a target of incompatible RBCs of <20 mL.
- The continuous production of antibodies against donor red cell's antigens can cause delayed erythropoiesis (up to 3-4 months), delayed red cell engraftment (up to 40 days post transplantation), and red cell chimerism (up to several months, especially after non-myeloablative HSCT). In severe cases, a pure red cell aplasia can ensue.
- Refer to the table below for selecting blood products at different phases of the transplant.

Minor incompatibility

- Donor has antibodies against recipient's red cell antigens, e.g. O donor and A recipient
- A potential serious adverse reaction is acute hemolysis secondary to production of anti-A and/or anti-B against the recipient's red cells. In most cases, hemolysis is self-limited as recipient red cells are cleared from circulation.
- Removal of donor plasma from HPC product minimizes residual antibodies in the graft.
- DAT+ until all recipient's red cells have been cleared from circulation. An eluate should identify the antibody against the recipient's ABO antigen.
- Very severe and life-threatening hemolysis may require emergency RCE with replacement donor compatible red cells – discuss with covering attending physician and primary team.
- Refer to the table below for selecting blood products at different phases of the transplant.

Bidirectional incompatibility

- Has consequences of both major and minor incompatibilities.
- Processing of HPC product should include both red cell and plasma depletion.
- Choose O RBC, and AB plasma until DAT becomes negative and recipient isoagglutinins are not detectable on reverse type.
- Isoagglutinin half-lives: IgM – 5 days; IgG – 3 weeks.

Transfusion support for ABO incompatible HSCT patients during peri-transplantation phase

Recipient	Donor	RBC	1 st choice platelets	2 nd choice platelets	Plasma
O	O	O	O	A, B, AB	O, A, B, AB
O	A	O	A	AB, B, O	A, AB
O	B	O	B	AB, A, O	B, AB
O	AB	O	AB	A, B, O	AB
A	O	O	A	AB, B, O	A, AB
A	A	A	A	AB	A, AB
A	B	O	AB	A, B, O	AB
A	AB	A, O	AB	A, B, O	AB
B	O	O	B	AB, A, O	B, AB
B	A	O	AB	B, A, O	AB
B	B	B	B	AB	B, AB
B	AB	B, O	AB	B, A, O	AB
AB	O	O	AB	A, B, O	AB
AB	A	A, O	AB	A, B, O	AB
AB	B	B, O	AB	B, A, O	AB
AB	AB	AB, A, B, O	AB	A, B, O	AB

Note: This table is used as a guideline for selecting blood products for BMT patients from the initiation of chemotherapy until 1) recipient has a negative DAT and 2) anti-donor isoantibodies are undetectable. All blood products before this phase should be compatible with the recipient, and all blood products after this phase should be compatible with the donor.

Other considerations for transfusion support of HSCT patients

1. Irradiated blood products are transfused to prevent transfusion associated GVHD. PRT substitutes for irradiation for platelets.
- CMV-safe products are used for HSCT patients: CMV-seronegative products or PRT platelets should be provided to CMV-seronegative recipients who receive CMV-seronegative allotransplants. Pre-storage LR components and PRT components may be substituted for CMV seronegative components.

Transfusion support for ABO-incompatible renal transplant recipients

- Choose red cells which are ABO/Rh compatible with the recipient. The product should also have an anti-donor ABO titer <200 or saline washed red blood cells.
- Choose plasma and platelets according to the following table:

Recipient	Donor	Platelets/Plasma
O	A	A, AB
O	B	B, AB
O	AB	AB
A	B	AB
A	AB	AB
B	A	AB
B	AB	AB

Cryoprecipitate

Cryoprecipitate is manufactured by thawing fresh frozen plasma at 1-6°C and separating the insoluble fraction by centrifugation. The supernatant is called cryo-reduced plasma, or cryosupernatant plasma. Each pool of cryoprecipitate contains the following:

1. Fibrinogen (150-250 mg/bag)
2. Von Willebrand factor
3. Factor VIII (80-120 U/bag)
4. Factor XIII (40-60 U/bag)
5. Fibronectin

BJC protocol:

- 1st cryo dose is released upon order receipt
- LMR is contacted by BB staff for additional cryo order(s).

Cryoprecipitate is occasionally ordered for bleeding patients who actually need plasma (e.g if the physicians is attempting to correct a coagulopathy while giving less volume). Cryoprecipitate is not a concentrated form of FFP; it does not contain significant amounts of coagulation factors not listed above. Cryoprecipitate is indicated for bleeding patients with low fibrinogen levels, as seen in DIC. Cryoprecipitate derived from one unit of FFP is expected to raise an adult patient's fibrinogen level by ~7 mg/dL. Currently, all cryoprecipitate at BJH is received from the ARC pre-pooled in 5-unit pools, so orders must be in multiples of 5 units.

Checking the patient's fibrinogen level might be helpful prior to cryoprecipitate transfusion; in the absence of data, the starting dose is 10 units. This dose has a volume of 100-150 mL and contains

approximately 2g of fibrinogen and at least 800 U Factor VIII. Note that the CTICU often gives cryoprecipitate to profusely bleeding patients empirically, and this may be reasonable in the circumstances they encounter. Medical judgment should be made on an individual basis. Currently, Humate P, a factor VIII and von Willebrand factor concentrate is used for Von Willebrand disease.

RhIg (Rh immune globulin, a.k.a. Rhogam)

One vial of RhIg is usually given intramuscularly (IM) and contains 300 µg of anti-D, a dose sufficient to “neutralize” 15 mL of D-positive packed RBCs or 30 mL of whole blood. The purpose is to prevent alloimmunization against the D-antigen. This is particularly important for women of child-bearing age, as it puts their future pregnancies at risk for hemolytic disease of the fetus and newborn (HDN). For men and older women, the main complication of D-alloimmunization is possible delays in obtaining compatible blood due to workup of positive antibody screens or during blood shortages (only 15% of the general population is D-negative).

Fetal-maternal hemorrhage

Either during pregnancy (in a D-negative woman) or delivery (in a D-negative woman delivering a D-positive baby), is an indication for RhIg administration in the **absence of current/historical allo-anti-D**. RhIg may also be given to pregnant D-negative women following D&C, amniocentesis, and trauma. RhIg is ideally given within 72 hours of exposure to fetal D antigen.

One vial of RhIg is administered at the 28-week prenatal visit, and one vial is administered once the baby is confirmed as D-positive following delivery. The need for additional doses of RhIg is assessed by a qualitative test for the presence of D antigen in maternal blood, called a "**Fetal screen**", or "**Rosette test**". This test involves first incubating a red cell suspension from the mother with reagent anti-D. The antibody will coat any RhD-positive fetal cells present. The suspension is then washed to remove unbound anti-D. Instead of adding Coombs serum to the washed cells, a suspension of D-positive indicator cells is then added, attaching to the antibodies already coating the RhD-positive fetal red blood cells. The mixture is then centrifuged and examined microscopically for rosettes formed by the RhD-positive indicator cells surrounding the antibody-coated fetal RBCs. The presence of even one rosette per 3 low-power fields constitutes a positive result and indicates the presence of RhD-positive red cells in significant numbers in the maternal blood. The number of clumps observed may be influenced by several variables and should not be used as a means of quantifying the amount of fetal blood in the maternal circulation. This is only a qualitative test. If this test is negative, no further action is needed, and one vial of RhIg is sufficient.

If the screening test is positive, a quantitative test is done by the Hematology Lab. Historically, this was the **Kleihauer-Betke (K-B)** acid elution technique (still done on nights and weekends, to be followed by the flow cytometry fetal RBC test the next working day), but this has now been replaced with the more precise flow cytometric determination of HbF-positive cells during the week. Either test determines the volume of fetal-maternal hemorrhage and thus can be used to estimate the amount of RhIg needed to prevent alloimmunization. The hematology lab will

do a STAT K-B test without LMR approval, when ordered from the ER or Labor and Delivery unit. This test is useful not only for Rh incompatibility but also for pregnant women with trauma or bleeding for assessment of fetal-maternal bleeds.

To calculate the number of vials of RhIg required, the following formula is used:

Number vials RhIg required = [% fetal red cells]/100 x [maternal blood volume (mL)] / 30*, rounded to nearest integer, + 1**

* 30 mL = amount of fetal whole blood neutralized per vial

** round up if decimal point is ≥ 0.5

For example, if flow cytometry or K-B result is 1.3% with maternal BV = 5000mL, $1.3/100 \times 5000/30 = 2.17$, round down to 2, then add one, so give 3 vials RhIg.

RhD exposure from Single Donor Platelets (SDPs)

RhIg may be indicated when a D-negative woman of child-bearing age has received D-positive platelets when no D-negative platelets were available (each platelet may contain up to 2mL donor RBCs). Should this be necessary in case of a severe platelet shortage, the attending physician is to be consulted and it is absolutely necessary for RhIg to be given as alloimmunization prophylaxis. In these cases, notify the patient's house staff. Explain that apheresis platelet units contain a very small volume of RBCs, and the D antigen is highly immunogenic. If the patient is not immunosuppressed then RhIg should be recommended. If the clinical team thinks it is necessary they should order 1 vial of RhIG.

Note: If an D-negative woman of child-bearing age is given a D-positive RBC unit, please discuss with attending as one may consider the risk/benefit of RBC exchange followed by RhIg

D-negative HSCT patients who received a D-positive HSCT do not require RhIg administration, as they will be producing D-positive RBCs from their transplanted stem cells. In general, oncology and HSCT patients have been found extremely unlikely to mount an antibody response to D-positive platelets and therefore do not require RhIg.

Before recommending RhIg, check the patient's type & screen. If they have a circulating anti-D antibody, they may not need RhIg (already sensitized, or received RhIg recently). If they already have an anti-D they do not need RhIg. If they have received RhIg recently, determine whether they need another dose. If anti-D is detectable, there is no need for another dose. Theoretically 1 dose of RhIg provides coverage for 6 units of Rh-positive platelets administered over 1-2 months. Sometimes RhIg is given subcutaneously, in contrast to the manufacturer's recommendation and in the absence of data on efficacy. This may be done because the patients are often still thrombocytopenic, and the IM route has the risk of producing hematomas. The RhIg product should never be used IV.

WinRho (RhD Immuno Globulin Intravenous)

WinRho is an IV preparation that can be used if the IM route is deemed too risky. This preparation is FDA approved for IV use, but there is a risk of an anaphylaxis (all products contain small quantities of IgA) or severe systemic reaction due to antibody aggregation and complement activation.

WinRho is also very costly. The product potency is expressed in international units by comparison to the World Health Organization (WHO) standard. A 1,500 International Unit [IU] (300 µg) vial contains sufficient anti-D to effectively suppress the immunizing potential of approximately 17 ml of D-positive RBCs. WinRho is also FDA-approved for treatment of ITP in D-positive individuals.

In Utero Umbilical Cord Blood Specimens

These are relatively uncommon, but intense interventions which can generate urgent calls for advice on diagnostic test selection, how to order tests, sample collection, processing and transport, and turnaround time. They are accessioned to the **mother's** BJH patient record, but visible in the baby's chart. These samples cannot be "redrawn". Give them and the ordering clinician your immediate, full attention, and call the appropriate laboratory director with questions and concerns. Testing to be performed at St. Louis Children's Hospital (SLCH) must go thru BJH customer service and is handled like a "send out". If taken directly to SLCH, the sample will be returned to BJH, causing delayed testing and risking specimen loss or contamination.

Red Blood Cell Antigens and Antibodies

RBC antigen frequency and clinical significance

A major goal of blood bank testing is to identify unexpected RBC antibodies. The blood bank may call you when the floor is requesting blood for a patient with a new antibody. Facilitate communication between the blood bank and the primary physicians regarding the clinical significance of the antibody and how long it may take to find compatible RBC units. Time required to find an antigen-negative unit depends primarily on antigen frequency in the donor population.

To calculate number of units that have to be screened to find compatible blood:

$$\text{# units to be screened} = \text{number of units ordered} / \text{frequency of antigen negative units}$$

Example: ~75% of RBC units are positive for Jk^a; the blood bank would have to screen 4 units on average to find one that is Jk^a-negative ($1/0.25 = 4$). If you need two units negative for both Jk^a and E; ($2 / (0.25 \times 0.70) = 11.4$), so 11-12 units will need to be screened.

ABO phenotype frequencies (A₂ is ~20% of all A)

Phenotype	Epitope	White	Black	Asian
A1	A, A1	34%	19%	27%
A2	A	10%	8%	rare
A1B	A,A1,B	3%	3%	5%
A2B	A,B	1%	1%	rare
B	B	9%	19%	25%
O	O	44%	49%	43%

Haplotypes of the Rh system

Haplotype			Frequencies in the US population			
Fisher	Race	Wiener	White	Black	Native American	Asian
Dce	R ⁰	Rh ₀	0.04	0.44	0.02	0.03
DCe	R ¹	Rh ₁	0.42	0.17	0.44	0.7
DcE	R ²	Rh ₂	0.14	0.11	0.34	0.21
DCE	R ^Z	Rh _Z	<0.01	<0.01	0.06	0.01
dce	r	rh	0.37	0.26	0.11	0.03
dCe	r'	rh'	0.02	0.02	0.02	0.02
dcE	r"	rh"	0.01	<0.01	0.01	<0.01
dCE	r ^y	rh _y	<0.01	<0.01	<0.01	<0.01

Notes:

1. Many Black recipients will lack both the C and E antigens (all of those who are R⁰R⁰, R⁰r, and rr will lack both of these), thus it is common for these recipients to have previously made anti-C and/or anti-E if they have been transfused previously. Units in the donor blood supply which lack both C and E are easier to find in D-negative units, as the majority of the donor supply is from White donors.
2. The overwhelming majority of Asians will be D-positive.

Functional Roles of Molecules Carrying Red Blood Cell Antigens

Blood Group Name	Number	Function
ABO	001	Glycosyltransferase
MNS	002	M, N: glycophorin A; S,s: glycophorin B
P1	003	Glycolipid (also serves as the receptor for <i>Parvovirus B19</i>)
Rh	004	NH ₄ Transport
Lutheran	005	Adhesion
Kell	006	Endopeptidase
Lewis	007	Fucosyltransferase
Duffy	008	Chemokine receptor although no clear signal transduction, receptor for <i>P. vivax</i> , CD234
Kidd	009	RBC Urea transport
Diego	010	Anion transport; links to cytoskeleton
Cartwright (Yt)	011	Acetylcholinesterase
Xg	012	Adhesion
Scianna	013	Unknown
Dombrock	014	Unknown
Colton	015	Aquaporin
Landsteiner-Wiener	016	Adhesion
Chido/Rodgers	017	Complement activation (C4A and C4B complement components, acquired from plasma by RBC)
Hh	018	Fucosyltransferase
Kx	019	Transport
Gerbich	020	Forms glycocalyx, links to cytoskeleton, glycophorin C & D
Cromer	021	CD55/DAF
Knops	022	Complement receptor (CR1, CD35)
Indian	023	Hyaluronate binding, CD44
OK	024	CD147
RAPH	025	MER2
JMH	026	CD108
I	027	GlcNAc transferase
Globoside	028	Ga1NAc transferase
GIL	029	Water channel

RBC Antigen/Antibody Quick Summary

Blood Group System	Antibody	Ig Class	Common reaction mode			Manner of Exposure		Clinical significance		% blood compatibility (% antigen negative)	
			RT	37C	AHG	Natural (stimulus unknown)	Immune (transfusion/pregnancy)	Transfusion reaction	HDFN	Caucasian	African American
Rh	D	IgG		X	X	Unlikely	Yes	Yes	Yes	15	8
	C	IgG		X	X	Unlikely	Yes	Yes	Yes	30	68
	E	IgG		X	X	Occasional	Yes	Yes	Yes	70	78
	c	IgG		X	X	Unlikely	Yes	Yes	Yes	20	1
	e	IgG		X	X	Unlikely	Yes	Yes	Yes	2	2
	f	IgG		X	X	Unlikely	Yes	Yes	Yes	35	8
	Cw	IgG		X	X	Occasional	Yes	Yes	Yes	98	100
Kell	K	IgG			X	Unlikely	Yes	Yes	Yes	91	97
	k	IgG			X	Unlikely	Yes	Yes	Yes	0.2	<0.1
	Kpa ^a	IgG			X	Unlikely	Yes	Yes	Yes	98	>99
	Kpb ^b	IgG			X	Unlikely	Yes	Yes	Yes	<0.1	<0.1
	Js ^a	IgG			X	Unlikely	Yes	Yes	Yes	>99	81
	Js ^b	IgG			X	Unlikely	Yes	Yes	Yes	<0.1	1
Duffy	Fy ^a	IgG			X	Unlikely	Yes	Yes	Yes	34	90
	Fy ^b	IgG			X	Unlikely	Yes	Yes	yes	17	77
Kidd	Jk ^a	IgG, IgM			X	Unlikely	Yes	Yes	Yes	23	9
	Jk ^b	IgG, IgM			X	Unlikely	Yes	Yes	Yes	28	52
Lewis	Le ^a	IgM	X	X	X	Yes	Unlikely	Rare	No	78	77
	Le ^b	IgM	X	X	X	Yes	Unlikely	Rare	No	28	45
MNS	M	IgM, IgG	X	X		Yes	Unlikely	Few	Rare, IgG	22	30
	N	IgM	X	X		Yes	Unlikely	Rare	Rare	28	26
	S	IgG				Unlikely	Yes	Yes	Yes	44	69
	s	IgG				Unlikely	Yes	Yes	Yes	11	3
	U	IgG				Unlikely	Yes	Yes	<0.1		1
P Globoside	P1	IgM	X	X		Yes	Unlikely	Rare	No	21	6
	P	IgM	X	X		Yes	Unlikely	Probable	Yes	<0.1	<0.1
	P+P1+Pk	IgG, IgM	X	X		Yes	Yes	Probable	Yes	<0.1	<0.1
Lutheran	Lu ^a	IgM	X	X		Yes	Yes	No	Rare	92	96
	Lu ^b	IgG				Unlikely	Yes	Yes	Mild	<0.1	<0.1

Cold Autoagglutinin (CA) and Thermal Amplitude Tests

CA testing needs LMR approval if DAT is **not** positive (for complement component C3) and when requested by a clinician, but not when initiated by the blood bank as a part of an antibody identification workup. Most individuals have benign cold IgM autoantibodies of anti-I and anti-i specificity that do not react at body temperature. Cold agglutinin disease, i.e., cold autoimmune hemolytic anemia, results when auto-anti-I or, less commonly, anti-i are of high titer and broad thermal range up to $\geq 30\text{-}32^\circ\text{C}$. Auto-anti-I is associated with *Mycoplasma* infection, and auto-anti-i is associated with EBV. Cold agglutinin (CA) titers of <64 are considered normal. Titers >64 are considered elevated although hemolytic anemia due to CA is rarely seen with titers <1000. The ability of the autoantibodies to react at temperatures close to 30°C might be evidence of its clinical significance (regardless of the CA titer), as skin temperature can drop to 30°C in cold weather resulting in CA hemolytic anemia. Cold agglutinins may also be of relevance to surgeries, especially cardiothoracic surgery. A positive DAT-C3 is very sensitive for clinically relevant CAs, and thus CA testing should be discouraged when the DAT-C3 is negative or not performed.

NOTE: Cold agglutinins are not cryoglobulins. Cryoglobulins are IgM immunoglobulins that, in the cold, precipitate from solution. Clinical presentation of cryoglobulinemia is highly variable, but usually involves immune-complex mediated vasculitis of skin, joints, kidneys etc. The immunology lab offers a test for cryoglobulins.

There are four different CA procedures in the blood bank:

1. **Cold Agglutinin Screen**- A 1:64 dilution of patient's plasma is incubated with a "trio" screening cell and incubated in an ice bath (0 to 4°C) for 60 min. Read macro- and microscopically for agglutination. Resulted as either positive or negative.
2. **Cold Study** may be requested when the CA screen is positive to determine the specificity of the CA. Patient's plasma is tested against several different cells; a) three screening cells (the "trio"), b) I antigen neg panel cells, c) warm washed autologous cells, d) washed cord blood cells (i positive), and e) cells expressing the same ABO antigen(s) as the patient. Incubated for 30 min at RT and in an ice bath.
3. **Cold Antibody Titration** may be requested to determine the strength of the CA. Serial two-fold dilutions of the patient's plasma are prepared (up to 2048) and tested against adult cells, cord cells, and autologous cells. Incubated in an ice bath for 60 minutes.
4. **Thermal Amplitude Study** is a screen that involves testing the patient's plasma against "trio" red cells, cord cells, and autologous cells at 37°C, 30°C, RT and 4°C for 30 minutes. Incubation at 15 to 18°C may be requested and is appropriate for CT surgery cases ("cold surgery"). A full study involves testing two-fold serial dilutions, each at different temperatures. *Note: reactivity at "warm" temperatures is suggestive of clinical significance.

Blood bank interpretive reports

Blood bank interpretative reports allow for the synthesis of information about a patient's new antibody in clinical context. Information in the report includes patient's relevant transfusion history, results of the testing performed, clinical relevance (potential to cause hemolytic transfusion reactions or hemolytic disease of the fetus and newborn) and therapeutic relevance (how difficult it might be to find compatible units, additional time needed for testing).

A few important notes about blood bank reports:

1. **Original blood bank panels and folders MUST NEVER leave the blood bank.**
2. **Review only the folders that are in the LMR review basket.** Blood bank folders are reviewed by blood bank staff before they are placed in the "LMR review" basket. Some workups might take longer to go through the review process.
3. **Do not write on the original blood bank folders, sheets or panels.** These are official documents that are part of the patient record, and it might be necessary to go back to the original work. If you want to practice cross outs, make a copy for mark up.
4. **Familiarize yourself with Softtech** (where all SOPs are kept electronically), where you will be able to find many answers regarding current BJH blood bank practices
5. **Interpretive reports are written only for new antibodies found in patients for the first time in the BJH system.**

6. These templates are expected to be customized within the note if needed. If you have questions, ask the attending. Please do not build new templates. Check with Dr. Thibodeaux, so consistency can be ensured throughout the process.
7. Resources can be found in WUSTLBox → LGM → Transfusion-Blood Bank → Blood bank interpretative reports resources folder and in the BB at the trainee workspace.

Handoffs and responsibilities:

Trainees:

- Trainee on the secondary service is responsible for reviewing and writing interpretative reports. If the trainee on service needs to function as primary, then the backup trainee will be responsible for reviewing and writing reports. If this is not possible, then the reports will go to the next day.
- Cutoff for writing new reports is 3pm, to allow for reports to be finished in a timely manner. Anything coming in after 3pm will be interpreted on the next working day.

Attendings:

- Assign notes to the attending on service for that week, until 3pm on Fridays. Assign reports starting on Friday after 3pm to the attending that starts the following Monday.

General timeline of result to finalized report in EPIC (exceptions are expected)

	Day 0	Day 1	Day 2	Day 3
Trainee	Report in BB bin	Review and interpret result/report		Ensure completed reports filed in BB
Attending			Review and interpret result/report	

Reviewing Results In Person In The Blood Bank

Trainees perform their blood bank interpretive report activities at a designated computer station in the blood bank.

Folders to be reviewed are placed in a set of bins in the back of the blood bank near the reference bench. Once the entire blood bank review process is complete, trainees can review and write reports. (**The original folder contents must remain in the blood bank at all times-If needed outside blood bank, make a copy**).

1. “LMR review” basket: reports that are ready for trainee review
2. “Reports requiring interpretation”: folders that require an interpretation note in EPIC
3. “To be filed”: folders have been reviewed/interpreted, ready to be filed by blood bank staff

Workflow for physical review of reports:

- In the blood bank, get the folders in the “LMR Review” basket.
- Review the most recent profile sheet (see example profile sheet)

- Patient information (including date of specimen, history of antibodies, and history of transfusion if known) - confirmation of transfusion history might be needed as it sometimes is requested as part of the workup
- ABO/Rh typing
- Antibody screen
- Antibody ID
- DAT
- Eluate
- Antibody titer
- Additional testing
- Conclusions and comments
- Review the panels associated with the profile sheet to familiarize yourself to patterns

Determination of whether a report needs to be written

A report is indicated for all new antibodies. A report is not indicated if there is evidence of this antibody being reported in our system prior to this test result (historical antibody before October 2020). Determination of this is critical before writing a report.

Scenarios not requiring a report

- If the section lists historical antibodies found in the BJH system that matches the antibodies listed in the conclusion section, then no report is needed.

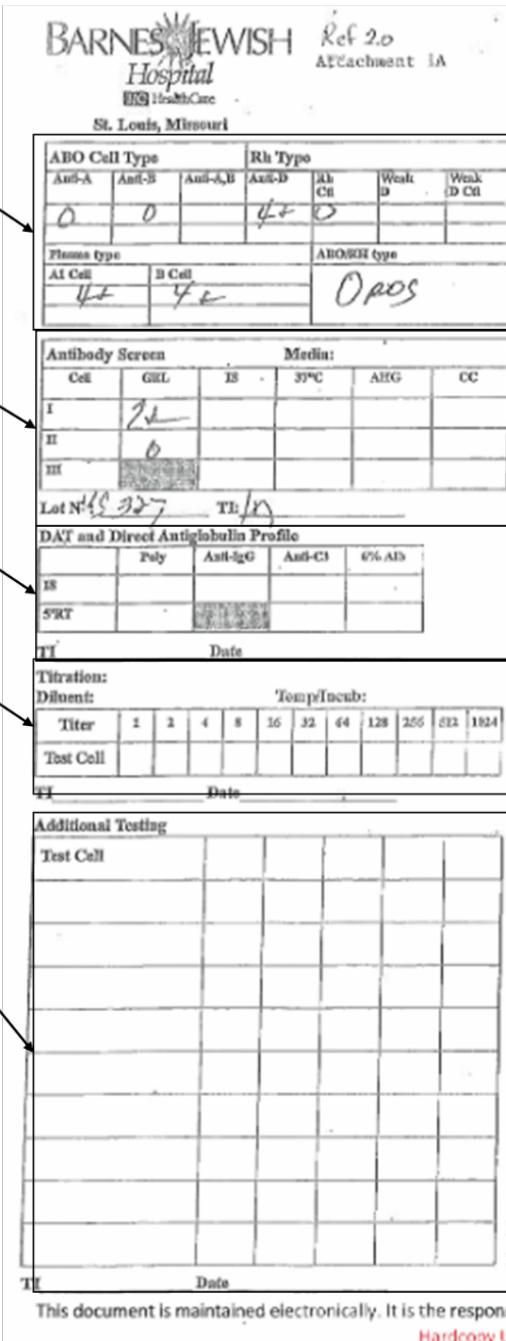
Scenarios requiring a report

- New antibodies reported for the first time in the BJH system
- Historical antibodies from other systems reported for the first time in the BJH system

Determination of whether a report needs to be written in EPIC

A report is indicated for all new antibodies reported for the first time in the BJH system. A report is not indicated if there is evidence of this antibody being reported at BJH prior to this test result (historical antibody). **Determination of this is critical before writing a report.**

Example of patient blood bank profile sheet:

<div style="border: 1px solid black; padding: 5px; display: inline-block;">ABO/Rh typing results</div>	 <p>This document is a Barnes-Jewish Hospital Blood Bank Profile Sheet. It includes sections for ABO/Rh typing, antibody screen, DAT, antibody titer, and other testing. Arrows from the left side point to specific sections: ABO/Rh typing results points to the ABO Cell Type and Rh Type tables; Antibody screen results points to the Antibody Screen table; DAT results points to the DAT and Direct Antiglobulin Profile table; Antibody titer points to the Titration table; and Other testing points to the Additional Testing table.</p>	<div style="border: 1px solid black; padding: 5px; display: inline-block;">Patient info: including date to use for reports, history of transfusion if known, and antibody history</div>																												
		<div style="border: 1px solid black; padding: 5px; display: inline-block;">REFERENCE PROFILE SHEET</div>																												
<div style="border: 1px solid black; padding: 5px; display: inline-block; width: 100%;"> <p>Patient Name: Ref 2.0 SP 00001 Blood Bank: B 11/09/13 0723 MRN: 5/8 Birthdate: 14327 Sex: Accession No: 8 102 884 85 0 887348 T 0 001 404 Locator No: 33333 101 F DR. 300000 2000 T Sample Date: Test Date: Diagnosis: Med: _____ Pregnancy: Number: _____ Transfusion History: unknown Blood Requested: Number of Units: _____ RN/MD: Patient Location: _____ Antibody History: New PT</p> </div>																														
		<div style="border: 1px solid black; padding: 5px; display: inline-block; width: 100%;"> <p>Eluate</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>Eluate Test</th> <th>37°C</th> <th>IgG</th> <th></th> </tr> <tr> <th>Cell</th> <th>Eluate</th> <th>Last Wash</th> <th>No. of Drops</th> </tr> </thead> <tbody> <tr> <td>I</td> <td></td> <td></td> <td>Elu-Kit</td> </tr> <tr> <td>II</td> <td></td> <td></td> <td>Lot No:</td> </tr> <tr> <td>III</td> <td></td> <td></td> <td></td> </tr> <tr> <td>A1</td> <td></td> <td></td> <td>Tech:</td> </tr> <tr> <td>B</td> <td></td> <td></td> <td>Date:</td> </tr> </tbody> </table> <p>Conclusion:</p> <hr/> <hr/> <hr/> <hr/> <p>Comments:</p> <hr/> <hr/> <hr/> </div>	Eluate Test	37°C	IgG		Cell	Eluate	Last Wash	No. of Drops	I			Elu-Kit	II			Lot No:	III				A1			Tech:	B			Date:
Eluate Test	37°C	IgG																												
Cell	Eluate	Last Wash	No. of Drops																											
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Historical antibody not requiring a report (evidence of this antibody already in the BJH system)

To find information regarding Blood bank antibody history in EPIC:

- go to “labs” → “blood bank” to bring up the blood bank testing results
 - **CRITICAL STEP** - To ensure you have checked all available results, go to result review→ at the top click the box “all rows”, highlight all rows under blood bank header, right click and select “dates and rows” to load all results.
 - If there is evidence of this antibody being resulted in the BJH system prior to this result, no report is needed.
- To check if a note has been written already, go to the search function at the top right of the page while in the patient chart. Type “antibody” or “Transfusion Medicine Blood Bank” and review the notes tab to see if there is a note already written on the antibody in question.
 - If there is a note on the antibody in question already, no note is written
 - If there is no note on the antibody in question, write a note.

To find information on patient antibody history in the folder:

- Review the top sheet, in the right column there is a section labeled “antibody history”, where the technologists will note any antibody history that is known at the time of review.
- This should not replace looking in the patient chart in EPIC to confirm antibody history and/or presence of a note

To check if there are results available at outside hospitals accessible through EPIC:

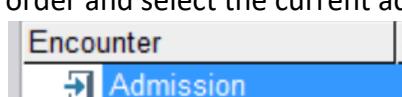
- Click on the Care Everywhere tab if available
 - For each health system check the “Lab Results” green button
 - Look in lab results for sections similar to (will be different for each institution) “Blood Bank”/“Blood Type”/“Transfusions” for identified antibodies
- Even if you find results, if they are not in the BJH system, you will write a note

New antibody requiring a report – there is no evidence of antibody being reported in the BJH system according to the above process

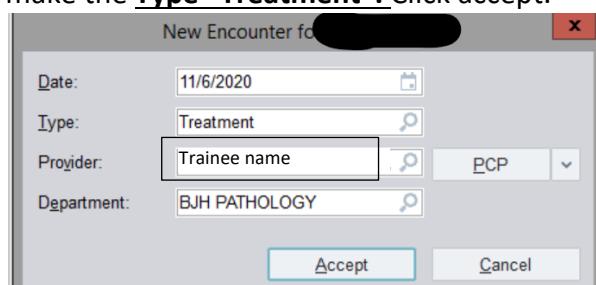
Writing A Report Once Indication Has Been Determined

Determine if this is an inpatient or outpatient encounter. Look up the patient in Epic with “Patient Lookup” Function. Inpatients will have a unit and room location in their information.

- If inpatient:
 - Go to the “Select Encounter” tab, confirm the admission during the type and screen order and select the current admission
- If outpatient:
 - Go to the “Select Encounter” tab, directly under the select encounter tab, click on the “New Encounter”button

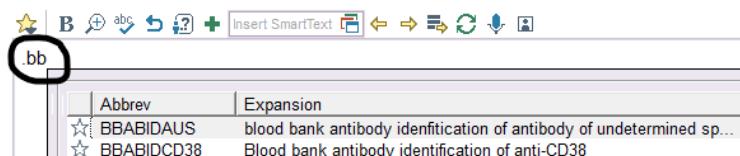


- In the resulting “New Encounter” pop up, make sure department is Pathology and make the **Type “Treatment”**. Click accept.



Once you are in an Encounter, make a new note

- Click on “notes” tab”, click on “new note”
 - “Type”: Progress Notes
 - “Service”: Pathology
 - Date of Service: date of the note, **NOT** the date of the test, defaults to current date/time
 - Cosign required: check box
 - Cosigner: select attending on service
- Use the “smarttext” function by entering “.bb” to bring up templates:
 - General Template (.BBABIDALLO)
 - Anti-CD38 (.BBABIDCD38)
 - Antibody of undetermined specificity (AUS) (.BBABIDAUS)
 - Passive anti-D (.BBABIDRHIG)
 - Warm autoantibody (.BBABIDWAA)
 - Cold autoantibody (.BBABIDCAA)



- **Patient information:**
 - Reminder: You can use F2 to jump to each section
 - ABO/Rh: select patient ABO/Rh type or *** if free text needed (such as no type determined)
 - If no type determined, add info regarding forward and reverse type results
 - Antibody screen: Positive (this is why the note is being written)
 - Previous Antibodies:
 - Present/known: select and list all present and or previous known antibodies
 - No known antibodies: if unknown or in system based on review of chart
 - Antibodies identified: list antibody or antibodies identified in this current workup
 - Additional testing performed: List results from additional testing performed with this workup if no additional workup, select “none”
 - RBC Phenotype: *** type results and list out all antigens and do not use haplotype abbreviations.
 - Example: Do not use R₁r for D positive, C positive, c positive, E negative, e positive
 - Direct antiglobulin test (DAT): select positive or negative (if performed), if not performed do not select
 - Eluate: select positive, negative or not performed, if positive type the findings (***)
 - If additional testing was performed that is outside the ones listed above, free text those results (such as adsorptions, titers, thermal amplitude, etc.)
- **Relevant Patient history** – narrative surrounding patient’s transfusion history
 - RELEVANT and BRIEF past medical history
 - do not copy and paste from other notes
 - avoid abbreviations
 - Transfusion history
 - if known include details of transfusions
 - including timing, at least of most recent if known
 - if unknown transfusion history, state this
 - Pregnancy history if known and/or relevant
 - Context around current care (i.e. what prompted this testing)
- **Testing information** – narrative surrounding meaning of testing results
 - Antibody screen – positive by definition of this report being needed
 - Antibody identification – list antibodies
 - DAT performed
 - If any additional testing was performed and resulted in EPIC this needs to be stated here
 - Eluate, Phenotype, titer, etc.
- **Clinical relevance** – narrative surrounding clinical importance of these antibodies
 - Implication in hemolysis and whether it’s intravascular and/or extravascular and or hemolytic disease of the fetus and newborn

- If they are considered to be clinically significant (see Table: Clinical Significance of Alloantibodies and Provision of Red Cells)
- **Therapeutic relevance** – narrative surrounding implications for patient if blood is needed
 - Antigen negative units provided
 - this is true in most cases but not all, so if not relevant, delete “negative for the *** antigen”
 - Add any information specific to antigens that will be considered (for example if antigen untested units will be issued based on crossmatch compatibility)
 - Use the table: Clinical Significance of Alloantibodies and Provision of Red Cells
 - Percent of donor population will be compatible (provide antigen negative blood)
 - Multiply frequencies of antigen negative population (See Red book, Ortho chart)
 - Take into account Rh(D) status (D+ multiple is 1, D- multiple is 0.15)
 - Use Caucasian (white) population (the majority of blood donors)
 - Yazer M et al. Transfusion 2017;57:1226–1234
 - Exception to simple multiplication – Rh haplotypes counted as one multiple, see table below
 - Approximate number of units needed to be screened to find one compatible unit
 - Do not count Rh status here (because units screened already account for it)
 - 1 (unit to be ordered)/frequency of units negative for the antigen(s)
 - The least amount of units in the report will be 1-2 units to be screened, if the result is close to 1 use this. If >2, then round up to the nearest whole numbers
 - **Contact information**
 - Blood bank general number
 - Person who prepared the report
 - Review the report and sign to send to attending for review and attestation
 - **Note:** If you made a new encounter you must also sign the encounter which usually found in the bottom right section of EPIC. Designate the attending on service as the co-signer for the encounter.

Table: Clinical Significance of Alloantibodies and Provision of Red Cells (from ML 10.0, Attachment 3, Softech)

Patient historically positive but current antibody screen is:		Antibodies to the Following:	Is Antigen Negative Blood Required?	Is a Full Serologic Crossmatch Required?
Positive or Negative	Clinically significant antibodies	D, C, E, c, e, K, S, s, Jk ^a , Jk ^b , Fy ^a , Fy ^b , f	Yes	Yes
Positive or Negative	Clinically insignificant antibodies	N, P ₁ , Le ^a , Le ^b , Lu ^a , A ₁	No (crossmatch compatible only) O cells for Anti-A1	Yes
Positive	Potentially clinically significant antibodies	Kp ^a , Wr ^a , Js ^a , Di ^a , Co ^b , C ^w , V or VS, Go ^a	No If patient's antibody screen is reacting 1+ or greater (HCLL will require override to issue)	Yes
Negative Sample must be tested with selected cell in Reference to determine degree of reactivity			Yes If patient is no longer reacting or reacting less than 1+ must provide antigen negative by screening if antisera is available at BJH or request antigen negative from ARC.	Yes
Positive or Negative	Anti-M (IS and IgG)		Crossmatch compatible is acceptable	Yes
			Yes if crossmatch compatible is not available	Yes
Positive or Negative	Passive anti-D <i>Note: Recent injection of Rh Immune Globulin must be documented</i>	D	Yes (Provide Rh Neg)	Yes
Positive or Negative	CD38 antibody No underlying alloantibodies	CD38	Yes, Kell Negative if DTT treated cells are used to perform antibody identification.	No
Positive or Negative	CD38 antibody underlying clinically significant antibody	CD38 See the list of clinically significant antibodies above.	Yes, Kell Negative if DTT treated cells are used to perform antibody identification and negative for underlying clinically significant antibody	Yes <i>Note: Donor cells will need to be DTT treated for XM.</i>
Positive or Negative	CD47 antibody No underlying alloantibodies	CD47	No <i>Note: Patient ABO type NTD requires patient receive O cells.</i>	Yes <i>Note:</i> Antibody screen Positive- Modified IgG crossmatch PeG or LISS. Antibody screen Negative-IgG crossmatch.
Positive	CD47 antibody underlying clinically significant antibody	CD47 See the list of clinically significant antibodies above	Yes, negative for underlying clinically antibody <i>Note: Patient ABO type NTD requires patient receive O cells.</i>	Yes <i>Note: Modified IgG crossmatch with Peg or LISS Without IS phase.</i>
Positive or Negative	Warm autoantibodies no underlying alloantibodies		No	No
Positive or Negative	Warm autoantibodies with underlying clinically significant antibody	See the list of clinically significant antibodies above.	Yes	Yes
Positive or Negative	Antibodies to High Frequency Antigens	K, Yt ^a , Kp ^b , Js ^b , U, Lu ^b , Co ^a , LW and all others	Yes	Yes
Positive	High Titer Low Avidity or HTLA-like antibody	Yk ^a , Kn ^a , Cs ^a , Ch ^a , Rg ^a , JMH, McC ^a	Yes If significant antibodies can not be ruled out	Yes Consult LMR if incompatible
Positive or Negative	Antibody of Unknown Specificity	All major blood group systems excluded	Not applicable	Yes
Negative	ABO Incompatible Platelet Transfusion >300 mls.		Not applicable	See Section 3.7

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Table: Percent compatible calculations and Rh(D), C/c, E/e considering Rh haplotypes

If patient is Rh (D) Positive

Anti-C (Big C)		Anti-c (Little c)		Anti-E (Big E)		Anti-e (Little e)	
Anti-C	32.20%	Anti-c	19.51%	Anti-E	71.40%	Anti-e	2.41%
rr	15.10%	R ₁ R ₁ or R ₁ r'	18.50%	R ₁ ' or R ₁ R ₀ or R ₀ r'	34.90%	R ₂ R ₂ or R ₂ r''	2.30%
R ₂ r or R ₂ R ₀ or R ₀ r''	11.80%	r'r	0.80%	R ₁ R ₁ or R ₁ r'	18.50%	R ₂ R ₂ or R ₂ r'' or R ₂ r _v	0.10%
R ₂ R ₂ or R ₂ r''	2.30%	R ₁ R ₂ or R ₂ r' or R ₁ r _v	0.20%	rr	15.10%	R ₂ R _v or R ₂ r _v	0.01%
r'r	0.90%	R ₂ R _v or R ₂ r _v	0.01%	r'r	0.80%	r'r _v or r'r'' or r _v r _v	rare
R ₀ r or R ₀ R ₀	2.10%	r'r _v or r'r''r _v	rare	R ₀ r or R ₀ R ₀	2.10%	r'r''	rare
r'r''	rare			r'r	rare		
Anti-C and Anti-E		Anti-c and Anti-E		Anti-c and Anti-e		Anti-c and Anti-e	
rr	15.10%	R ₁ R ₁ or R ₁ r'	18.50%	R ₁ R ₁ or R ₁ r'	18.50%	R ₂ R ₂ or R ₂ r _v	0.01%
R ₂ r or R ₀ R ₀	2.10%	r'r	rare	r'r	rare	r'r''	rare
Anti-C and Anti-e		2.30%		0.01%		0.01%	
R ₂ R ₂ or R ₂ r''	2.30%	r'r''	rare	R ₂ R _v or R ₂ r _v	0.01%	r'r''	rare

If patient is Rh (D) negative (with or without Anti-D)

(% of ABO compatible donor population 16.85%)

Anti-C	% ABO/Rh comp	94.96%	Anti-c	% ABO/Rh comp	rare	Anti-E	% ABO/Rh comp	94.36%	Anti-e	% ABO/Rh comp	rare
rr	% ABO comp	16.00%	% ABO comp	rare		% ABO comp	15.90%	% ABO comp	rare		
r' r'	% ABO comp	15.10%	r' r'	rare		r' r''	15.10%	r' r''	rare		
r' r	% ABO comp	0.90%	r' r or r' y	rare		r' r_y or r' y	0.80%	r' r_y or r' y	rare		
r' r''			r' r'			r' r'		r' r'			

NOTE - Since Rh(D)- patients or patients with anti-D can only receive Rh(D)- blood:
% compatible units: put in % ABO/Rh compatible corresponding to the antibodies (gray box)
units to screen: use 1/%ABO/Rh compatible to calculate number of units needed to screen since only Rh negative units would be used for screening

Reid and Lomas-Francis, 2007. p 191-192.

Transfusion Reactions

Transfusion reactions are reported to the blood bank by the transfusing service. The blood bank then initiates a workup consisting of (1) a clerical check to verify the product has not gone to the wrong patient, and (2) a screen for hemolysis consisting of a Direct Antiglobulin Test (DAT), an inspection of post-transfusion samples for visible hemoglobin and icterus, and a check for urine hemoglobin if sent. A form will be generated for you and left in a bin near the logbook. **When you have determined whether a patient should receive additional blood products after a reported transfusion reaction, you must call back the blood bank to inform them;** blood bank staff will document this in HCLL and the logbook. The blood bank will not release further blood products to any patient following a transfusion reaction without the approval of the LMR. **If the floor asks to transfuse a patient after a reaction has been called, or when the laboratory workup is complete, the blood bank will call you.**

Protocol for ALL acute transfusion reactions from clinical perspective:

- STOP THE TRANSFUSION immediately
- Maintain IV assess with 0.9% NaCl
- Check blood component for patient ID
- Notify Blood Bank(BB)
- Send blood sample and urine to BB
- Send blood unit and anything attached to BB in case culture becomes necessary
- Support patient as necessary

Questions to ask when discussing the reaction with the blood bank include:

- 1) What product was transfused and how much?
- 2) What was the nature of the transfusion reaction? Was there a change in vital signs?
- 3) What are the results of the transfusion reaction work-up done in the blood bank?
- 4) Has the patient had any previous transfusion reactions?
- 5) Does the patient have any anti-RBC antibodies?
- 6) Are they requesting blood products? What product are they now requesting?

The LMR must perform their own investigation, including chart review, discussion with the clinical team and if needed the transfusion attending to determine the nature of the reaction, the patient's status, and safety to transfuse additional blood products. Inform the blood bank if it is acceptable to release more blood products based on the reaction history and workup. If acceptable, tell the BB Desk Tech to add note in HCLL "OK to transfuse" and with any transfusion recommendations. **The LMR is expected to follow up on the results of each investigation with the clinical team taking care of the patient in which a transfusion reaction has been called. The transfusion reaction must be reviewed by the attending on service within 24 hours and presented at the next rounds or over the phone on weekends.** The LMR then writes a transfusion reaction note in EPIC, which will be reviewed and signed by the attending (see section on transfusion reaction interpretive reports). **Having the results documented in the computer is not good enough.** A table of the most clinically important transfusion reactions is presented in subsequent pages.

Situations requiring immediate attention and discussion with the TM attending

Suspicion for TRALI, bacterial contamination, possible hemolysis, and/or severe reactions (e.g. anaphylaxis) necessitates an immediate discussion with the TM attending on call to determine course of action. If TRALI or bacterial contamination are suspected, inform the charge technologist as soon as possible to notify the ARC so that additional products from that donor may be sequestered to avoid potential release of a concurrent product to another patient. Do not wait until investigation is completed or until the next day if after hours or over the weekend. Complete a "Recipient Complications" form and send to BB, who will then send to ARC. The form can be found at <https://www.redcrossblood.org/> → Biomedical services → Hospital Partner Resource Guide → Blood Bank Resources and Documents → Transfusion Reaction Case Report.

Special considerations for suspected TRALI (transfusion related acute lung injury)

TRALI is very serious and potentially fatal with understanding of pathogenesis, treatment, and prevention of TRALI evolving. Criteria include all the following: acute onset of respiratory distress, hypoxemia, bilateral infiltrates on CXR, onset <6 hours of transfusion (usually <2 hours), and absence of other causes of acute lung injury. It is thought that alloantibodies in the donated blood directed against HLA class I or II antigens and/or human neutrophil antigens (HNA) interact with the recipient's leukocytes in the pulmonary tissue. Although any blood products can be implicated in TRALI, high plasma-volume components, including platelets and FFP, have the highest risk.

When TRALI is suspected the LMR initiates a workup which includes the following:

1. Review clinical information (symptoms, CXR, etc.) and determine TRALI likelihood. Complete transfusion reaction form (copies available in blood bank).
2. **Discuss the case with the TM attending as soon as possible (do not wait until A.M. rounds).**
3. Call the BB Desk Tech: retrieve any associated products and notify the collection facility.
4. Order the testing needed for the patient/donor as indicated below:
 - a. If the implicated unit is a platelet or FFP product from the ARC:
 - i. Donor HLA antibody screening, done at ARC after receipt of TRALI investigation form.
 - ii. Recipient HLA typing (EDTA tube; performed at BJH).
 - b. If the implicated unit is a RBC product from the ARC:
 - i. Donor HLA typing screening, done at ARC after receipt of TRALI investigation form.
 - ii. Recipient HLA antibody screen (red-gray top SST; performed at BJH).
 - iii. Recipient HNA screen if HLA antibody screen is negative (1 red top and 1 purple top tube; send-out to Versiti WI) (may not always be performed, depends on clinical scenario)
 - iv. Donor HLA typing (per ARC if necessary).
 - v. Recipient HLA typing (green top tube; performed at BJH)
5. **Fill out the "Recipient Complications" Form (see above for location on ARC website)**
6. Review the form with the attending.
7. Return signed and completed form to the Compliance Coordinator for faxing to the donor center (and FDA if a fatality occurs).
8. LMRs must keep track of each TRALI case and follow-up on the test results so that TRALI can be confirmed (or not). If the donor has HLA or HNA antibodies directed against the patient (e.g., donor has anti-B7 and patient types B7), then this finding, together with the clinical picture, is taken as confirmation of TRALI.

Transfusion Reactions (Quick Summary Table)

Reaction Type	Mechanism	Signs/Symptoms	Lab Diagnosis	Treatment
Acute Hemolytic Transfusion Reaction	Pre-formed red cell antibody	fever, hypotension, flank pain, chest pain, nausea/vomiting, chills, shock, renal failure, DIC	clerical error? DAT positive hemoglobinemia, hemoglobinuria	Stop transfusion; Maintain IV access; Hydrate w/ NS, Pressors as needed
Delayed Hemolytic Transfusion Reaction	Anamnestic red cell antibody response ~2-10 days aftertransfusion	Usually asymptomatic Rarely, clinical picture similar to acute hemolytic txn rxn.	↓Hgb/Hct ↑bilirubin DAT positive (usually)	Monitor CBC and renal status and markers to assess hemolysis if indicated.
Febrile Nonhemolytic Transfusion Reaction	Antibody to donor WBCs or Cytokine-mediated	Fever $\geq 1^{\circ}\text{C}$ AND $>38^{\circ}\text{C}$ or Chills/rigors	Blood bank hemolytic workup negative; culture of unit negative	Stop transfusion; R/O acute hemolysis or bacterial contamination. Premedicate w/ acetaminophen; Use leukoreduced blood products.
Transfusion of bacterially contaminated product	Product seeded by donor skin flora, or donor bacteremic; growth in storage	Fever, shock, Hemoglobinuria, renal failure, DIC	Culture of product and patient	Broad-spectrum antibiotics, fluids, pressors
Allergic Reaction	Allergy to donor plasma protein	Hives, itching Occ. wheezing, ↓BP	N/A	If urticaria only sign , may restart transfusion. Consider premedication w/ diphenhydramine if repeated or severe.
Anaphylactic Reaction	Antibody to IgA or other plasma protein	Hypotension/shock	↓IgA levels and anti-IgA Ab. In most cases, allergen not identified	Epinephrine, fluid resuscitation, intubation; If due to anti-IgA, use IgA-negative platelets, FFP and RBCs or washed RBCs.
Hypotensive Transfusion Reaction	Unknown; may involve bradykinin activation.	Drop in systolic BP of ≥ 30 mmHg and systolic BP ≤ 80 mmHg and all other causes of hypotension excluded	N/A	Stop transfusion and give vasopressors as needed.
Transfusion-associated circulatory overload (TACO)	Volume overload, usually in pts. w/ heart disease getting pRBCs	Signs of congestive heart failure	↓pO2 pulmonary edema on CXR	Transfuse slowly; Diuretics.

Reaction Type	Mechanism	Signs/Symptoms	Lab Diagnosis	Treatment
Transfusion Related Acute Lung Injury (TRALI)	Ab to recipient WBCs, usually anti-HLA or anti-HNA	Acute respiratory distress, within 6 hours of transfusion +/- fever, <u>no</u> evidence of volume overload	↓pO2; pulm edema on CXR; Work up donor for anti-HLA and/or anti-HNA	Supportive care; usually resolves within 96 hrs. Permanently defer implicated donor
Transfusion-associated dyspnea (TAD)	Unknown	Acute respiratory distress within 24 hours of transfusion cessation and Allergic reaction, TACO, and TRALI are ruled out.	↓pO2, ↑ RR	Supportive care
Transfusion Related Graft-Versus-Host-Disease (GVHD)	Donor lymphocytes vs host; occ. seen in immunocompromised pts sharing HLA w/ donor	Fever, rash, diarrhea, severe pancytopenia	CBC, ↑LFTs skin biopsy	Supportive care; immunosuppression; Prevent w/ irradiated blood products. High mortality rate.
Post-Transfusion Purpura (PTP)	Ab-mediated platelet destruction; usually in multiparous women who are PI ^{A1} negative.	Severe thrombocytopenia ~ 1 week after transfusion, may be acute with further transfusions	CBC, PI ^A typing send PTP panel to Blood Center of Wisconsin	Plasma exchange or IVIG

Reporting a Transfusion-related Death

Section 606.170(b) of Title 21, Code of Federal Regulations (21 CFR 606.170(b)), requires that facilities notify the Food and Drug Administration (FDA), Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ), as soon as possible after confirming a complication of transfusion to be fatal. The regulation also requires submitting an investigation report to the FDA within 7 days after the fatality. Please work with your attending, the Blood Bank Medical Director (Brenda Grossman), Quality Coordinator (Marcella Hermann) and the Blood Bank manager (Cindy Ingold) to comply with the regulation in a timely manner.

CDC Hemovigilance Module of Transfusion Reactions

(see TRddx.com for electronic algorithm)

Transfusion-associated circulatory overload (TACO)

Case Definition	Severity	Imputability
Definitive: New onset or exacerbation of 3 or more of the following within 6 hours of cessation of transfusion: <ul style="list-style-type: none"> • Acute respiratory distress (dyspnea, orthopnea, cough) • Elevated brain natriuretic peptide (BNP) • Elevated central venous pressure (CVP) • Evidence of left heart failure • Evidence of positive fluid balance • Radiographic evidence of pulmonary edema Probable: N/A	Non-severe: Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function. Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a body function. Life-threatening: Major intervention required following the transfusion (e.g. vasopressors, intubation, transfer to intensive care) to prevent death. Death: The recipient died as a result of the adverse transfusion reaction . Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction. Not Determined: The severity of the adverse reaction is unknown or not stated.	Definite: No other explanations for circulatory overload are possible. Probable: Transfusion is a likely contributor to circulatory overload AND EITHER <ul style="list-style-type: none"> The patient received other fluids as well OR The patient has a history of cardiac insufficiency that could explain the circulatory overload, but transfusion is just as likely to have caused the circulatory overload. Possible: The patient has a history of pre-existing cardiac insufficiency that most likely explains circulatory overload.
Possible: N/A		OPTIONAL
		Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded. Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion. Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.

Transfusion-related acute lung injury (TRALI)

Case Definition	Severity	Imputability
<p>Definitive: NO evidence of acute lung injury (ALI) prior to transfusion AND ALI onset during or within 6 hours of cessation of transfusion AND Hypoxemia defined by any of these methods:</p> <ul style="list-style-type: none"> • PaO₂/FiO₂ less than or equal to 300 mm Hg • Oxygen saturation less than 90% on room air • Other clinical evidence <p>AND Radiographic evidence of bilateral infiltrates AND No evidence of left atrial hypertension (i.e., circulatory overload)</p> <p>Probable: N/A</p> <p>Possible: N/A</p>	<p>Non-severe: Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function.</p> <p>Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a body function.</p> <p>Life-threatening: Major intervention required following the transfusion (e.g. vasopressors, intubation, transfer to intensive care) to prevent death.</p> <p>Death: The recipient died as a result of the adverse transfusion reaction. Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction.</p> <p>Not Determined: The severity of the adverse reaction is unknown or not stated.</p>	<p>Definite: There are no alternative risk factors for ALI present.</p> <p>Probable: N/A</p> <p>Possible: There is evidence of other causes for acute lung injury such as:</p> <p>Direct Lung Injury</p> <ul style="list-style-type: none"> • Aspiration • Pneumonia • Toxic inhalation • Lung contusion • Near drowning <p>Indirect Lung Injury</p> <ul style="list-style-type: none"> • Severe sepsis • Shock • Multiple trauma • Burn injury • Acute pancreatitis • Cardiopulmonary bypass • Drug overdose
OPTIONAL		
		<p>Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded.</p> <p>Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion.</p> <p>Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.</p>

Transfusion-associated dyspnea (TAD)

Case Definition	Severity	Imputability
Definitive: Acute respiratory distress occurring within 24 hours of cessation of transfusion AND Allergic reaction, TACO, and TRALI definitions are not applicable.	Non-severe: Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function. Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a body function. Life-threatening: Major intervention required following the transfusion (e.g. vasopressors, intubation, transfer to intensive care) to prevent death. Death: The recipient died as a result of the adverse transfusion reaction . Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction. Not Determined: The severity of the adverse reaction is unknown or not stated.	Definite: Patient has no other conditions that could explain symptoms. Probable: There are other potential causes that could explain symptoms, but transfusion is the most likely cause. Possible: Other present causes are most likely, but transfusion cannot be ruled out.
Probable: N/A		OPTIONAL
Possible: N/A		Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded. Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion. Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.

Allergic reaction

Note: Minor allergic reactions (Non-severe) do not have to be reported to NHSN.

Case Definition	Severity	Imputability
Definitive: 2 or more of the following occurring during or within 4 hours of cessation of transfusion: <ul style="list-style-type: none"> • Conjunctival edema • Edema of lips, tongue and uvula • Erythema and edema of the periorbital area • Generalized flushing • Hypotension • Localized angioedema • Maculopapular rash • Pruritus (itching) • Respiratory distress; bronchospasm • Urticaria (hives) Probable: ANY 1 of the following occurring during or within 4 hours of cessation of transfusion: <ul style="list-style-type: none"> • Conjunctival edema • Edema of lips, tongue and uvula • Erythema and edema of the periorbital area • Localized angioedema • Maculopapular rash • Pruritus (itching) • Urticaria (hives) 	Severe, Life-threatening, Death: Involves respiratory and/or cardiovascular systems and presents like an anaphylactic reaction. There is anaphylaxis when, in addition to mucocutaneous symptoms, there are airway symptoms, hypotension, or associated symptoms like hypotonia and syncope. The respiratory signs and symptoms may be laryngeal (tightness in the throat, dysphagia, dysphonia, hoarseness, stridor) or pulmonary (dyspnea, cough, wheezing, bronchospasm, hypoxemia). Such a reaction usually occurs during or shortly after cessation of transfusion. Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction. Not Determined: The severity of the adverse reaction is unknown or not stated.	Definite: Occurs during or within 2 hours of cessation of transfusion AND No other evidence of environmental, drug or dietary risks. Probable: Occurs during or within 2 hours of cessation of transfusion AND There are other potential causes present that could explain symptoms, but transfusion is the most likely cause. Possible: Occurs 2 - 4 hours after cessation of transfusion OR Other present causes are most likely, but transfusion cannot be ruled out.
OPTIONAL	OPTIONAL	OPTIONAL
Possible: N/A	Non-severe: There is no immediate risk to the life of the patient, and the patient responds quickly to symptomatic treatment.	Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded. Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion. Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.

Hypotensive transfusion reaction

Case Definition	Severity	Imputability	
<p>Definitive: All other adverse reactions presenting with hypotension are excluded AND Hypotension occurs during or within 1 hour after cessation of transfusion.</p> <ul style="list-style-type: none"> Adults (18 years and older): Drop in systolic BP of greater than or equal to 30 mmHg and systolic BP less than or equal to 80 mmHg. Infants, children and adolescents (1 year to less than 18 years old): Greater than 25% drop in systolic BP from baseline (e.g., drop in systolic BP of 120mmHg to below 90mmHg). Neonates and small infants (less than 1 year old OR any age and less than 12 kg body weight): Greater than 25% drop in baseline value using whichever measurement is being recorded (e.g., mean BP). <p>Probable: N/A</p>	<p>Non-severe: The recipient required no more than discontinuation of transfusion and symptom management and no long-term morbidity resulted from the reaction.</p> <p>Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to hypotension, or hypotension led directly to long-term morbidity (e.g., brain damage)</p> <p>AND Vasopressors were not required.</p> <p>Life-threatening: The recipient required vasopressors.</p> <p>Death: The recipient died as a result of the adverse transfusion reaction.</p> <p>Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction.</p> <p>Not Determined: The severity of the adverse reaction is unknown or not stated.</p>	<p>Definite: Occurs less than 15 minutes after the start of the transfusion AND Responds rapidly (i.e., within 10 minutes) to cessation of transfusion and supportive treatment AND The patient has no other conditions that could explain hypotension.</p> <p>Probable: Onset is between 15 minutes after start and 1 hour after cessation of transfusion OR The patient does not respond rapidly to cessation of transfusion and supportive treatment OR There are other potential causes present that could explain hypotension, but transfusion is the most likely cause.</p> <p>Possible: Other conditions that could readily explain hypotension are present.</p>	
OPTIONAL		OPTIONAL	
<p>Possible: Hypotension occurs, does not meet the criteria above. Other, more specific reaction definitions do not apply.</p>	<p>Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded.</p> <p>Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion.</p> <p>Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.</p>		

Febrile non-hemolytic transfusion reaction (FNHTR)

Note: Reactions may be classified as FNHTRs in the absence of fever if chills or rigors occur.

Case Definition	Severity	Imputability
Definitive: Occurs during or within 4 hours of cessation of transfusion AND EITHER Fever (greater than or equal to 38°C/100.4°F oral and a change of at least 1°C/1.8°F) from pre-transfusion value OR Chills/rigors are present. Probable: N/A	Non-severe: Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function. Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a body function.	Definite: Patient has no other conditions that could explain signs/symptoms. Probable: There are other potential causes present that could explain signs/symptoms, but transfusion is the most likely cause. Possible: Other present causes are most likely, but transfusion cannot be ruled out.
OPTIONAL		OPTIONAL
Possible: FNHTR is suspected, but reported symptoms and/or available information are not sufficient to meet the criteria defined above. Other, more specific adverse reaction definitions do not apply.	Life-threatening: Major intervention required following the transfusion (e.g. vasopressors, intubation, transfer to intensive care) to prevent death. Death: The recipient died as a result of the adverse transfusion reaction . Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction. Not Determined: The severity of the adverse reaction is unknown or not stated.	Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded. Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion. Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.

Acute hemolytic transfusion reaction (AHTR)

Note: Report hemolytic reactions resulting from immune or non-immune causes, including when the recipient is **intentionally** transfused with incompatible blood components.

Case Definition	Severity	Imputability
Definitive: Occurs during, or within 24 hours of cessation of transfusion with new onset of ANY of the following signs/symptoms: <ul style="list-style-type: none"> • Back/flank pain • Chills/rigors • Disseminated intravascular coagulation (DIC) • Epistaxis • Fever • Hematuria (gross visual hemolysis) • Hypotension • Oliguria/anuria • Pain and/or oozing at IV site • Renal failure AND 2 or more of the following: <ul style="list-style-type: none"> • Decreased fibrinogen • Decreased haptoglobin • Elevated bilirubin • Elevated LDH • Hemoglobinemia • Hemoglobinuria • Plasma discoloration c/w hemolysis • Spherocytes on blood film AND EITHER (IMMUNE-MEDIATED) Positive direct antiglobulin test (DAT) for anti-IgG or anti-C3 AND Positive elution test with alloantibody present on the transfused red blood cells OR (NON-IMMUNE MEDIATED) Serologic testing is negative, and physical cause (e.g., thermal, osmotic, mechanical, chemical) is confirmed. Probable: Meets signs and symptoms criteria for acute hemolysis AND EITHER (IMMUNE MEDIATED) Physical cause is excluded but serologic evidence is not sufficient to meet definitive criteria OR (NON-IMMUNE MEDIATED) Physical cause is suspected and serologic testing is negative.	Non-severe: Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function. Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a body function. Life-threatening: Major intervention required following the transfusion (e.g. vasopressors, intubation, transfer to intensive care) to prevent death. Death: The recipient died as a result of the adverse transfusion reaction . Death should be used if death is possibly , probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction. Not Determined: The severity of the adverse reaction is unknown or not stated.	Definite: ABO or other allotypic RBC antigen incompatibility is known OR Only transfusion-related (i.e., immune or non-immune) cause of acute hemolysis is present. Probable: There are other potential causes present that could explain acute hemolysis, but transfusion is the most likely cause. Possible: Other causes of acute hemolysis are more likely, but transfusion cannot be ruled out. OPTIONAL Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded. Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion. Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.
OPTIONAL		
Possible: AHTR is suspected within 24 hours of cessation of transfusion, but symptoms, test results, and/or information are not sufficient to meet the criteria defined above. Other, more specific adverse definitions do not apply.		

Delayed hemolytic transfusion reaction (DHTR)

Note: Report all hemolytic reactions, including when the recipient is **intentionally** transfused with incompatible blood components.

Case Definition	Severity	Imputability
<p>Definitive: Positive direct antiglobulin test (DAT) for antibodies developed between 24 hours and 28 days after cessation of transfusion</p> <p>AND EITHER</p> <ul style="list-style-type: none"> Positive elution test with alloantibody present on the transfused red blood cells OR Newly-identified red blood cell alloantibody in recipient serum <p>AND EITHER</p> <ul style="list-style-type: none"> Inadequate rise of post-transfusion hemoglobin level or rapid fall in hemoglobin back to pre-transfusion levels OR Otherwise unexplained appearance of spherocytes. <p>Probable: Newly-identified red blood cell alloantibody demonstrated between 24 hours and 28 days after cessation of transfusion</p> <p>BUT Incomplete laboratory evidence to meet definitive case definition criteria.</p> <p>NOTE: Patient may be asymptomatic or have symptoms that are similar to but milder than AHTR; symptoms are not required to meet case definition criteria.</p>	<p>Non-severe: Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function.</p> <p>Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a body function.</p> <p>Life-threatening: Major intervention required following the transfusion (e.g. vasopressors, intubation, transfer to intensive care) to prevent death.</p> <p>Death: The recipient died as a result of the adverse transfusion reaction. Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction.</p> <p>Not Determined: The severity of the adverse reaction is unknown or not stated.</p>	<p>Definite: No other explanation for symptoms or newly-identified antibody is present.</p> <p>Probable: An alternate explanation for symptoms or newly-identified antibody is present, but transfusion is the most likely cause.</p> <p>Possible: Other explanations for symptoms or newly-identified antibody are more likely, but transfusion cannot be ruled out.</p>
OPTIONAL		OPTIONAL
<p>Possible: DHTR is suspected, but reported symptoms, test results, and/or available information are not sufficient to meet the criteria defined above. Other, more specific adverse reaction definitions do not apply.</p>		<p>Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded.</p> <p>Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion.</p> <p>Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.</p>

Delayed serologic transfusion reaction (DSTR)

Note: Delayed serologic reactions should only be reported for patients **transfused by your facility**.

Case Definition	Severity	Imputability
Definitive: Absence of clinical signs of hemolysis AND Demonstration of new, clinically-significant antibodies against red blood cells BY EITHER Positive direct antiglobulin test (DAT) OR Positive antibody screen with newly identified RBC alloantibody.	Not Determined: Since this is by definition a reaction with no clinical symptoms, severity of the reaction cannot be graded.	Definite: New alloantibody is identified between 24 hours and 28 days after cessation of transfusion AND Transfusion performed by your facility is the only possible cause for seroconversion. Probable: New alloantibody is identified between 24 hours and 28 days after cessation of transfusion AND The patient has other exposures (e.g. transfusion by another facility or pregnancy) that could explain seroconversion, but transfusion by your facility is the most likely cause.
OPTIONAL		
		Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded.
		Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion.
		Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.

Transfusion-associated graft vs. host disease (TAGVHD)

Case Definition	Severity	Imputability
<p>Definitive: A clinical syndrome occurring from 2 days to 6 weeks after cessation of transfusion characterized by:</p> <ul style="list-style-type: none"> • Characteristic rash: erythematous, maculopapular eruption centrally that spreads to extremities and may, in severe cases, progress to generalized erythroderma and hemorrhagic bullous formation. • Diarrhea • Fever • Hepatomegaly • Liver dysfunction (i.e., elevated ALT, AST, Alkaline phosphatase, and bilirubin) • Marrow aplasia • Pancytopenia <p>AND Characteristic histological appearance of skin or liver biopsy.</p> <p>Probable: Meets definitive criteria EXCEPT Biopsy negative or not done.</p> <p>Possible: N/A</p>	<p>Non-severe: N/A</p> <p>Severe: Patient had marked symptoms and responded to treatment.</p> <p>Life-threatening: Patient had severe symptoms and required life-saving treatment (e.g., immunosuppression).</p> <p>Death: The recipient died as a result of the adverse transfusion reaction. Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction.</p> <p>Not Determined: The severity of the adverse reaction is unknown or not stated.</p>	<p>Definite: WBC chimerism present in the absence of alternative diagnoses.</p> <p>Probable: WBC chimerism present BUT Other potential causes are present (e.g., stem cell transplantation).</p> <p>Possible: WBC chimerism not present or not done OR Alternative explanations are more likely (e.g., solid organ transplantation).</p> <p>OPTIONAL</p> <p>Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded.</p> <p>Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion.</p> <p>Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.</p>

Post transfusion purpura (PTP)

Case Definition	Severity	Imputability
<p>Definitive: Alloantibodies in the patient directed against HPA or other platelet specific antigen detected at or after development of thrombocytopenia AND Thrombocytopenia (i.e., decrease in platelets to less than 20% of pre-transfusion count).</p> <p>Probable: Alloantibodies in the patient directed against HPA or other platelet specific antigen detected at or after development of thrombocytopenia. AND Decrease in platelets to levels between 20% and 80% of pre-transfusion count.</p>	<p>Non-severe: Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function.</p> <p>Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a body function.</p> <p>Life-threatening: Major intervention required following the transfusion (e.g. vasopressors, intubation, transfer to intensive care) to prevent death.</p> <p>Death: The recipient died as a result of the adverse transfusion reaction. Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction.</p> <p>Not Determined: The severity of the adverse reaction is unknown or not stated.</p>	<p>Definite: Occurs 5-12 days post-transfusion AND Patient has no other conditions to explain thrombocytopenia.</p> <p>Probable: Occurs less than 5 or more than 12 days post-transfusion OR There are other potential causes present that could explain thrombocytopenia, but transfusion is the most likely cause.</p> <p>Possible: Alternate explanations for thrombocytopenia are more likely, but transfusion cannot be ruled out.</p>
OPTIONAL		OPTIONAL
<p>Possible: PTP is suspected, but laboratory findings and/or information are not sufficient to meet defined criteria above. For example, the patient has a drop in platelet count to less than 80% of pre-transfusion count but HPA antibodies were not tested or were negative. Other, more specific adverse reaction definitions do not apply.</p>	<p>Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded.</p> <p>Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion.</p> <p>Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.</p>	

Transfusion-transmitted infection (TTI)

Case Definition	Severity	Imputability
Definitive: Laboratory evidence of a pathogen in the transfusion recipient.	Non-severe: Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function.	Definite: ONE or more of the following: <ul style="list-style-type: none"> • Evidence of the pathogen in the transfused component • Evidence of the pathogen in the donor at the time of donation • Evidence of the pathogen in an additional component from the same donation • Evidence of the pathogen in an additional recipient of a component from the same donation AND No other potential exposures to the pathogen could be identified in the recipient. AND EITHER <ul style="list-style-type: none"> Evidence that the recipient was not infected with the pathogen prior to transfusion OR Evidence that the identified pathogen strains are related by molecular or extended phenotypic comparison testing with statistical confidence ($p<0.05$).
Probable: N/A	Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a body function.	Probable: ONE or more of the following: <ul style="list-style-type: none"> • Evidence of the pathogen in the transfused component • Evidence of the pathogen in the donor at the time of donation • Evidence of the pathogen in an additional component from the same donation • Evidence of the pathogen in an additional recipient of a component from the same donation. AND EITHER: <ul style="list-style-type: none"> Evidence that the recipient was not infected with this pathogen prior to transfusion OR No other potential exposures to the pathogen could be identified in the recipient. Possible: Case fails to meet definite, probable, doubtful, or ruled out imputability criteria.
OPTIONAL		OPTIONAL
Possible: Temporally associated unexplained clinical illness consistent with infection, but no pathogen is detected in the recipient. Other, more specific adverse reactions are ruled out. Note: Possible cases cannot meet the definite or probable imputability criteria.	Life-threatening: Major intervention required following the transfusion (e.g. vasopressors, intubation, transfer to intensive care) to prevent death. Death: The recipient died as a result of the adverse transfusion reaction. Not Determined: The severity of the adverse reaction is unknown or not stated.	Doubtful: Laboratory evidence that the recipient was infected with this pathogen prior to transfusion OR Evidence is clearly in favor of a cause other than transfusion, but transfusion cannot be excluded. Ruled Out: ALL of the following (where applicable): <ul style="list-style-type: none"> • Evidence that the transfused component was negative for this pathogen at the time of transfusion • Evidence that the donor was negative for this pathogen at the time of donation • Evidence that additional components from the same donation were negative for this pathogen OR There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion. Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.

Transfusion-transmitted infection (TTI)

(continued)

Pathogens of well-documented importance in blood safety.

These pathogens have public health significance for hemovigilance, are well-documented blood stream pathogens, and/or are routinely screened for in blood donors. A full list of potentially infectious organisms is available in the drop-down pathogen list in NHSN.

Bacterial	Viral	Parasitic	Other
<i>Enterobacter cloacae</i>	Cytomegalovirus (CMV)	Babesiosis (<i>Babesia spp.</i>)	Creutzfeldt-Jakob Disease, Variant (vCJD)
<i>Escherichia coli</i>	<i>Enterovirus spp.</i>	Chagas disease (<i>Trypanosoma cruzi</i>)	
<i>Klebsiella oxytoca</i>	Epstein Barr (EBV)	Malaria (<i>Plasmodium spp.</i>)	
<i>Klebsiella pneumoniae</i>	Hepatitis A		
<i>Pseudomonas aeruginosa</i>	Hepatitis B		
<i>Serratia marcescens</i>	Hepatitis C		
<i>Staphylococcus aureus</i>	Human Immunodeficiency Virus 1 (HIV-1)		
<i>Staphylococcus epidermidis</i>	Human Immunodeficiency Virus 2 (HIV-2)		
<i>Staphylococcus lugdunensis</i>	Human Parvovirus B-19		
<i>Syphilis (<i>Treponema pallidum</i>)</i>	Human T-Cell Lymphotropic Virus-1 (HTLV-1)		
<i>Yersinia enterocolitica</i>	Human T-Cell Lymphotropic Virus-2 (HTLV-2)		
	West Nile Virus (WNV)		
	Zika Virus (ZIKAVI)		

Note: If there is sufficient evidence of TTI to warrant culture of the unit, the ARC (or blood supplier) **must** be notified so that they can remove any additional products associated with that donation from distribution. The LMR must notify the blood bank not only to send the unit for culture, but also to access our inventory for associated products for quarantine, and to contact the blood supplier and notify them of our concern.

Cultures are performed in the BJH microbiology lab, under the following “patient” account:
Transfusion, Reaction
Cerner MRN 9937181486
Cerner FIN 701072083

Although this “patient” exists in EPIC, results of the Gram stain and culture do not cross over from Cerner into EPIC. Microbiology should contact the blood bank with positive results, but the LMR must follow up on the final report for negative cultures, which may take up to 10 days to complete due to plate subcultures. Call the “Bloods” bench in Microbiology (273-1827) for results. **Obtaining the accession number** from a technologist at an initial call will make it easier for the Micro technologist to look up the culture for follow up calls. A copy of the final culture must be provided to the blood supplier.

Other or Unknown

Other: Use this option if the recipient experienced an adverse reaction that is not defined in the Hemovigilance Module surveillance protocol (e.g., transfusion-associated acute gut injury (TRAGI), transfusion-associated immunomodulation (TRIM), iron overload, microchimerism, hyperkalemia, thrombosis).

Unknown: Use this category if the patient experienced transfusion-related symptoms, but the medical event that caused those symptoms could not be classified.

Note: Reporting 'Other' and 'Unknown' reactions is not required by CDC.

REPORTING OPTIONAL		
Case Definition	Severity	Imputability
<p>Not Applicable: CDC does not specifically define the 'Other' or 'Unknown' adverse reaction categories, therefore the case definition criteria may only be reported as N/A.</p>	<p>Non-severe: Medical intervention (e.g. symptomatic treatment) is required but lack of such would not result in permanent damage or impairment of a bodily function.</p> <p>Severe: Inpatient hospitalization or prolongation of hospitalization is directly attributable to the adverse reaction, persistent or significant disability or incapacity of the patient occurs as a result of the reaction, or a medical or surgical intervention is necessary to preclude permanent damage or impairment of a body function.</p> <p>Life-threatening: Major intervention required following the transfusion (e.g. vasopressors, intubation, transfer to intensive care) to prevent death.</p> <p>Death: The recipient died as a result of the adverse transfusion reaction. Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction.</p> <p>Not Determined: The severity of the adverse reaction is unknown or not stated.</p>	<p>Definite: Conclusive evidence exists that the adverse reaction can be attributed to the transfusion.</p> <p>Probable: Evidence is clearly in favor of attributing the adverse reaction to the transfusion.</p> <p>Possible: Evidence is indeterminate for attributing the adverse reaction to the transfusion or an alternate cause.</p> <p>Doubtful: Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded.</p> <p>Ruled Out: There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion.</p> <p>Not Determined: The relationship between the adverse reaction and the transfusion is unknown or not stated.</p>

Transfusion reaction interpretive reports

Transfusion reaction notes allow for the synthesis of information regarding a patient's transfusion, the reaction, and surrounding clinical context. Information in the report includes transfusion reaction interpretation and classification, transfusion information, the patient's relevant transfusion history, results of the testing performed, clinical relevance (immediate treatment recommendations for transfusion reaction), and therapeutic relevance (recommendations for future transfusions).

A few important notes about transfusion reaction reports:

1. Resources can be found in WUSTLBox à LGM à Transfusion-Blood Bank à Blood bank interpretative reports resources.
2. Initial notification of a transfusion reaction work up includes getting the paperwork from the bin in the blood bank or call from the blood bank informing the trainee of the work up.
3. The original transfusion reaction paperwork must be returned with the final report. The written and attested note from EPIC will need to be printed out and attached to the paperwork before turning in.
4. Transfusion reaction notes must be written by the trainee within 24 hours of the initial notification of a transfusion reaction workup by the blood bank.
5. Transfusion reaction notes must be attested by the attending within 48 hours of the initial notification of a transfusion reaction workup by the blood bank.
6. Notes that go over 48 hours without being finalized will be escalated to the Director of Transfusion Services for follow up.

Handoffs and responsibilities:

Trainees: The trainee on the primary service (the trainee who takes calls about transfusion reactions) is responsible for reviewing and writing transfusion reaction notes.

Attendings:

Weekdays:

- Present at the next day's rounds
- Assign notes to the attending on service for that week

Weekends until 8am on Mondays (when the attendings switch service)

- Present at the next day's rounds if you did not contact the attending at the time
 - Friday night - discuss Saturday morning
 - Saturday - discuss Sunday morning
 - Sunday - discuss Monday morning (the next attending on service)
- If you present/discuss the case with the attending, assign the note to that attending

General timeline of result to finalized report in EPIC (exceptions are expected)

	Notification	Day 1	Day 2	Day 3
Trainee	Notification, address clinical situation	Review, write note		Return paperwork with printed EPIC note to BB
Attending			Review report, attest note	

Reviewing Transfusion Reaction Results

Trainees can generally incorporate preparation of the transfusion reaction reports into the current workflow for transfusion reaction evaluations.

Workflow for physical review of transfusion reaction paperwork and writing report:

- In the blood bank, get the transfusion reaction paperwork in the “transfusion reaction” bin.
- Review the transfusion reaction sheet (see example with numbered boxes on the following page):
 1. Product information – unit number, product type, time start, time stopped, amount transfused
 2. Vital signs: pre and post transfusion
 3. Symptoms and signs of transfusion reaction
 4. Reason for transfusion
 5. Summary of reaction from reporting clinical team member, current medications, and any premedications given
- Review the blood bank evaluation (attached to transfusion reaction report and also in EPIC):

Component	
Product Unit Number	W#####H
Type of Product Transfused	Pack Red Blood Cells
Clerical check	Satisfactory
Visible Serum Icterus	No Visible Icterus
Visible Serum Hemoglobin	No Visible Hgb
ur hemoglobin	Not Performed
Resulting Agency	BJH

Example from
EPIC

- Additional information surrounding the transfusion reaction:
 - This information should be obtained from chart review AND speaking to physician
 - Patient general condition prior to needing transfusion especially those relevant to transfusion reactions such as previous fevers, known infections, volume status, history of previous transfusion reactions, etc.
 - Any updates since transfusion reaction (interventions, response to interventions, etc.)
- Write the note in EPIC
- Once the attending has attested and signed the note, print the note and attach it to the transfusion reaction paperwork
- Turn back into the blood bank

Example of transfusion reaction sheet:



NATIONAL LEADERS IN MEDICINE

REPORT OF A SUSPECTED TRANSFUSION REACTION

PATIENT IDENTIFICATION

Please check (✓) the appropriate box(es) (□) and fill in the blank(s) as needed.

Nursing Staff-Submit this form, unit bag(s), transfusion slip(s), Type and Screen specimen and urine sample to Blood Bank

Immediate Reaction Date - This area must be completed by transfusionist

Date/Time of Reaction: _____ Previous Reactions Yes No Unk

Unit #	Product	Started	Ended	Volume
1				

2	Vital Signs	
	Pre	Post
B/P		
Pulse		
Temp		
RR		
O ₂ sat		

Check all that apply: Rash/Hives Shortness of Breath BP change

3

Chills Abd/Flank Pain Other: _____
 Fever Nausea/Vomiting _____

Primary reason for transfusion: Coagulopathy Genetic Disorder Hematology Disorder Hemolysis
 Internal Bleeding Malignancy Medical Surgery Unknown Other (specify) _____ 4

Patient History and Summation of Reaction: 5

List of Current Medications:

Premedication:

Completed by:

Date:

Time:

*Blood Bank - Attach screen print of completed "Immediate Transfusion Reaction" workup before submitting to LMR
 BELOW THIS AREA FOR BLOOD BANK LMR/MEDICAL DIRECTOR USE ONLY*

Recommendations:

Date Entered:

*****Note:** This section of the transfusion reaction report page will no longer need to be filled out or signed – instead printing out the note AFTER the attending has attested it will contain all of this information and will be used as documentation.

Lab Medicine Resid

SIGNATURE REQUIRED

PRINTED NAME REQUIRED

SIGNATURE REQUIRED

PRINTED NAME REQUIRED

Date:

Telephone #/Pager #

Date:

Telephone #/Pager #

Required Information*THIS AREA FOR BLOOD BANK LMR/MED
Investigation Results (Use case definition criteria in protocol)**

*Adverse reaction: (check one)

- Allergic reaction, including anaphylaxis
 Delayed hemolytic transfusion reaction (DHTR) Acute hemolytic transfusion reaction
 Immune Antibody: _____ Non-immune antibody: _____
 Delayed serologic transfusion reaction (DSTR) Antibodies: _____
 Febrile non-hemolytic transfusion reaction (FNHTR) Hypotensive transfusion reaction
 Infection

Was a test to detect a specific pathogen performed on the recipient post-transfusion?

- Yes No If yes, positive or reactive results: Yes No

Org 1 _____ Org 2 _____ Org 3 _____

Was a test to detect a specific pathogen performed on the donor post-donation?

- Yes No If yes, positive or reactive results: Yes No

Org 1 _____ Org 2 _____ Org 3 _____

Was a test to detect a specific pathogen performed on the unit post-transfusion? (i.e., culture, serology, NAT)

- Yes No If yes, positive or reactive results: Yes No

Org 1 _____ Org 2 _____ Org 3 _____

- Post transfusion purpura (PTP) Transfusion associated circulatory overload (TACO)

- Transfusion associated dyspnea (TAD)

- Transfusion associated graft vs. host disease (TA-GVHD)

Did patient receive non-irradiated blood product(s) in the two months preceding the reaction? Yes No

- Transfusion related acute lung injury (TRALI) Antibody studies performed: (optional)

	Not Done	Negative	Test Result Positive		
			Cognate or cross reacting antigen present	No cognate or cross reacting antigen present	Not tested for cognate antigen
Donor or unit HLA specificity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Donor or unit HNA specificity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Recipient HLA specificity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Recipient HNA specificity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

- Unknown

Other (specify) _____

*Case definition criteria: Definitive Probable Possible N/A

*Severity: Non-severe Severe Life-threatening Death Not determined

*Imputability: Definite Probable Possible Doubtful Ruled Out Not determined

*Outcome: Death Major or long-term sequelae Minor or no sequelae Not determined

Date of Death: _____ / _____ / _____ †Deaths attributable to transfusion must be reported to FDA.

If recipient died, relationship of transfusion to death:

- Definite Probable Possible Doubtful Ruled Out Not determined

Was a particular unit implicated in (i.e. responsible for) the adverse reaction? Yes No

If Yes, which unit (provide at least the last six digits of unit #)? _____

Lab Medicine Resident:

Transfusion Medicine Attending:

SIGNATURE REQUIRED

PRINTED NAME REQUIRED

SIGNATURE REQUIRED

PRINTED NAME REQUIRED

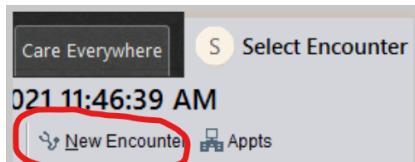
Date: _____ Telephone #/Pager # _____ Date: _____ Telephone #/Pager # _____

Writing A Transfusion Reaction Note

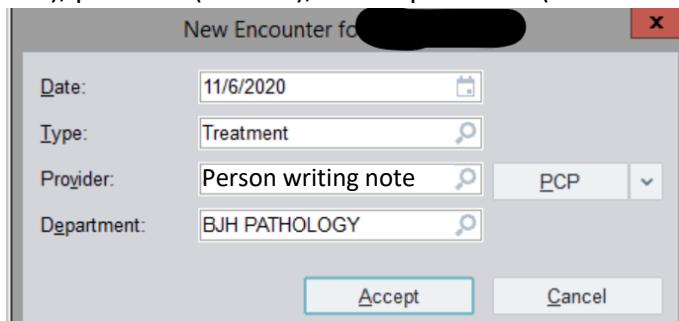
Creating a note

Determine if this is an inpatient or outpatient encounter. Look up the patient in EPIC with "Patient Lookup" Function – inpatients will have a location and unit.

- If inpatient – note is written during encounter
 - Go to the "Select Encounter" tab, confirm the admission during which the transfusion reaction occurred, and select the current admission
- If outpatient - if encounter is closed, a new encounter is needed
 - Go to the "Select Encounter" tab, directly underneath select "New Encounter"

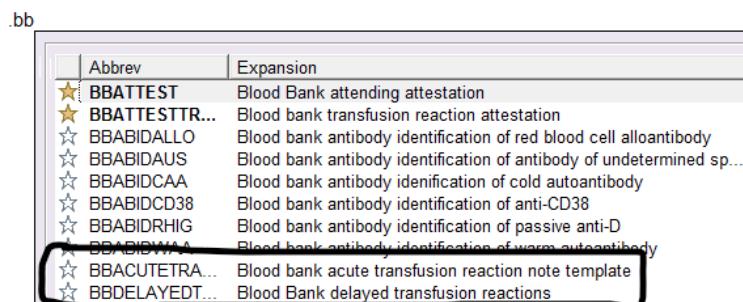


- In the "New Encounter" pop up, enter the date the note is written, encounter type (treatment), provider (trainee), and department (BJH Pathology), and click accept.



Once you are in an encounter, create a new note

- Click on "notes" tab", click on "new note"
 - Type: Progress Notes
 - Service: Pathology
 - Date of Service: date of note (defaults to current date/time) **NOT** the date of reaction
 - Cosign required: check box
 - Cosigner: select attending on service
- Use the "smarttext" function - enter ".bb" and select template:
 - use "delayed" for: DSTRs and DHTRs
 - use "acute" for reactions occurring within 24 hours of transfusion



Completing the transfusion reaction note:

Reminders: Use F2 to jump to each section and answer according to the hemovigilance module (p89-106 in red book, AABB quick reference and CDC hemovigilance doc in resources)

Acute transfusion reactions (blood bank acute transfusion reaction note template)

- **Transfusion reaction interpretation**

- Written as a “top line diagnosis”: “imputability” “transfusion reaction type”, severity
 - Example: Definitive febrile nonhemolytic transfusion reaction, nonsevere
- Imputability: level of confidence that the transfusion caused the reaction in question
- Transfusion reaction type: select the type of reaction you think it is
- Severity: how severe the reaction was
- Case definition: how sure are you that this is the type of reaction as defined by criteria
 - This will be directly underneath the “top line”
- **Note:** If additional information is pending, add a statement that this report is preliminary based on additional information (and state what further workup is being done). This can be removed when the report is appended to additional information is added to the note to complete the workup

- **Transfusion information – information about the implicated transfusion event**

- Recipient ABO/Rh: what is the blood type of the patient
- Donor ABO/Rh: what is the blood type of the transfused blood product
- Blood product type: select type of product transfused
- Blood product modifications: select all modifications of blood products that apply
- Unit numbers: **cut and paste this from the chart to avoid transcription errors**
 - “Chart review” à “snapshot” à “transfusion summary” or “blood administration”
 - Note: only add the unit numbers investigated in the transfusion reaction work up
- Time started: time that transfusion was started
- Time stopped: time the transfusion was stopped
- Volume transfused: amount of blood product transfused

- **Relevant patient history** – narrative surrounding patient’s transfusion reaction

- RELEVANT and BRIEF past medical history – focus on pertinent positives and negatives
- **Do not** just copy/paste from other notes – this is a synthesis of information gathered from multiple sources focused on information immediately relevant to the transfusion reaction
- Avoid abbreviations, use language that any clinician reading the note will understand
- Important components of the narrative
 - Describe the clinical status of the patient within the last ~24 hours, with details relevant to transfusion reaction differential diagnoses (for instance, febrile, received fluids, etc.)
 - The reason for transfusion they received that resulted in the suspected reaction
 - Note any history of previous transfusion reactions and types, if known

- Premedications - types, dose, and approximate timing with respect to transfusion
 - **Describe the transfusion reaction** – when reaction occurred after transfusion started, description of symptoms, medications and interventions,
 - Describe clinical testing done as part of the workup by the clinical team as it relates to the transfusion reaction work up: chest X-rays, EKGs, blood cultures drawn, etc.
 - Describe the resolution of the transfusion reaction, including status of the patient (did symptoms completely resolve? Did the patient need escalation of care?)
- Pre-transfusion and post-transfusion vital signs: can be transcribed from report or found in “Chart review” à “snapshot” à “transfusion summary” or “blood administration”
- **Blood Bank testing information**
 - Enter blood bank evaluation results that were performed as part of the workup on pre- and post-transfusion reaction patient samples. If a test was not performed, put N/A
 - Patient ABO/Rh: enter ABO/Rh from pre- (last type and screen) and post-transfusion
 - Crossmatch compatibility: select if compatible or not if performed or N/A if not
 - DAT results: put result for post-transfusion sample, if positive and pre-transfusion sample was done put that, if not put N/A for pre-transfusion
 - Visible hemolysis: put result for post-transfusion sample, if positive and pre-transfusion sample was done put that, if not put N/A for pre-transfusion
 - Visible icterus: put result for post-transfusion sample, if positive and pre-transfusion sample was done put that, if not put N/A for pre-transfusion
 - Hemoglobinuria: this is only done post-transfusion if specimen sent
 - Correlate with recent UA (if available) if positive to determine if due to RBCs in urine from another cause or if could be attributed to hemolysis of transfused RBCs
 - Clerical check: only performed post-transfusion
 - Indicate if satisfactory or unsatisfactory (is a discrepancy is found)
 - Blood product culture: only done post-transfusion if indicated (if decided to pursue evaluation for septic transfusion reaction)
 - Report will need an addendum once the culture results to finalize the interpretation
 - Additional testing: if indicated, usually none, but not always (depending on the type of transfusion reaction)
- **Clinical relevance** – briefly explain how the transfusion reaction was categorized according to this patient’s transfusion reaction and clinical context
 - Case definition – describe the criteria this case met to justify case definition chosen
 - Severity – describe the criteria this case met to justify severity level chosen
 - Imputability – describe criteria this case met to justify imputability descriptor chosen
- **Therapeutic relevance** – how transfusion reaction could be treated now and how risk could be mitigated in the future
 - These will be specific to the type of transfusion reaction and multiple choices can be selected if indicated
 - There is a sentence regarding premedication and masking fever as a sign of hemolysis – leave this regardless of the type of transfusion reaction

- **Contact information**
 - Blood bank general number
 - Person who prepared the report
 - Attending who this was presented to and who will sign the note

Delayed transfusion reactions - DSTRs and DHTRs (delayed transfusion reactions template)

- **Transfusion reaction interpretation**
 - Written as a “top line diagnosis”: “imputability” “transfusion reaction type”, severity”
 - Example: Probable delayed serologic transfusion reaction, severity not determined
 - Imputability: confidence that the transfusion caused the reaction in question
 - Transfusion reaction type: select the type of reaction you think it is
 - Severity: how severe the reaction was
 - Case definition: how sure are you that this is the type of reaction as defined by criteria
 - This will be directly underneath the “top line”
- **Relevant patient history** – narrative surrounding the transfusion reaction
 - RELEVANT and BRIEF past medical history – focus on pertinent positives and negatives
 - **Do not** just copy/paste from other notes – this is a synthesis of information gathered from multiple sources focused on information immediately relevant to the transfusion reaction
 - Avoid abbreviations, use language that any clinician reading the note will understand
 - Important components of the narrative
 - Describe the patient’s clinical status within the last ~24 hours, with details relevant to transfusion reaction differential diagnoses (for instance, dropping hemoglobin, suspicion for hemolysis, etc.)
 - Describe clinical testing done as part of the workup by the clinical team as it relates to the transfusion reaction: suspicion for hemolysis, related labs (LDH, haptoglobin, hemoglobin trend, urine hemoglobin)
- **Clinical relevance** – briefly explain how the transfusion reaction was categorized according to this patient’s transfusion reaction (use the hemovigilance terms and tables)
 - Case definition – describe the criteria this case met to justify case definition chosen
 - Severity – describe the criteria this case met to justify severity level chosen
 - Imputability – describe criteria this case met to justify imputability descriptor chosen
- **Therapeutic relevance** – how transfusion reaction could be treated now and how risk could be mitigated in the future
 - These will be specific to the type of transfusion reaction and multiple choices can be selected if indicated
 - There is a sentence regarding premedication and masking fever as a sign of hemolysis – leave this regardless of the type of transfusion reaction

- **Contact information**
 - Blood bank general number
 - Person who prepared the report
 - Attending who this was presented to and who will sign the note

Finalizing the transfusion reaction note:

Sending the note to attending for review and attestation in EPIC

- Review the report and sign if considered complete. Signing the note will send it to the designated attending for review and attestation.
- **Note:** If you made a new encounter you must also sign the encounter (the bottom right section of EPIC. Designate the attending on service as the co-signer for the encounter).
- **Note:** If additional information is pending (such as blood product culture), write up the complete report with what you suspect is the cause add the additional information that is pending below the Transfusion Reaction interpretation. Once available, the report must be addended with the additional information and finalize the interpretation.

Returning the completed transfusion reaction forms to the blood bank

- Print the transfusion reaction note complete with the attending attestation
- Return it to the blood bank to Fairfax Altheimer (can put in her mailbox)
- Note: this workflow replaces filling out the bottom of the first page and the second page of the transfusion reaction report (which was previously done by hand)

Cellular Therapy Product Reactions

Cell therapy products include a variety of cell types infused for therapeutic purposes, including:

- Hematopoietic progenitor cell (HPC) products – majority of products at BJH
 - Anatomic source of cells
 - HPC-A: collected by apheresis (most often),
 - HPC-M: bone marrow (less common but regularly), and
 - HPC-C: cord blood (very uncommon at BJH)
 - Donor source of cells
 - Autologous – frozen between collection and infusion
 - Allogeneic – can be fresh or frozen between collection and infusion
- Chimeric antigen receptor (CAR) -T cell products – genetically modified T cells
 - Autologous cells collected by apheresis
 - Cells sent fresh or frozen (depends on which product) to manufacturer
 - Cells received frozen

Allogeneic HSCT products are frequently infused fresh, but autologous HSCT products are usually frozen for infusion at a later date. Before freezing, cells are mixed with a cocktail resulting in a final concentration of 10% cytoprotective DMSO (Dimethyl Sulfoxide). Typically, 1 to 5 bags of HSCT products (each bag is 100 mL, therefore 10 mL DMSO per bag) are thawed at the patient's bedside and infused over a few minutes.

Adverse reactions to cell therapy product infusions:

The primary LMR reviews adverse effects of cell therapy product infusions. Patients receiving fresh or frozen HSCT infusions can experience a range of adverse effects. **Note: Only frozen products contain DMSO.**

The Circular of Information for the use of Cellular Therapy Products is a useful resource regarding information on cellular therapy products and associated adverse reactions.

Adverse reactions are categorized by the Circular of information according to mechanism:

- **Nonimmunologic:** DMSO toxicity*, circulatory overload*, septic infusion reaction**, transmission of infectious disease or disease agents, fat emboli, bleeding due to excessive anticoagulation, hypothermia, nonimmunologic hemolysis
- **Immunologic, immediate:** febrile nonhemolytic reaction*, acute hemolytic reaction, allergic reaction, TRALI
- **Immunologic, delayed:** alloimmunization to antigens, delayed hemolytic reaction, graft-vs-host disease

*Common cell therapy product reactions include:

- DMSO toxicity:
 - Histamine release
 - Signs/symptoms: coughing, flushing, rash, chest tightness, wheezing, nausea/vomiting, unpleasant taste in mouth, hypoxia

- Leukocyte/cytokine (febrile nonhemolytic reaction):
 - Cytokines, present in product or infused white cells destroyed
 - Signs/symptoms: temperature elevation, chills, +/- dyspnea, hypoxia
- Volume/circulatory overload:
 - Volume overload due to rapid product infusion
 - Signs/symptoms: similar to TACO (dyspnea, hypertension)

****Septic infusion reactions:**

- Every collected cellular therapy product is cultured at least once.
- If a septic reaction is suspected from an infusion reaction, confirm the result of cultures on the product with the cell therapy lab
- If a product culture results as positive off hours, the LMR may be contacted
 - Immediately relay the results to the clinical team taking care of the patient
 - Blood cultures and prophylactic antibiotics might be considered
 - Contact the cell therapy lab the following morning

Each case is discussed at rounds before it is signed off by the attending. Present all relevant data, including relevant patient history, vital signs before, during and after infusion, treatment and recovery. Check 2 boxes: Outcome Analysis and Product Reaction Likely Cause (drug reaction is due to patient medications; DMSO is a product reaction) and sign the form.

IgA Deficiency

Transfusion of a patient with IgA deficiency can manifest as an acute allergic reaction with the following signs and symptoms:

1. Pulmonary/ventilatory: bronchospasm, glottic and/or pharyngeal edema
2. Dermatologic: urticaria
3. Hemodynamic: hypotension, tachycardia

Prediction of anaphylaxis secondary to IgA deficiency is difficult:

Presence of anti-IgA is not a good predictor of reactions in the absence of a prior history of anaphylaxis. The prevalence of anti-IgA antibodies in asymptomatic IgA deficient patients is variable:

- 10-50% of severely IgA deficient patients
- 50-100% of patients with coexisting immune dysregulation (e.g. IgG2 subclass deficiency, rheumatoid arthritis, SLE)
- 25-50% of severely IgA deficient persons with anti-IgA antibodies have been transfused or pregnant

For suspected IgA deficiency:

- Confirm IgA concentration <25 mg/dL using in-house test.
- If less than <25 mg/dL, send for IgA Deficiency Panel which includes a more sensitive quantitative IgA level and Anti-IgA detection.

- Check "IgA Deficiency Panel" (403107P) on the requisition and provide 2 mL of serum (red top tube). Send to Chemistry Send-Outs (Viracor IBT Laboratories).
 - **DO NOT SEND TO MAYO CLINIC (The lower limit of detection is too high)**
- IgA deficient products require IgA concentrations < 0.05 mg/dL (<1:900 US blood donors).
- Consider haptoglobin assay for Asian patients (estimated incidence of homozygous haptoglobin deficiency is ~1:4,000 in Japanese; 1:1,500 in Korean; and 1:1,000 in Chinese). Haptoglobin deficiency can also cause anaphylaxis in the setting of blood transfusion.

Management:

When the diagnosis of IgA deficiency has not been confirmed with serologic testing, or when IgA deficient products are not available:

- Use double washed RBCs or frozen, deglycerolized RBCs (also washed).
- Use volume-reduced PRT platelets with saline re-suspension (4-hour expiration after re-suspension, and variable reduction of *in vivo* recovery).
- Use factor concentrates (e.g. Kcentra, fibrinogen) instead of FFP or Cryo.

When IgA deficiency has been confirmed:

Use IgA deficient plasma and other blood components from IgA deficient donors, when available. If not available, manage as stated above.

Acute Management:

Stop the procedure or transfusion of potential allergen immediately. If anaphylaxis and anaphylactoid reactions develop treat according to BCLS and ACLS protocols.

Discuss with attending need to consult Allergy/Immunology to guide the therapy.

Pharmacologic support includes:

- Antihistamines: H1 (e.g. Benadryl 1 mg/kg) and H2 blockade (e.g. ranitidine, cimetidine, Pepcid).
- Inhalation therapy: use B2 agonists like albuterol for bronchospasm and racemic epinephrine for glottic/pharyngeal edema.
- Steroids: Solucortef or solumedrol.
- For more severe cases: administer 1:1000 epinephrine 0.2-0.5 mL for adults and 0.01 mL/Kg for children (IM or SubQ) and consider intravenous use of vasopressors like epinephrine, norepinephrine or vasopressin for refractory hypotension.

Common Send-Out Tests

Molecular testing (Whole Blood or Fetal Amniocytes)

Occasionally Blood Bank Technologists will ask you to request the team order RBC Genotyping. Or a clinician may request genotyping. Common Indications for RBC Genotyping include:

1. Individuals on a medication interfering with RBC antibody workup.
2. Individuals with complex antibody work up due to multiple alloantibodies
3. Discrepant Serologic Results – Anti-D in individual typing as D positive
4. Weak D Typing
5. Individuals with recent transfusion
6. Hemolytic Disease of the Newborn (fetal testing)

Molecular testing can be performed at the American Red Cross Reference Laboratory, Versiti, or MVBC. Tests include analysis of red blood cell antigens including Rh (D, C, E) variants as well as MNS, Kidd, Kell, and Duffy, molecular analysis of platelet antigens (HPA-1a/b, 2a/b, etc.).

Sample requirements:

- Whole Blood: 5-10 ml EDTA (lavender top) or ACDA (yellow top) whole blood tube (ARC, MVBC, Versiti)
- Amniocytes: 1-5 ml amniotic fluid or 1-5 x 10⁶ cultured amniocytes. (Versiti only)

For more information, contact: pjmolecular@usa.redcross.org, or call: 215-451-4917.

Contact BJH blood bank send outs and ordering physician to coordinate.

The most common genotyping indication, patients on anti-CD38 (daratumumab) or an anti-CD47 medication, is usually ordered by trial coordinators. Individuals with weak D on forward type may or may not be at risk for developing an anti-D if given D positive.

There are three major RBC genotyping panels that are commonly sent out, Human Erythrocyte Antigen (HEA) panel, RhD, and RhCE panel. All 3 genotyping panels are utilizing Immucor's BeadChip arrays based on their proprietary elongation-mediated multiplex analysis of polymorphism (eMAP). The HEA panel genotypes the most common polymorphisms responsible for the major RBC antigens and is useful for patients with difficult antibody workups. The RhD and RhCE panels are necessary in individuals with seemingly auto-antibodies to RhD or RhCE. Rh variants are commonly seen in African American individuals.

Clinicians may order RBC genotyping in Epic by searching in Epic “RBC antigen genotyping” or “RBC genotyping.” A screenshot of the order form is below. They must select the antigen type discussed above. Other is reserved for rare instances in which Sanger Sequencing of an entire gene may be necessary.

RBC antigen genotyping - ✓ Accept | ✗ Cancel

Process Instructions: Select "human erythrocyte antigen panel" for patients taking monoclonal antibody therapy that interferes with blood bank testing (e.g. daratumumab, anti-CD47).

Frequency: Once (Routine) Once STAT

At
 Today Tomorrow
 Add

Specimen Type: Blood Search

⚠ Antigen Types: Human erythrocyte antigen panel RhD variant RhCE variant Other (describe)

Comments: [+ Add Comments](#)

CC Results: [+ My List](#) [+ Other](#)

? Next Required Link Order ✓ Accept | ✗ Cancel

Platelet Antibody Testing

- Platelet serology testing can aid in diagnosing antibody-mediated thrombocytopenia and in investigating the cause of platelet refractoriness.
- Indicated for diagnosis of suspected: Neonatal allo-immune thrombocytopenia (NAIT), Post-transfusion purpura (PTP), autoimmune thrombocytopenic purpura (AITP), platelet refractoriness, drug-induced thrombocytopenia.
- Sample Requirements: 5 mL serum (red top). Send sample refrigerated.
- For more information, contact Platelet & Neutrophil Immunology Lab at Versiti Wisconsin. Call 800-245-3117 x6255.
- Contact BJH chemistry send out lab and ordering physician to coordinate.

Drug-Induced Immune Hemolytic Anemia

- For patients with hemolytic anemia with a temporal relationship to drug therapy, in addition to (usually) a positive direct antiglobulin test and (sometimes) non-reactive eluate.
- Sample Requirements: 2 full red top tubes, 2 full EDTA (lavender top) tubes, **and implicated drug** (lyophilized powder, pills or tablets – no solutions or suspensions).
- Contact BJH blood bank send outs and ordering physician to coordinate.
- For more information contact Missouri-Illinois Region American Red Cross at 314-658-2084.

ADAMTS-13 Inhibitor Assay

BJH Immunology lab performs the Technozym ELISA functional assay for ADAMTS-13 activity on the Quant Lyzer automated DLISA platform (INOVA). This is not FDA cleared, so it was validated as a laboratory developed test.

- The assay consists of ELISA wells coated with antibody to GST (glutathione S transferase). The plates are incubated with reconstituted vWF A-2 domain 73 amino acid peptide

containing the target for ADAMTS-13 cleavage which is attached to GST to bind it to the wells. Following a wash, calibrators, and QC and patient plasma samples are diluted, added to wells, and incubated to allow time for ADAMTS-13 to cleave the vWF substrate creating a new C terminus. After washing, an antibody specific for the vWF ADAMTS-13 cleavage which is linked to horse radish peroxidase (HRP) is added, incubated, and the plate is washed. Finally, HRP substrate is added and change in OD is measured. A curvilinear calibration curve is derived from the 6 calibration points and the average OD of QC and patient samples run in triplicate are compared to the calibration curve to obtain ADAMTS-13 activities.

- Reportable range (AMR) 5% to 64%
- Batched on Fridays at 11AM. Runs take approximately 3-4 hours for results.
- LMR may be asked to approve a STAT run on other days (only on day shift, sample in lab by 11AM) if patient scenario warrants urgent testing.
- ADAMTS-13 activity is stable in citrated plasma at room temperature for at least 4 hours and refrigerated for at least 24 hours. Therefore, it is OK to obtain an in lab blue top tube from the Coag lab area (typically moved from room temperature to refrigerator within 4 hours) to perform an urgent ADAMTS-13 test, especially if the patient has been transfused with FFP or undergone an initial plasma exchange.
- Activity <20% will reflex to a send out ADAMTS-13 inhibitor assay at Versiti Wisconsin
- For more information on inhibitor testing, contact: call (800) 245-3117.
- Sample Requirements: Citrated Plasma (light blue top), fresh or frozen.

SLCH Blood Bank

Special considerations in pediatric blood bank practice

Although you are unlikely to be paged about the following considerations (they are standard practice), it is important to know how pediatric (and particularly neonatal) blood banking is different from adult blood banking. The two most important differences are:

Neonatal compatibility testing: Neonates (<4 months) do not require reverse (plasma) ABO typing, as their circulating antibodies are likely to be maternal in origin. Forward ABO typing and standard IAT are sufficient. Electronic crossmatch is allowed if no antibodies are detected on IAT and may be used until the neonate is 4 months old or discharged (unlike adults, who require a new sample after 3 days if recently transfused). Full crossmatch or appropriate antigen-negative blood is required if IAT is positive. If non-O RBCs are to be given, a reverse ABO type *in Coombs phase* is necessary to detect maternal IgG anti-ABO antibodies. DAT is sometimes performed on request to identify maternal IgG antibodies attached to neonatal RBCs, when hemolytic disease is suspected.

Aliquoting: Single-donor units are often too large for a single transfusion event in small children. The blood bank may use a sterile welding device to “split” off a smaller portion of a blood product into a syringe or separate bag. The original bag retains its shelf life, while the syringe (considered an “open” system because it is an unlicensed container) is given a 24-hour shelf life for RBCs/plasma or a 4-hour shelf life for platelets. A neonate may be “assigned” to a single unit if multiple transfusions will be needed, in order to reduce donor exposure. Standard dosing for small children is weight-based:

- RBCs: 10-15 ml/kg (expected to increase Hgb by 2-3 g/dL)
- Plasma: 10-15 ml/kg
- Platelets: 5-10 ml/kg (15 ml/kg may be requested for severe thrombocytopenia)

Common LMR Calls from SLCH Blood Bank

While serving as primary LMR, you will also take patient-related calls from the SLCH blood bank. These calls are similar in nature to BJH, but several differences are noted below. Discuss issues with Dr. Jackups (SLCH Blood Bank Medical Director), regardless of which attending is on service at BJH. **Our service does not perform or manage apheresis at SLCH;** pediatric nephrology does.

Complicated or unusual serology interpretations: As the SLCH blood bank does not perform complex reference work, additional testing will usually be sent to the Red Cross reference lab automatically. You may be called about what work-up should be performed.

Neonates with Weak D (<2+) **on forward typing:** Obtain birth history (where, manner, complications), transfusion history, and cord blood ABO/Rh type results (with attention to Rh strength). The question will likely need to be resolved with molecular typing; however, if the neonate is small this can be delayed until they can tolerate the blood draw. A comment should

be added in the blood bank stating “Rh weakly reactive, possible Rh variant,” and D-negative blood should be dispensed until molecular typing has been performed. Additionally, the LMR will need to notify the clinical team of the results when molecular typing is resulted.

Unusual blood product requests: The blood bank may occasionally question the use of unusual or excessive blood product requests and ask you to investigate. You may need to discuss options with the ordering physician.

Special processing requests: There is a detailed blood bank policy regarding which patients should receive special processing such as irradiation (see below). PRT platelets are considered equivalent to both irradiated and CMV-seronegative platelets. If a physician requests processing outside of this policy, attempt to determine why and contact Dr. Jackups for approval. **These indications may be different from BJH!**

Special Product Request Guidelines

Indications for Irradiated Products
0-4 month old neonate, Congenital immunodeficiency, solid organ transplant recipient, oncology patient, immunosuppressive therapy/chemotherapy for hematologic disorder, aplastic anemia, HSCT candidate or recipient, allogeneic HSCT donor
CMV negative Products: No longer offered at SLCH

Product (un)availability: As SLCH’s blood bank inventory is smaller than BJH’s and pediatric patients often require very specific (and rare) products, the desired product may not be available. When this occurs, you need to contact the physician and determine if they can wait for the Red Cross to provide the product (the blood bank tech should be able to give you a rough estimate of the delay) or, if the patient needs blood sooner, what is the “best” product available in inventory. Some considerations:

- ABO-incompatible plasma in platelet components: While this is an acceptable option, physicians are often unwilling to give ABO-incompatible plasma to small patients due to the hemolytic risk. SLCH policy allows up to one unit, or 15 ml/kg in a smaller child, of ABO-incompatible plasma in a 24-hour period without approval or volume reduction.
- Rh-positive platelets to an Rh-negative recipient: This is an option for patients who are severely immunosuppressed (e.g. BMT during engraftment) and thus unlikely to make anti-D, or to neonates who have not made antibodies. In others, especially females, the option of using a dose of RhIG should be offered.
- Leukoreduced (LR) blood instead of CMV-seronegative: The AABB currently considers LR to be equivalent to CMV-seronegative blood for CMV risk reduction, though studies in children are limited. **PRT platelets are a substitute product for CMV-seronegative platelets.**

Requests for HLA-compatible platelets: Request 5-60 min post-transfusion platelet counts and an HLA antibody screen. Discuss new requests with Dr. Jackups. The heme/onc service is usually quite good at obtaining corrected count increments (CCIs) and communicating with the

blood bank. HLA-compatible products will be obtained from the Red Cross, *not BJH*, so you do not need to fill out forms or handle donor issues on a regular basis. **BJH will not provide products to SLCH.**

Heme/Onc algorithm for platelet refractoriness:

1. If platelet refractoriness is suspected, then calculate the corrected count increment (CCI).
 - a. As an example, if the platelet count increases by 10,000 approximately 30 minutes after 1 unit of platelets is given in a patient with a body surface area of 1.5, then the CCI is $10,000 \times 1.5 \div 3.5 \div 1$ or 4,286.
 - b. As another example, if the platelet count increases by 50,000 approximately 15 minutes after 2 units of platelets are given one after the other in a patient with a body surface area of 2, then the CCI is $50,000 \times 2 \div 3.5 \div 2$ or 14,286.
2. CCI = [increase in platelet count 5 to 60 minutes after the transfusion] × [body surface area] ÷ [3.5] ÷ [number of units].
3. If the CCI is less than 7,500, platelet refractoriness is possible.
4. If platelet refractoriness is possible, transfusions with ABO-matched platelets should be ordered.
5. If the CCI continues to be less than 7,500 after each of two consecutive transfusions of ABO-matched platelets, platelet refractoriness is likely.
6. If platelet refractoriness is likely, testing for the presence of class 1 HLA antibodies should be performed.
 - a. Order HLA typing and Antibody screen under “HLA Testing for Transfusion Support/Platelet refractoriness”.
 - b. After submitting the requisition, notify Dr. Jackups so he can look for the results and assist with future platelet transfusions.
7. If the class 1 HLA antibody screen is positive, transfusions with HLA-compatible or HLA-matched platelets should be tried.
8. “Fresh” platelets (stored fewer than 48 hours) and/or ABO-matched platelets may be used if the results of the class 1 HLA antibody screen are still pending or are ultimately negative.

Massive transfusion protocol policy: Product delivery for MTP is usually handled by the SLCH blood bank, but the LMR may be involved if needed products are unavailable or clinical questions arise. Products are dispensed according to the algorithms below. Because of inventory reasons, plasma is not routinely pre-thawed, and thus may not be available for the activation pack. O-negative RBCs and AB plasma are used before the patient's ABO type is confirmed (unlike BJH, which uses O-positive RBCs for men and A plasma in order to conserve inventory). ABO confirmation may be performed with a sample from the core lab that is labeled with a different timestamp (unlike BJH, which requires a new second draw).

Children <30 kg

Activation Pack Emergency Release (w/in 5 mins.)	Pack 1 and 2*	Pack 3 until stop*
2 units PRBCs	2 units PRBCs	2 units PRBCs
0-2 units plasma, <i>as available</i>	2 units plasma	2 units plasma
½ to 1 Single Donor Platelet	½ SDP	½ SDP 3 units cryoprecipitate

Children ≥30 kg

Activation Pack Emergency Release (w/in 5 mins.)	Pack 1 and 2*	Pack 3 until stop*
4 units PRBCs	4 units PRBCs	4 units PRBCs
0-4 units plasma, <i>as available</i>	4 units plasma	4 units plasma
1 Single Donor Platelet	1 SDP	1 SDP 1 pool of cryoprecipitate (5 units)

* Pack 1 shall be ready 20 minutes from activation. All other packs shall be ready within 20 minutes from release of the previous pack. The blood bank will not prepare the next pack until dispense of the previous pack.

Transfusion reactions: Transfusion reaction summaries will be emailed to the LMR, who will need to look up the patient's chart or speak with the clinician, answer the 5 questions listed at the bottom of the email (shown below), and write a note in Epic similar to the BJH process, but with Dr. Jackups as co-signer. If there is an urgent need for additional blood products, the LMR will be called. "Reply All" on your email response; Dr. Jackups may revise the answers as needed. Although SLCH does not currently use the CDC Hemovigilance definitions for transfusion reactions (pg. 82), these definitions serve as a good guide for reviewing reactions at SLCH. **Additionally, make distinctions between “minor allergic” reactions (local urticaria), “major allergic” reactions (generalized urticaria, mild swelling, or cough that is not clearly associated to the reaction), and anaphylaxis (signs of respiratory compromise or angioedema).** Note that pre-medications (diphenhydramine and acetaminophen) are not recommended for children unless there have been multiple allergic or febrile reactions.

As BJH employees, we do not have privileges to obtain SLCH physicians' pager numbers from the main SLCH operator.

Should you need to identify and/or contact a SLCH physician, use the SmartWeb System. Steps are outlined in the following pages.

Transfusion reaction questions:

1. What type of reaction should be reported (allergic, febrile non-hemolytic, TRALI, other)?
2. Is there any special processing that should be done with future transfusions (washing, etc.)?
3. Should pre-medications be given in addition to the current protocol?
4. Are there additional comments/recommendations that should be included in the result?
5. Is it okay to transfuse the patient with additional products?

Protocol Exceptions: All exceptions to laboratory protocols, which by definition arise in unusual clinical situations, must be approved by Dr. Jackups. The LMR will facilitate communication between the blood bank and clinicians as needed.

Directed donor policy: It is SLCH policy not to accept blood for directed donation and to dissuade directed donation requests, unless there is a clear clinical purpose (e.g. maternal platelets for NAIT). It is worth noting that donors need to meet allogeneic donor screening criteria (e.g. Hgb/Hct), except as waived by the donor center medical director, so a woman trying to donate platelets for her newborn with NAIT may still be rejected for donation. Data from the Red Cross suggest that directed donors, particularly first-time donors, are 2-5 times more likely to test positive for transfusion-transmitted diseases. The LMR should *not* contact prospective donors (often relatives of the patient), as this is a very delicate issue. If contacted with such a request, contact Dr. Jackups.

If a directed donation is approved, the prospective donor(s) must coordinate with ARC themselves to set up the donation (Ph. 1-800-RED CROSS). Instruct the clinical team they must complete a “Special Collections Order” form and send it to ARC. The form can be found here: https://www.redcrossblood.org/content/dam/redcrossblood/controlled-documents/Special_Collections_Autologous_Directed_ARC-DOC-017795.pdf

Guide to SLCH SmartWeb paging system

To Identify a SLCH clinician based on patient location:

1. From any BJC/SLCH computer, enter into the URL: **SLCHoncall** or enter the following URL: http://smartweb.carenet.org/smartweb/pages/oncall/oncall_search.jsf?COG=SLCH

2. Click the arrows to “RESIDENTS/INTERNS SCLH” or type “residents / interns” in search bar.

Assignment	Start Time	End Time	Clinician	Message Count
ANESTHESIA IN-HOUSE CALL AND EMERGENCY PAGER - SLCH [104906]	All day		ANESTHESIA IN HOUSE AND EMERGENCY PHONE [Msg Id 314491111]	0
Anesthesia PAIN Service Pager - SLCH [103999]	All day		SLCH PAIN SERVICE ON CALL PHONE [Msg Id 102699]	0
A TO Z PEDIATRICS [113808]	7:00AM		Herkenhoff, Andrea Nicole [Msg Id 102916]	0
ACADEMIC PEDIATRICS [110475]	8:00AM		Dorfman, Julie R [Msg Id 114915]	0
ADMINISTRATOR ON CALL - SLCH [8825]	All day		WOLF, MAGGIE [Msg Id 3143740629]	0
ADOLESCENT CENTER / MEDICINE -SLCH [8084]	All day		MONDAY-FRIDAY 8AM-4:30PM, CALL THE OFFICE AT 454-2468, [Msg Id 10449]	1
ADOLESCENT CENTER / MEDICINE -SLCH [8084]	All day		Pax, Kathryn L. [Msg Id 3143600304]	2
AFFINIA ADULT [117089]	7:00AM		Moore, Catherine Ruth [Msg Id 110185]	0
AFFINIA DENTAL [117092]	7:00AM		DENTAL STUDENT - SLCH ANSWER LINE [Msg Id 117125]	0
AFFINIA OB [117091]	7:00AM		ONEIL-CALLAHAN, MICHAEL E MD [Msg Id 110021]	0

3. Scroll through the listing of residents and interns to find the trainee associated with the patient's location.

The screenshot shows a list of trainees assigned to various teams on Wednesday, June 8. The columns include the trainee's name, team, start date, end date, and status. The data is as follows:

RESIDENTS / INTERNS - SLCH [6967]	All day	10100 TEAM SENIOR RESIDENT ON CALL [Msg Id 3142263432]	0	10100 Team Senior Resident On Call
RESIDENTS / INTERNS - SLCH [6967]	All day	11100 TEAM INTERN ON CALL [Msg Id 3142268252]	0	11100 Team Intern On Call
RESIDENTS / INTERNS - SLCH [6967]	All day	11100 TEAM SENIOR RESIDENT ON CALL [Msg Id 3145366676]	0	11100 Team Senior Resident On Call
RESIDENTS / INTERNS - SLCH [6967]	All day	12 INTERN ON CALL [Msg Id 3142809607]	0	12 Intern On Call
RESIDENTS / INTERNS - SLCH [6967]	All day	12 INTERN ON CALL [Msg Id 3142809607]	0	12 Intern On Call
RESIDENTS / INTERNS - SLCH [6967]	All day	12 SENIOR RESIDENT ON CALL [Msg Id 3145655953]	0	12 Senior Resident On Call
RESIDENTS / INTERNS - SLCH [6967]	All day	7100 TEAM RESIDENT ON CALL [Msg Id 3142805327]	0	7100 Team Resident On Call
RESIDENTS / INTERNS - SLCH [6967]	All day	9 SR RESIDENT [Msg Id 3145749899]	0	9 Senior Resident
RESIDENTS / INTERNS - SLCH [6967]	All day	SILVER TEAM SENIOR RESIDENT PHONE 1 - SLCH [Msg Id 108848]	0	Silver Team Senior Resident
RESIDENTS / INTERNS - SLCH [6967]	All day	10100 TEAM INTERN ON CALL [Msg Id 3142616149]	0	10100 Team Intern On Call

4. Click on the appropriate trainee's designation (blue text) and popup will display.

5. Click on the pager icon in the top left corner of the popup to send a text page.

The screenshot shows a detailed view of the 11100 TEAM INTERN ON CALL assignment. The data is as follows:

Directory Detail View for 11100 TEAM INTERN ON CALL		Status: ON PAGE			
Msg Id:	3142268252	Current Exception:	Covered By Kessler, Haeja Annamarie (ID: 117991)		
Member Of					
RESIDENTS / INTERNS - SLCH [6967]					
Directory Info					
Title	Phone	Phone Type	Department		
3142268252	CORPORATE CELL	HOUSE STAFF			
314-454-8006	EXT	HOUSE STAFF			
Address Info					
Building	Room / Floor	Address	Address Type		
Current On Call Info					
Start date	End date	Group Name	Group Path	Time Zone	Priority
20-Jan-2022 07:00 AM	20-Jan-2023 07:00 AM	RESIDENTS / INTERNS - SLCH		CENTRAL	0

To Identify a SLCH clinician based on clinician:

1. From any BJC/SLCH computer, enter into the URL: **SLCHoncall** or enter the following URL:
http://smartweb.carenet.org/smartweb/pages/oncall/oncall_search.jsf?COG=SLCH

2. Click on the tab labelled “paging”

3. Enter the SLCH clinician’s contact information into the fields

The screenshot shows the Smart Web interface with the 'Paging' tab selected. In the 'Messaging Search' section, fields for Last Name, First Name, Department, Group/Function Name, and ID are present, along with a 'Search' button. To the right is a 'Recipient List' panel containing buttons for 'Compose Message', 'Clear Recipients', 'Personal Message Group', and 'Save'. Below these are sections for 'PC Based Personal Message Groups' and 'Children's Hospital St. Louis' branding.

4. Click on the pager icon to send a text page.

The screenshot shows the Smart Web interface with the 'Paging' tab selected. In the 'Messaging Search' section, fields for Last Name, First Name, Department, Group/Function Name, and ID are present, along with a 'Search' button. Below is a table titled 'Displaying 1 - 1 of 1' showing one result: ID 101614, Name Physician name, Department PATHOLOGY & IMMUNOLOGY, Status ON PAGE, Type SPRINTWCTP (Alpha). A 'Compose A Message' dialog is open over the main interface, prompting the user to 'Compose and send your message' with a text input field. The dialog also includes fields for 'Remaining Char's: 1478', 'Messaging Type: Alpha', and 'Maximum Char's: 1500'. Buttons at the bottom of the dialog include 'Send Message', 'Clear', and 'Close'.

5. The clinician's direct pager number is also listed in the box labelled "ID"

The screenshot shows a web browser window titled "Smart Web - Windows Internet Explorer". The URL is <http://www.silverspoon.org/SmartWeb/pager/paging/paging.pdf>. The page is titled "Smart Web" and has a navigation bar with links like "Smart Web", "Compose Message", "Personal Message", "Patient List", and "Clinical Search". A red arrow points to the "ID" column in a search results table.

Last Name	First Name	Department		Status	Type
BALDRIDGE	DUSTIN M.D.	HOUSE STAFF	ON PAGE	SUCHVRZ5MP (Alpha)	

Below the table, there is a message: "Displaying 1 - 1 of 1" and a footer note: "© Silverspoon Today, LLC. Version 11-Nov-14 10:51".

Hematology and Coagulation

Hematology LMRs will split their rotation between hematopathology (bone marrow, lymph nodes/consult, flow cytometry services) and laboratory hematology and coagulation. There may be minor updates throughout the year regarding hematology and coagulation. Please refer to the Hematopathology “Orange” Survival guide.

Hematology LMR duties

There are currently three hematopathology (HP) services with the following responsibilities:

HP1: In-house bone marrow biopsies and in-house lymph node biopsies

HP2: In-house bone marrow biopsies and extramural consult materials

HP3: In-house bone marrow biopsies (no-trainee) and peripheral blood/ body fluid flow cytometry; physician review of peripheral blood smears/ body fluid specimens originating in the hematology laboratory

Hematology LMRs are assigned to the **HP3** service and have the following responsibilities:

Flow cytometry service (HP3): The Hematology LMR on service will be stationed at the flow cytometry lab, review flow cytometry results for the specimens assigned to the HP3 service (see above), prepare reports for sign out with the HP3 attending and investigate any flow cytometry lab issues that arise. Please refer to Hematopathology Survival Guide for details.

Hematology on-call phone: The phone operates between 8AM and 5PM on weekdays ONLY. On nights and weekends, calls are automatically forwarded to the transfusion LMR. This ensures there are no duty hour violations. You will answer calls for alert values, heme/coag test approvals, test interpretations, and special requests. While there is not a weekly beeper report, you **should log your calls and send out approvals in the Call Log**. You will **present select calls at the heme/coag beeper report**.

Peripheral blood senior staff review: CBCs and other body fluids that are flagged or ordered for morphologic examination that meet certain criteria (see below) must be reviewed by a pathologist, who in general is the HP3 attending. These will be sent to the Hemepath inbox in the IOH3 slide mailroom in between 10-11AM Monday-Friday for you to preview. Gather basic clinical information on the patient (including pathology diagnoses), review the smear, fill out a goldenrod-colored billing sheet (available at CP residents’ room, core lab flow desk, and Administrative “pod” on IOH3), and sign out with the HP3 attending. Schedule sign out times with the HP3 attending in person or via email. After sign out, turn the slides and paperwork in to the designated Hemepath Admin to be processed and returned to the lab. If a smear is suspicious for a previously undiagnosed, critical finding (e.g. new leukemia), and the patient is not currently being followed by the BMT service (floors 8800, 9800, 24/7 clinic, etc.), **contact the patient’s clinician with the result**, and document the exchange on the differential sheet. This is a service we provide to the hospital, as the clinician may not always see the results of our review.

Criteria for pathologist review include:

- Lymphocytosis, abs lymph > 3.3 with any number of variant lymphs
- ≥ 10% Prolymphocytes
- Hairy cells, Sezary cells, or Plasma cells
- 1 % Blasts on first-time patients
- 1 % Promonocytes with > 1.2 abs monocytes
- > 1.0 abs large granular lymphocyte counts
- Malignant non-hematopoietic cells
- Any cells with questionable identification

Hemoglobin Analysis: Hemoglobin capillary electrophoresis is performed twice weekly on Tuesdays and Thursdays. Patients with new findings of abnormal hemoglobins will have gel electrophoresis performed on Thursday. Acid gel will be performed if HbS or HbC was identified, while acid and alkaline gels will be performed if abnormal Hb other than HbS and HbC was identified. Cases for which gel electrophoresis was performed and other cases for review (e.g. MCV ≤70 fl with normal hemoglobin pattern) are placed in a folder on the Immunology lab bench on Thursday afternoon (usually by 3PM) for you to preview and sign out with Dr. Frater, or his substitute, on Friday. Coordinate the sign out time with Dr. Frater, preview the results, and gather a short history on each patient to facilitate sign out. Pertinent patient history includes demographics (e.g. African American, SE Asian), indication for Hgb analysis, past Hgb analyses, past CBCs (red cell indices), and iron studies. Return paperwork to the Immunology lab when complete.

Hematology Service Conference Schedule

Conferences you are expected to attend:

- Week long Laboratory Hematology boot camp (formerly coag boot camp, typically in the 1st or 2nd week of the rotation; Julie Shafferkoetter will provide details on dates, times, locations). It includes didactic lectures on coagulation/hemostasis (Dr. Eby), automated hematology (Dr. Jackups), flow cytometry (Cara Shirai PhD), and peripheral blood morphology (Dr. Frater).
- Hematology Case Conference by inpatient hematology fellows (Mondays, noon, CSRB 8841)
- Friday Heme noon conferences (include Non-Malignant Case Conference, formerly called Coag Beeper Report, Hemopath journal club, Heme didactics by faculties)
- LGM-wide weekly conferences (Case Conference, Grand Rounds)
- Pathology department-wide conferences (RFM, Management Series, Computational & Digital Pathology Series)

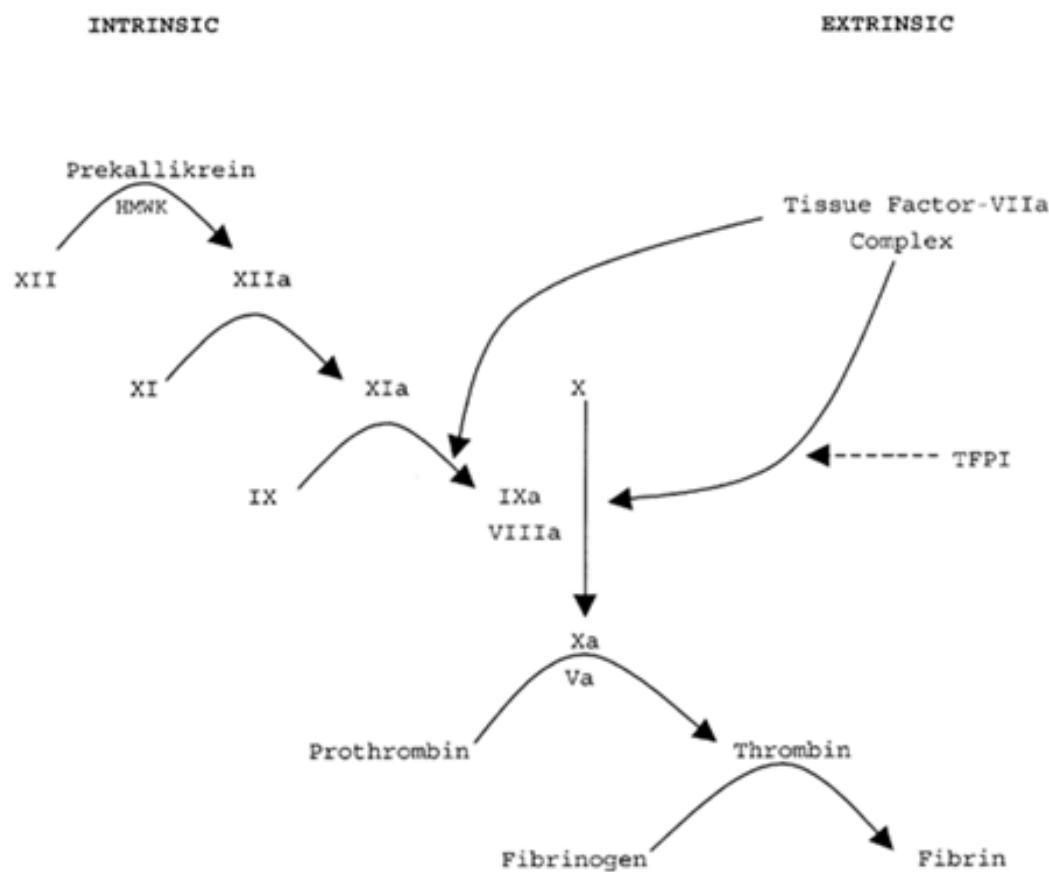
Optional – Hematology Grand Rounds (Fridays, 8AM, CSRB 8841)

Conferences you are expected to present:

- Non-Malignant Hematology Case Conference beeper report – once (4th Friday of month, noon
 - Discuss 3 interesting patients that you encountered while on the Hematology service: hemostasis, non-malignant flow cytometry, peripheral smears, hemoglobinopathies, pediatric hematology/hemostasis cases. Check with the following attendings for cases: Dr. Frater, Eby, Jackups, Shirai, and Brestoff (assistant medical director of flow lab for immunodeficiency).
 - Review your slides with Drs Eby / Jackups before your presentation
- LGM Case conference on Hematology topic – once
 - Discuss with Drs Eby / Jackups if you need help choosing a topic

Suggested readings:

- Rodak's Hematology: Clinical Principles and Applications, 6th edition, by Elaine Keohane, Catherine Otto, Jeanine Walenga
- An Algorithmic Approach to Hemostasis Testing, 2nd edition, by Kandice Kottke-Marchant



Testing For Coagulopathies

Prothrombin time (PT) and international normalized ratio (INR)

How the PT is performed: Citrated plasma (prepared from blood collected in a blue top tube) is incubated with thromboplastin, which contains tissue factor (initiates the extrinsic pathway by activating factor VII), phospholipid, and calcium (reverses citrate inhibition of clotting), and time to clot is measured.

Clinical disorders with prolonged PT: Deficiency of factor VII, common pathway factors (II, V, X), and fibrinogen.

Anticoagulants that prolong the PT: Warfarin, superwarfarins (*e.g.* brodifacoum), direct thrombin inhibitors (dabigatran), anti-Xa inhibitors (*e.g.* rivaroxaban, less so for apixaban and edoxaban).

INR: Harmonizes PT ratios (patient divided by mean normal PT) among commercial PT reagents with different sensitivities to depletion of vitamin K dependent clotting factors (International Sensitivity Index, ISI) so that warfarin can be dosed consistently. The ratio is calculated as: INR = ((PT patient)/ (PT laboratory mean))^{ISI}. See discussion on warfarin monitoring in the Anticoagulants section.

Activated partial thromboplastin time (aPTT)

How the aPTT is performed: Citrated plasma (blue top tube) is first incubated with partial thromboplastin (contains phospholipid) and a negatively-charged contact activator of the intrinsic pathway such as kaolin, then calcium (reverses citrate inhibition of clotting), and time to clot is measured.

Clinical disorders with prolonged aPTT: Deficiency/inhibitors of intrinsic pathway factors (VIII, IX, XI), common pathway factors (II, V, X), fibrinogen, and the “contact activators” (factor XII, pre-kallikrein high-molecular-weight kininogen, which greatly prolong the aPTT but do not impose a bleeding risk). Lupus anticoagulants can prolong the routine aPTT without significantly affecting the PT.

Anticoagulants that prolong the aPTT: Unfractionated heparin and low-molecular-weight heparin (minimal if any prolongation), direct oral anticoagulants: anti-thrombin and anti-Xa.

Patients on warfarin with a therapeutic INR (2-3) may have a high normal or slightly elevated aPTT. As the INR climbs > 3.0, so will the aPTT.

Thrombin Time (TT)

How the TT is performed: Citrated plasma is incubated with human thrombin, and time to clot is measured. If prolonged, a corrected TT (TTc) is run in the presence of protamine to neutralize heparin.

Clinical disorders with prolonged TT: Hypo- and dysfibrinogenemia, very high levels of fibrinogen degradation products, monoclonal gammopathies, and thrombin antibodies. Insensitive to coagulopathies that occur above thrombin in the cascade.

Anticoagulants that prolong the TT: Unfractionated heparin (very sensitive) and low-molecular-weight heparin (pretty insensitive) (normal TTc), direct thrombin inhibitors (very sensitive and not corrected by protamine-prolonged TTc).

Fibrinogen activity

How the fibrinogen activity is performed: Citrated plasma is diluted and incubated with human thrombin, time to clot is measured, and a concentration is reported based on a calibration curve using a fibrinogen standard. The methodology is the same as the TT but uses very diluted plasma in order to be sensitive to defects in fibrinogen.

Clinical disorders with low fibrinogen activity: Hypofibrinogenemia, including DIC, and dysfibrinogenemia. In dysfibrinogenemia, fibrinogen activity is reduced but fibrinogen antigen (a send-out immunoassay) is normal. We get very few requests for fibrinogen antigen and it should only be ordered if the fibrinogen activity assay is low, typically < 100 mg/dL.

Anticoagulants that cause artificially low fibrinogen activity: Usually none, as they are effectively diluted out and reagent contains heparin neutralizer.

Factor activity (other than fibrinogen)

How the factor activity is performed: Serial dilutions of the patient's citrated plasma are mixed with plasma deficient for the factor of interest; a PT (factors VII, X, V, II) or aPTT (factors XII, XI, IX, VIII) is run; and the activity is reported as a % using a standard curve and comparing with dilutions of normal pooled plasma with factor deficient plasma. If the activity increases with increasing dilution, an inhibitor pattern will be reported.

Clinical disorders with low factor activity: Factor deficiency (if no inhibitor reported) or inhibitor (if inhibitor pattern reported). The etiologies of factor deficiencies include hemophilia, liver dysfunction (in which case most factors are decreased, but factor VIII, an acute phase reactant, is *increased*), vitamin K deficiency (in which II, VII, IX, and X are selectively decreased), and DIC. This test is also used to monitor dosing of factor VIII and IX concentrates.

Bethesda titer

If a factor inhibitor is detected, a Bethesda titer may be indicated to quantify the strength of the inhibitor (usually only for factor VIII inhibitors). Serial doubling dilutions of the patient's plasma are mixed 1:1 with normal pooled plasma, and the factor activity is performed on each dilution after a 2 hour incubation, since FVIII inhibiting antibodies are sluggish. The Bethesda titer (in units, or BU) is the reciprocal of the dilution of the patient's plasma that inhibits 50% of the factor activity in normal pooled plasma. Interpretation:

- BU<5: mild inhibitor; may be overcome by increased doses of FVIII concentrate.
- 5<BU<10: a moderate inhibitor; the effectiveness of FVIII concentrate is questionable.
- BU>10: a strong inhibitor, FVIII administration is not effective, and recombinant porcine FVIII, Novoseven, or Prothrombin complex concentrate should be infused.

Chromogenic Factor VIII activity – starting May 2022

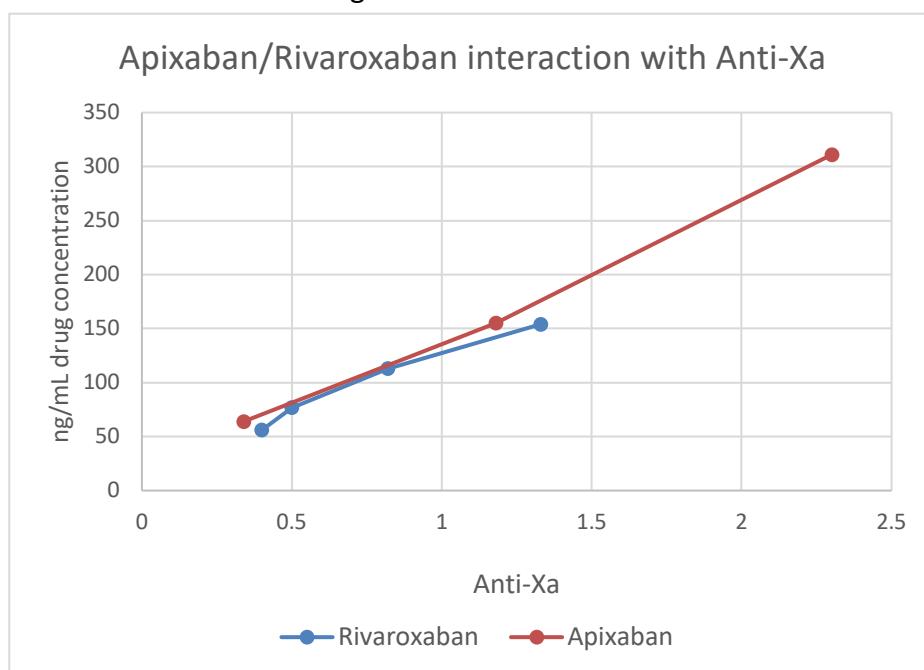
How the assay is performed: Chromogenic FVIII activity assay is a two-stage assay, that measures FVIII activity levels based on generation of FXa. During the first stage, patient's citrated plasma is incubated with an optimal amount of Ca²⁺ and phospholipids, as well as excess FIXa and FX and FII. This ensures that the rate of generation of FXa is solely dependent on FVIII activity level. In the second stage, a chromogenic substrate of FXa is added. Cleavage of this substrate by FXa produces a colored substance. FVIII activity level is inferred based on the absorbance value on the calibration curve. The chromogenic FVIII assay at BJH uses bovine FX).

Indications: Chromogenic FVIII assay correlates well with the clotting FVIII assay. Hence, it can be used to diagnose hemophilia A, vWD and to measure FVIII activity level after plasma derived or equivalent recombinant FVIII replacement therapy. To monitor newer, modified, recombinant, extended half-life FVIII concentrates (which can produce inaccurate clot-based FVIII activities) and to measure endogenous production, or infusion of, FVIII in presence of the FIXa-FX bi-functional antibody-emicizumab (Hemlibra). The use of clotting FVIII assay in this specific patient population can lead to overestimation of FVIII activity level, while the chromogenic FVIII assay with bovine reagents (which do not interact with emicizumab) provide a more accurate assessment of the replaced FVIII activity level. This test will be restricted to ordering by pediatric and adult hematology services.

Anti-factor Xa activity

How the anti-factor Xa activity is performed: Citrated plasma (containing the anticoagulant to be measured and endogenous antithrombin) is mixed with factor Xa and a chromogenic substrate of Xa. Hydrolysis of the substrate by FXa generates color or OD which is inversely related to the amount of heparin, or LMWH or antithrombin in the plasma, depending upon the calibrator. The anti-Xa test is calibrated with both UFH and LMWH standards and can measure both types of anticoagulants. The antithrombin activity assay is calibrated with an antithrombin calibrator in the presence of excess heparin.

Indications: Monitoring treatment by unfractionated and low-molecular-weight heparin; antithrombin deficiency (<40-50%) results in a lower than expected value. Also used to qualitatively assess anticoagulant potency of oral factor Xa inhibitors (*e.g.* rivaroxaban and apixaban), which do not require antithrombin to neutralize FXa. This graph shows the response of the BJH anti-Xa assay calibrated with UFH/LMWH to known concentrations of apixaban and rivaroxaban. Anti-Xa activity < 0.5 is associated with anti-Xa DOAC concentrations < 100 ng/ml. this can be very helpful to clinicians managing bleeding patients or patients requiring urgent interventions who have been taking one of these DOACs.



General work-up of prolonged PT or aPTT

Consider preanalytical variables first:

1. Incomplete filling of blood collection tubes
2. Heparin in intravenous lines (screen with TT)
3. High hematocrit (>55%)
4. Plasma turbidity (lipemia or hemolysis)

Mixing study: Performed by mixing patient plasma with an equal amount of normal pooled plasma (NPP), which supplements coagulation factors. The PT or aPTT is performed on the mixture at 0 min (and at 60-min incubation for aPTT) to determine if the PT or aPTT corrects (*i.e.* clots within the reference range) or does not correct (*i.e.* remains prolonged). TT is performed before mixing to rule out heparin or a direct thrombin inhibitor or severe hypofibrinogenemia. Interpretation, with most likely diagnosis:

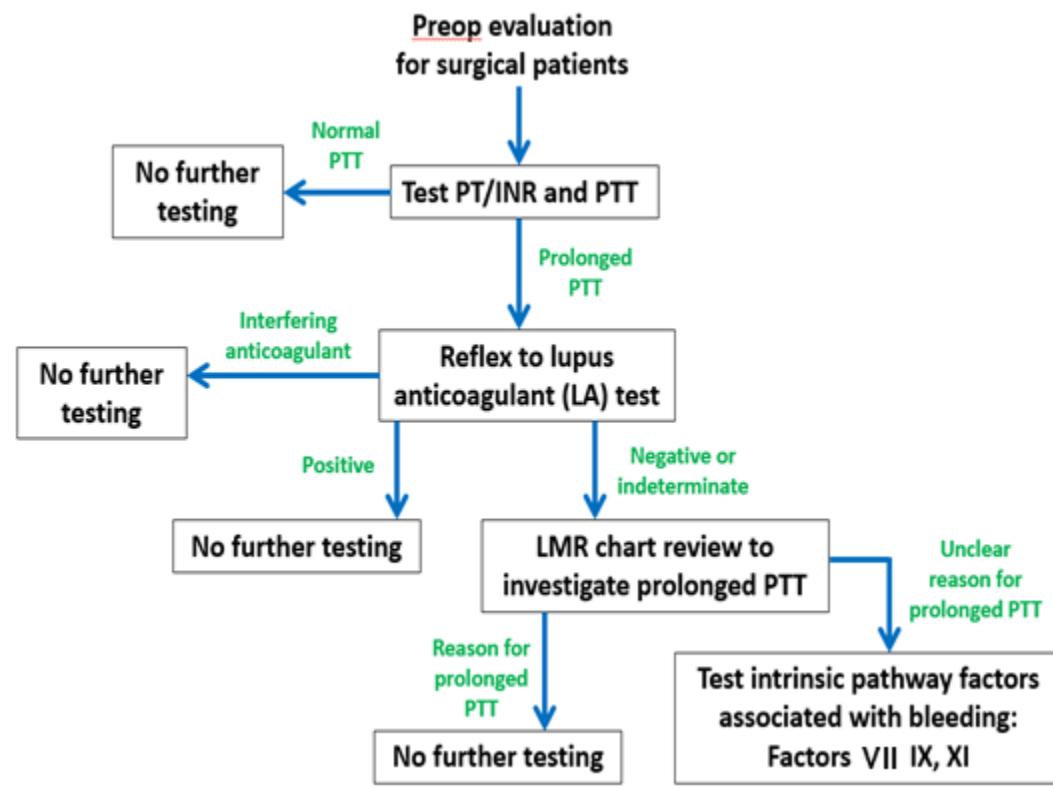
- Correction or nearly corrects (no perfect rules): simple deficiency of factor(s), depending on whether PT and/or aPTT is prolonged
- No/minimal correction: factor inhibitor, depending on whether PT and/or aPTT is prolonged
- aPTT with minimal correction, similar prolongation at 0 and 60 min: most likely lupus anticoagulant
- aPTT with partial correction at 0 min that becomes more prolonged at 60 min: most likely factor VIII inhibitor

Causes of PT and aPTT Prolongations:

Liver dysfunction	PT affected earlier and more than aPTT.
DIC	PT may be affected earlier and more than aPTT.
Vitamin K deficiency	PT affected earlier and more than aPTT.
Warfarin	PT affected earlier and more than aPTT.
Lupus anticoagulants	aPTT prolonged, PT is rarely prolonged.
Heparin	PT normal (reagent has heparin neutralizing additive), aPTT prolonged, TT prolonged, TTc not prolonged.
Direct thrombin inhibitor	aPTT prolonged more than PT, TT and TTc prolonged.
Factor Xa inhibitor	PT may be affected earlier and more than aPTT, TT not prolonged. Depends upon the DOAC (rivaroxaban>edoxaban>apixaban) and PT reagent.
Specific factor inhibitors	Depends on the location of the factor in the coag cascade: intrinsic pathway - aPTT prolonged; FVII (super rare) - PT prolonged; factors X, V, II, and fibrinogen - aPTT and PT prolonged.
Fibrinogen < 80 mg/dl	PT prolongation slightly more sensitive than aPTT

CPAP aPTT algorithm

Numerous studies have demonstrated that preoperative screening of coagulation function does not improve outcome in patients without a personal or family history of bleeding. Nonetheless, surgeons referring patients to CPAP (center for preoperative assessment and planning) often order "screening" preop PT and aPTT. To address unexpected prolonged aPTT in these patients without requiring a second blood draw, an algorithm called "CPAP aPTT" was designed:



If the patient has a prolonged aPTT (>40s), tests will be performed to identify interfering oral anticoagulants (via INR and thrombin time) and lupus anticoagulant. If these tests are negative, the lab will contact the LMR, who will need to review the patient's history. If the history can provide an explanation for the prolonged aPTT, e.g. liver disease, concurrent warfarin, or use of a DOAC or UFH/LMWH that was not caught by testing, no further action is required. If no other explanation is found, the LMR should contact the lab to add testing for clinical significant factor deficiencies, particularly XIII, IX, and XI. For major surgical procedures, it may be necessary to contact the anesthesiologist who initiated the workup in order to coordinate clinical decisions.

Testing For Hypercoagulability

Hypercoagulable states are considered in patients with idiopathic thrombotic events and/or recurrent fetal losses. It is preferable to delay testing in the setting of an acute thrombosis, or during any acute medical or surgical illness. The following tests are frequently ordered for a hypercoagulable workup: Activated Protein C Resistance, Factor V Leiden (FVL) mutation, Prothrombin G20210A mutation, Antithrombin deficiency, Protein C deficiency, Protein S deficiency, lupus anticoagulant, and cardiolipin/B2GP1 IgG and IgM autoantibodies. Heparin-induced thrombocytopenia (HIT) can cause thrombosis, and laboratory testing for HIT is discussed below. With the exception of anti-phospholipid syndrome and HIT, these are risk factors only for *venous* thromboembolism (VTE).

Activated protein C resistance (APCr), Epic order name: Factor V Leiden screen

How the assay is performed: The aPTT is performed on diluted patient's plasma with and without activated protein C (APC) reagent, and a ratio of the clotting times (with divided by without, *i.e.* [APC+ aPTT]/aPTT) is reported.

Interpretation: A ratio ≤ 2.3 suggests that APC does not adequately deactivate factor Va, usually due to the factor V Leiden (FVL) mutation (heterozygous: 1.5-2, homozygous: < 1.5), which disrupts a cleavage site for APC. A positive result is automatically reflexed to the fVL mutation analysis (see below).

Notes: This test is recommended as a screen prior to mutation testing (below) for FVL only. If both FVL and prothrombin gene mutation are requested, these tests can be performed on a single cartridge in the molecular diagnostics lab. An order set in Epic facilitates these decisions.

Factor V Leiden (fVL) mutation analysis

How the assay is performed: Invader method for a point mutation (G1691A in DNA, R506Q in protein). Requires an EDTA tube sent to molecular lab; performed in-house.

Interpretation: Can distinguish heterozygous and homozygous mutations, but only at one position. Other mutations very rarely cause hypercoagulable states and will not be detected by this assay. About 5% of Caucasians are positive for FVL.

Prothrombin gene mutation analysis

How the assay is performed: Invader method for a point mutation (G20210A). Requires an EDTA tube sent to molecular lab; performed in-house.

Interpretation: Can distinguish heterozygous and homozygous mutations. About 2% of Caucasians are positive for this mutation.

Notes: Risk for VTE is much higher when this mutation is concurrent with FVL.

Antithrombin activity

How the assay is performed: Citrated plasma is mixed with an excess concentration of heparin, factor Xa, and a chromogenic substrate of Xa. Color generation measures the degree to which antithrombin inhibits Xa in the presence of heparin (inverse relationship, calibrated with AT standard).

Interpretation: Congenital partial antithrombin deficiency is rare (about 1 in 2,000 to 5,000 blood donors); acquired deficiency may be due to hemodilution, anticoagulant therapy,

concurrent unfractionated heparin infusion, nephrotic range proteinuria, and liver disease. This test may also be used to guide dosing of antithrombin concentrate.

Notes: Similar in methodology as the Anti-factor Xa assay (see above). Testing is offered 24/7.

Protein C activity

How the assay is performed: Citrated plasma is mixed with an activator of protein C and a chromogenic substrate of APC. Color generation directly measures protein C activity. Batched testing performed on Mondays and Thursdays.

Interpretation: Congenital partial protein C deficiency is rare (about 1 in 300 blood donors); acquired deficiency may be due to warfarin and liver disease. This test should not be ordered on patients taking warfarin in the past 4 weeks.

Protein S free antigen

How the assay is performed: Immunoassay; this is an *antigenic*, not functional, assay. Batched testing performed on Mondays and Thursdays.

Interpretation: Congenital protein S deficiency is rare (about 1 in 750 blood donors); acquired deficiency may be due to warfarin, liver disease, and (possibly) an increase in C4bBP, which binds to free protein S. This test should not be ordered on patients taking warfarin in the past 4 weeks. As this test is antigenic, it will miss the very rare type II deficiencies (normal amount, but reduced function) that make up ~5% of cases.

Lupus Anticoagulants (LA)

Las are autoantibodies that recognize proteins (typically prothrombin and B2GP1) bound to phospholipids that have been associated with the following: unexplained thrombocytopenia, recurrent fetal loss, venous or arterial thromboembolic disease, false positive VDRL. These antibodies may occur in the presence or absence of SLE or other autoimmune diseases. Some patients have a prolonged aPTT that fails to correct when assayed immediately after a 50:50 mix with normal pooled plasma (although an LA can be present with a normal aPTT because the routine aPTT reagent is not as sensitive to LA). The principle of LA testing is to demonstrate 1) a prolonged clotting time (screen) designed to be sensitive to LA, 2) persistent prolongation of the clotting time after replacing possible missing clotting factors by adding normal pooled plasma (mixing study), 3) the neutralization of the inhibitor with excess phospholipid, and 4) ruling out a specific factor inhibitor (such as anti-FVIII autoantibody). Performing LA testing while patients are taking anticoagulants can cause false positive results if not recognized, so the lab does an extensive screen if the routine PT or aPTT is prolonged. The lab accepts samples containing heparin (neutralizes first with heparinase) and patients on warfarin if INR <3.0. The lab rejects samples with direct thrombin or FXa inhibitors. Current testing strategy uses two assays:

Dilute Russell's viper venom time (dRVVT): A multi-step algorithm is performed. In each step, plasma is incubated with dRVV, which activates factor X, time to clot is measured, and a ratio is calculated between the plasma tested and normal pooled plasma (NPP).

1. Screen: Patient's neat plasma is used. A ratio of clot time in patient's plasma vs. clot time in NPP must be >1.2 to move onto the next step.

2. Confirm: Patient's plasma is mixed with excess phospholipids, and the "screen" is repeated. The phospholipids should neutralize the LA and result in a lower ratio.
3. Normalization: A final "ratio of ratios" is calculated by dividing the screen ratio by the confirm ratio. A normalized ratio >1.2 is a positive result. If the baseline PT/INR is WNL, DRVVT testing stops at this point and is reported as positive for LA. If the baseline PT/INR is elevated, a mixing study (step 4) is performed.
4. 50:50 mix: Patient's plasma is mixed with an equal amount of NPP, and the screen steps repeated. The ratio must still be >1.2 , i.e. defect does not correct to conclude DRVVT + for LA. If the mix screen ratio is ≤ 1.2 then factor deficiencies are responsible for the apparent DRVVT LA+ pattern, or there is a very weak LA which has been diluted below detection in this assay by the 50:50 mix step. Therefore, a positive DRVVT confirm result and a mixing step which shows correction is signed out as INDETERMINATE. We see very few of these results.

Silica Clotting Time (SCT): This test uses the same methodology as the aPTT but uses an activator (colloidal silica) that is much more sensitive to antiphospholipid antibodies.

1. Screen: Patient's plasma is added to reagent with low phospholipid concentration. A ratio of clot time with patient's plasma vs. clot time with NPP is calculated. If the ratio is ≤ 1.16 , LA not present, stop. If ratio is > 1.16 , LA screen positive, go on to Confirm step.
2. Confirm: The test is repeated with patient's plasma added to reagent with excess phospholipids. The excess phospholipids should neutralize the LA and result in a shorter clot time. A ratio of clot time with patient's plasma vs. clot time with NPP is calculated.
3. Normalization: A final "ratio of ratios" is calculated by dividing the screen ratio by the confirm ratio. A normalized ratio >1.16 is a positive result. If the baseline PT/INR is WNL, testing stops at this point and is reported as positive for LA. If the baseline PT/INR is elevated, a mixing study (step 4) is performed.
4. 50:50 mix: Patient's plasma is mixed with an equal amount of NPP, and the screen steps repeated. The ratio must still be >1.16 , i.e. defect does not correct to conclude SCT + for LA. If the mix screen ratio is ≤ 1.16 then factor deficiencies are responsible for the apparent SCT LA+ pattern, or there is a very weak LA which has been diluted below detection in this assay by the 50:50 mix step. Therefore, a positive SCT confirm result and a negative 50:50 mix screen (50:50 mix screen ratio ≤ 1.16) is signed out as INDETERMINATE.

Interpretation: A positive for either dRVVT or SCT is considered a positive LA to maximize sensitivity. Regardless, a single positive LA test result may have no clinical implications, as many LAs are transient. In order to diagnose antiphospholipid syndrome (APS), a positive LA must persist after 12 weeks, in addition to specific thrombotic clinical criteria. Often LA is ordered simply to explain an elevated aPTT in a patient without a history of thrombotic or obstetric complications. In this case, a positive LA can remove concerns that the patient is at increased risk for bleeding. As for future risk of thrombotic/obstetric complications, at least one prospective study did demonstrate an increased risk of thrombotic events in asymptomatic LA-positive cases compared to controls.

In addition to the LA test, **Anticardiolipin (ACA)** and **Anti- $\beta\alpha$ 2-glycoprotein I (B2GP1) IgG** and IgM **antibody** tests may be ordered; these are performed by the Immunology lab. Both

are components of the criteria for diagnosing Anti-Phospholipid Syndrome (J Thromb Haemostasis 4:295-306;2006). In June, 2022, a new Epic order appeared:

Antiphospholipid antibody and lupus anticoagulant screen. This test combines LA and ACA and B2GP1 into one orderable test.

Heparin-induced thrombocytopenia (HIT)

Testing for HIT is indicated when clinical suspicion exists for the condition. The platelet count typically shows a rapid decrease to below 50% of baseline (rarely <10K) between days 5-14 of heparin exposure (rarely < 24 hours if exposed to heparin within the past 30 days and antibodies are still circulating), and patients are at risk of thrombosis (arterial or venous) rather than bleeding. It should be noted that **diagnosing HIT is a combination of clinical assessment of the likelihood, and in some situations, combined with laboratory testing to detect autoantibodies**: heparin is stopped and the platelet count rises; heparin is re-started and the platelet count falls.

A patient with moderate/high pre-test probability should be initially treated as having HIT regardless of lab tests. Treatment for HIT includes substitution of another anticoagulant for heparin to avoid thrombosis: most likely this is a DTI (e.g. argatroban, bivalirudin), since warfarin can actually induce thrombosis in the short term by inhibition of protein C, and HIT antibodies sometimes cross-react with LMWH. Some clinicians substitute fondaparinux (a synthetic LMWH with minimal cross-reactivity to HIT antibodies), or a DOAC, but this is controversial.

Pre-test probability for HIT can be assessed using the "4 T's" (see table below). Scores range from 0-8. A low probability patient (score 0-3) generally does not require further testing, as the risk of HIT is low (<5%). Intermediate probability patients (score 4-5) require laboratory work-up (risk for HIT 30-50%). A high probability patient (score 6-8) should be treated for HIT without delay until test results return, as the risk of HIT is very high (>95%) (J Thromb Haemostasis 4:759-765; 2006). Unfortunately, such treatment decisions can be difficult in patients on cardiac bypass, as IV DTIs have half-lives of several hours and are non-reversible in the setting of unexpected bleeding.

4 T's	0 point	1 point	2 points
Thrombocytopenia	Platelet count fall < 30% or platelet nadir <10	Platelet count fall between 30-50% or platelet nadir 10-19	Platelet count fall >50% and platelet nadir ≥ 20
Timing of platelet count fall	Platelet count fall <4 days without recent exposure	Onset after 10 days or unclear exposure	Platelet count fall between 5 to 10 days or Day 1 with recent heparin exposure
Thrombosis or other sequelae	None	Progressive or recurrent thrombosis	New thrombosis or anaphylactoid reaction after exposure
Other causes for thrombocytopenia	Definite	Possible	None apparent
Total score	0-3; low score	4-5; intermediate score	6-8; high score

Laboratory testing for HIT involves two assays:

- **Anti-heparin/PF4 antibodies:** An on demand/24/7 latex immunoassay (LIA) test performed on the automated coagulation instruments detects IgG, IgM, and IgA antibodies in the patient's plasma (blue top tube) against a heparin/PF4-like antigen. These antibodies may form immune complexes which activate platelets and cause HIT with or without new thrombi, but most patients who make anti-PF4 antibodies have no consequences. Antibody detection is a sensitive but non-specific test for HIT. The test result is negative (< 1.0 AU) or positive (\geq 1.0 AU). In addition, the test will also report absorbance units, with a comment that higher positive AU results (reportable range 1.0 to 16) have been associated with a higher chance of active HIT. Please note the LIA test cannot detect PF4 antibodies associated with the very rare Vaccine-induced Thrombotic Thrombocytopenia (VITT) associated with recombinant adenovirus vector vaccines (Johnson & Johnson and AstraZeneca). Talk to your attending regarding sending out an ELISA if the clinical team is requesting a workup for VITT. Versiti now has a specific test and requisition for VITT workup. A HIT ELISA is the first test (very sensitive) and if positive, SRA is performed with no heparin (+ in VITT cases, negative in most HIT cases) and with heparin (positive with VITT and HIT).
- **Serotonin release assay (SRA):** Patient plasma is incubated with specialized donor platelets in the presence of low and high concentrations of heparin. Clinically important HIT antibodies only activate platelets and release radiolabeled serotonin at low heparin concentration. This test is a send-out to Versiti (formerly Blood Center of Wisconsin) and is only run Mon-Sat. SRA results automatically populate in Epic. The SRA test is only performed as a reflex test from a positive anti-PF4 (Epic order = HIT Antibodies w/ Reflex to SRA). Only the first positive anti-PF4 during a single hospitalization will be reflexed to the SRA. The SRA is not available to be ordered as a stand-alone. When clinicians request the SRA as a stand-alone or when the anti-PF4 is negative, you will be asked to investigate the request. You will occasionally get pulled in to expedite or coordinate delivery of a sample to the chemistry send out lab. The FedEx pick up time is around 5 PM. If SRA testing is requested after Friday afternoon, it will not be performed and resulted until Monday late afternoon.

Interpretation: The LIA has higher sensitivity but lower specificity than the SRA and should always be performed first. The SRA performed at Versiti has a sensitivity of ~85% for HIT based on a 2021 publication in Blood. Therefore, there will be patients who have high 4T scores, high HIT Ab units, and whose platelet counts recover after stopping heparin yet have a negative SRA. Sensitivity may be improved by repeating the SRA on a new plasma sample $>$ 24 hours after the original negative result. This requires repeating the HIT ab test and then coordinating with send outs to order another SRA.

Testing for Platelet Disorders

von Willebrand Disease (vWD)

Patients suspected of vWD should have the following testing; 1) von Willebrand Factor Antigen, 2) Factor VIII Activity, and 3) von Willebrand factor activity. No single test is adequate to diagnose vWD. In patients with previously documented vWD, it may be appropriate to order just one of the above tests to monitor vWF treatment or response to DDAVP. Pregnancy increases the levels of FVIII and vWF making the diagnosis more difficult. Testing is only performed on Monday and Thursday except by special request (e.g. daily on dayshift for monitoring inpatients on vWF treatment).

vWF antigen concentration-adult reference range: 55%-180%

How the assay is performed: Immunoturbidimetric.

Interpretation: See vWF classification chart on subsequent pages; decreased in type 1 vWD (quantitative defect), low normal/decreased in type 2 (functional defect), and absent in type 3 (no expression of protein). Normal individuals with blood type O may have slightly low vWF concentration outside of the reference range which is a combination of O, A, B, and AB donors.

vWF activity-adult reference range: 50%-180%

How the assay is performed: Immunoassay which targets the GP1b platelet binding site on vWF and is a sensitive screening test for quantitative and qualitative defects in vWF activity.

Interpretation: See vWF classification chart below; decreased in type 1 vWD, variably decreased in type 2 depending on functional defect, and absent in type 3. If the first time testing is done at BJH the result is < 50%, a reflex, confirmatory functional assay is performed. This used to be the in-house Ristocetin cofactor assay (described below for background information).

Ristocetin cofactor assay-RCo (vWF activity)-RETIRED

How the assay is performed: The ability of the patient's plasma specimen to aggregate normal, formalin-fixed platelets in the presence of ristocetin (an antibiotic known to stimulate vWF binding to GPIb receptor on platelets) is compared with that of a normal pooled plasma specimen, by use of aggregometry.

In spring 2020 the RCo assay was retired and replaced with a send-out test:

Von Willebrand Factor GP1M Activity-at Blood Center of Wisconsin (Versiti). This assay measures binding of patient vWF to mutant platelet GPIba synthetic peptide which is independent of ristocetin. The assay's precision and accuracy is superior to the RCo activity assay. Sample: 0.5 ml frozen citrated plasma. TAT is ~ 7 days.

Interpretation: See vWF classification chart below; decreased in type 1 vWD, variably decreased in type 2 depending on functional defect, and absent in type 3. Normal individuals with blood type O may have slightly low vWF activity outside of the reference range. A vWF activity: antigen ratio ≤ 0.7 suggests a diagnosis of vWD type 2A, 2B or 2M and requires further specialized testing for discrimination.

Ristocetin-induced platelet aggregation (RIPA)-to aid in classification of types 2A, 2B, and 2M

How the assay is performed: The ability of the patient's plasma specimen to aggregate the patient's own platelets in the presence of different concentrations of ristocetin, by use of aggregometry.

Interpretation: See vWF classification chart below; only used to distinguish type 2B (increased, due to gain of function) from types 2A and 2M (decreased, due to loss of function).

vWF multimer analysis

How the assay is performed: A send-out, qualitative test using gel electrophoresis to separate vWF multimers by size. Sent to Wisconsin Blood Center (Versiti).

Interpretation: See vWF classification chart below; only used to distinguish different type 2 defects. This test should only be approved after the vWF antigen and activity assays are abnormally low and a type 2A, 2B, or 2M is suspected due to vWF act/vWF/antigen ratio < 0.7.

FVIII-vWF Binding assay-send out to Blood Center of Wisconsin (Versiti)

Type 2N vWD is due to vWF mutations which reduce binding of FVIII, but do not affect amount of vWF protein or platelet binding activity. Decreased FVIII binding leads to reduced FVIII half-life and a clinical picture of mild Hemophilia A, except inheritance is autosomal recessive (2N/2N) or compound heterozygous (type 1/2N). This is extremely rare, but should be considered in a patient (especially a woman) with isolated low FVIII and no clear X linked inheritance pattern of FVIII deficiency in the kindred. The test immobilizes patient's vWF, adds FVIII, washed away unbound FVIII, and measures both vWF antigen and FVIII activity to produce a ratio of FVIII to vWF.

CLASSIFICATION OF von WILLEBRAND DISEASE

* Type 2B often presents with mild thrombocytopenia due to platelet clearance. These patients are hyperresponsive to DDAVP treatment, exacerbating vWF-platelet binding and subsequent platelet clearance. DDAVP is therefore *contraindicated* for type 2B.

Platelet function studies

PFA-100 (platelet function screen)

How the assay is performed: Citrated whole blood is aspirated through an aperture in a membrane coated with 2 activators of platelet aggregation: collagen (COL) and either epinephrine (EPI) or ADP, and measure time to closure due to aggregation of activated platelets. Both cartridges are performed on every sample.

Interpretation: Prolonged closure time for either cartridge (>160 s for COL/EPI, >110 s for COL/ADP) is considered indicative of platelet dysfunction (antiplatelet drugs, vWD, and other genetic disorders). COL/EPI is more sensitive to aspirin than COL/ADP, and both are insensitive

to clopidogrel (Plavix). Notably, platelet counts <100 and hematocrits <30% may result in spuriously prolonged closure times.

Indications: Rapid (24/7) and non-specific screen to detect platelet dysfunction. Unfortunately, this test is also used by neurosurgery to assess the need for platelet transfusion to reverse antiplatelet therapy in patients with intracranial bleeds. This is *not* an FDA-approved indication, and has never been investigated, but neurosurgery is insistent. Be diplomatic, explain the limitations, and encourage them not to go overboard on platelet transfusion just because of an increased PFA-100.

VerifyNow

How the assay is performed: Citrated whole blood is incubated with fibrinogen-coated beads and a platelet agonist (arachidonic acid for aspirin response [ARU], ADP for Plavix response [PRU]). Platelet aggregation is measured by turbidimetry. A special blue top tube from the hematology lab is required.

Interpretation: Higher values = more aggregation, lower values = better “response” to aspirin/Plavix. Correlation with clinical outcome is not well known, so interpretive criteria are weak.

Indications: Currently used by neuroradiology and neurosurgery to assess aspirin and Plavix platelet inhibition before catheter directed carotid artery aneurysm coiling or intracranial carotid stenosis stenting. Increasing use in ER and neuro ICU for neurosurgery consults/admissions for patients with history of ingestion, or to “rule out” aspirin/Plavix. Occasionally ordered by the CCU for patients suspected of Plavix resistance. ***Our goal is to not see this test creep into general use.***

Platelet aggregation

How the assay is performed: A labor-intensive test in which platelet-rich plasma from the patient is induced with several different platelet activators, and aggregation is measured. The test requires advance notice and approval from the heme lab director, must be scheduled on a weekday, and requires blood from a normal control individual for comparison.

Interpretation: See chart below for possible diagnoses. The patient must be off any antiplatelet medication (not simply aspirin or clopidogrel) for at least 7 days and NSAIDs for 72 hours.

Indications: Comprehensive work-up of platelet dysfunction that is not clearly explained by testing for vWD or a history of antiplatelet therapy. Physicians looking for the PFA-100 may erroneously order this; they need to order the “platelet function screen” instead.

Please note there may be other rare tests on the Hematology LMR list for approval. Remember to check the living document for advise on approval for these tests. For those not discussed on this list please contact the Hematology attending on service on a case by case basis to review the background/contact the ordering MD if necessary.

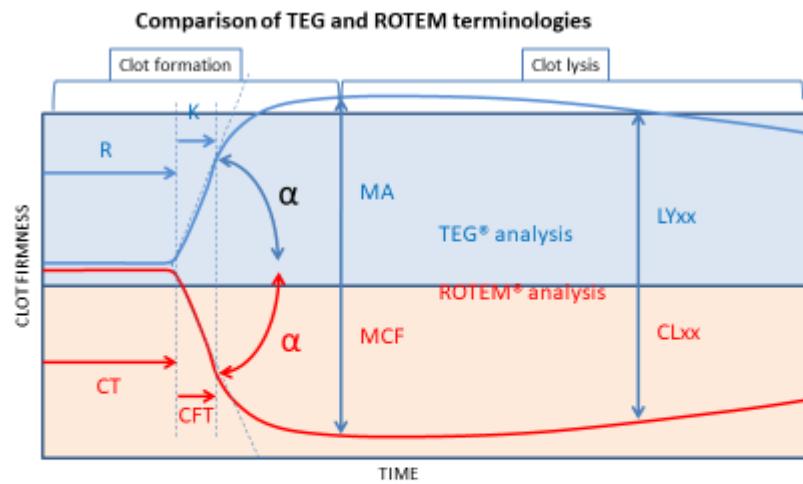
ROTEM

Background: Viscoelastic assays, including thromboelastography (TEG) and rotational thromboelastometry (ROTEM) are being used in many hospitals to provide rapid

assessment of hemostasis. ROTEM is utilized here at BJH and TEG at SLCH. LMRs are not expected to approve or to interpret Rotem results.

How the assay is performed: There are different modifications of ROTEM that mimic coagulation tests performed in the core lab: Extem (PT), Intem (aPTT), fibtem (fibrinogen) Heptem (aPTT with heparin neutralization), and Aptem (addition of a plasmin inhibitor to detect hyperfibrinolysis-unique to liver transplant cases).

Interpretation: Please see figure below. Interpretation of ROTEM assays and requires a multifactorial approach to interpretation. ROTEM reports give clotting time (CT), clot formation time (CFT), alpha (α) angle, maximum clot firmness (MCF), and Clot Lysis 30 min.



Clot formation phase	TEG® parameter	ROTEM® parameter
Initial fibrin formation (period to 2 mm amp.)	R time (reaction time)	CT (clot time)
Rate of clot development (2-20 mm amp.)	K time	CFT (clot formation time)
Alpha angle	α (slope between R and K)	α (angle of tangent at 2 mm amp.)
Maximum clot strength	MA (maximum amplitude)	MCF (maximum clot firmness)
Rate of clot lysis	LYxx (percentage lysis at xx min)	LI30 (clot lysis at 30min)

Indications: Major trauma in ER or OR; Peri-partum massive hemorrhage in L+D; Post-cardiac surgery in 56-ICU; during liver transplant surgery. Rotem testing is performed on the ABG/Rotem bench in the core laboratory and results can be viewed in realtime at computer terminals in select patient locations. Liver transplant surgery is an exception, in which case a core lab technologist takes an ABG and Rotem instrument on a cart, puts on scrubs, and stays outside the OR room to provide testing during surgery.

Further Reading (optional):

Carll T, Wool GD. Basic principles of viscoelastic testing. Transfusion. 2020 Oct;60:S1-9.

Selby R. "TEG talk": expanding clinical roles for thromboelastography and rotational thromboelastometry. Hematology 2014, the American Society of Hematology Education Program Book. 2020 Dec 4;2020(1):67-75.

Testing for Red Blood Cell Disorders

Anemia

Overview: Anemia can roughly be divided into 3 categories:

1. Bleeding
2. Hemolysis
3. Reduced RBC production, *e.g.* iron deficiency, anemia of chronic disease, etc

History: Previous diagnoses of anemia, malignancies (particularly hematopoietic), medications, etc. Common symptoms include fatigue and SOB. More specific signs/symptoms:

- Bleeding – hematuria, hematemesis, hematochezia, melena, fecal occult bleeding
- Hemolysis – usually rapid onset of symptoms, jaundice, possibly hemoglobinuria
- Reduced RBC production – gradual onset of signs/symptoms

CBC: Note the speed of reduction in Hgb. The MCV is particularly helpful:

- Microcytic – iron deficiency, thalassemia
- Normocytic – hemolysis, acute bleeding, anemia of chronic disease
- Macrocytic – vitamin B12/folate deficiency, myelodysplasia, chemotherapy

Reticulocyte count:

- Includes absolute retic count, percentage of retic and reticulocyte hemoglobin (Ret-He)
- High retic count – rapid turnover, suggesting hemolysis or acute bleeding
- Low retic count – poor turnover (aplasia), suggesting iron deficiency, anemia of chronic disease, etc.
- Ret-He measures the amount of hemoglobin in the reticulocytes and can be used to screen for iron deficiency (<27 pg), but should not be used as an individual diagnostic marker.

Other studies: Should be ordered based on a careful consideration of the above criteria.

- Ferritin: specific for iron deficiency
 - Normal/high – anemia of chronic disease (acute phase reactant)
 - Low – iron deficiency
- Iron studies: particularly check the transferrin saturation (serum iron divided by TIBC)
 - High – anemia of chronic disease (due to high iron and low transferrin)
 - Low – iron deficiency (due to low iron and high transferrin)
- Hemolysis labs
 - LDH: very sensitive for both intravascular and extravascular hemolysis, but non-specific
 - Haptoglobin: sensitive for intravascular hemolysis, but spuriously increased by inflammation (acute phase reactant), and only performed once a day
 - Direct antiglobulin test (Coombs): differentiates immune vs. non-immune causes
 - Anti-IgG positive: suggests warm autoantibody or alloantibody
 - Anti-C3 positive: suggests cold agglutinin or complement-mediated

- Vitamin B12: should only be ordered for macrocytic anemia
- Folate: folate deficiency is *extremely* rare outside of chronic alcoholism or extreme diet
- Hemoglobin analysis: useful for suspicion of thalassemia or hemoglobinopathy (see below for interpretation); TAT is 3-9 days, so you should rule out more obvious diagnoses like iron deficiency before ordering this!

Hemoglobin Electrophoresis

Quick texts for hemoglobin electrophoresis sign outs

HEMOGLOBIN ANALYSIS MNEMONICS

Mnemonic Template Text

Procedural

NORMAGE	Normal hemoglobin pattern for age
PREVHGB	Previously identified hemoglobinopathy
PREVHGBID	Previously identified hemoglobinopathy- pattern suggest recent RBC transfusion.

Gel electrophoresis

HGBS	Hemoglobin S identified.
HGBC	Hemoglobin C identified.
HGBABNORM	Presence of abnormal hemoglobin confirmed by alternative methods.

Microcytosis/thalassemias

MICRO	Severe microcytosis; must consider iron deficiency, cannot rule out underlying alpha thalassemia.
IRONDEF	Severe microcytosis; must consider iron deficiency.
ATHAL	This pattern is consistent with alpha thalassemia trait.
BTHAL	This pattern is consistent with beta thalassemia trait.
DBTHAL	This pattern is consistent with delta beta thalassemia.

Hgb F

HIGHF	Elevated hemoglobin F; differential includes hereditary persistence of fetal hemoglobin Or drug effect.
HPFH	This pattern is consistent with hereditary persistence of fetal hemoglobin
HIGHFNORM	Slightly elevated hemoglobin F, not considered clinically significant.

Hgb A2

HIGHA2NORM	Slightly elevated hemoglobin A2, not considered clinically significant.
A2PRIME	Hemoglobin A2 prime identified; this is a clinically insignificant delta globin mutation.
HGBA2	Unable to quantitate Hgb A2-probable Hgb O Arab interference.

Common hemoglobinopathies

SS	SS disease (sickle cell disease)
SC	SC disease (sickle cell disease)
SD	SD disease (sickle cell disease)
CC	Homozygous hemoglobin C disease
STRAIT	This pattern is consistent with hemoglobin S trait.

CTRAIT	This pattern is consistent with hemoglobin C trait.
DTRAIT	This pattern is consistent with hemoglobin D trait.
ETRAIT	This pattern is consistent with hemoglobin E trait.
GTRAIT	This pattern is consistent with hemoglobin G trait.
OTRAIT	This pattern is consistent with hemoglobin O trait.
SATHAL	This pattern is consistent with hemoglobin S trait and coinherited alpha thalassemia trait.
SBTHAL	This pattern is consistent with hemoglobin S trait and coinherited beta thalassemia trait.
SBTHALZERO	This pattern is consistent with hemoglobin S trait and coinherited beta thalassemia zero.
CTRANS	This pattern consistent with C Trait if not recently transfused.
STRANS	This pattern consistent with S Trait if not recently transfused.
FAST	Abnormal hemoglobin identified- Fast moving variant.
SLOW	Abnormal hemoglobin identified- Slow moving variant.

Transfusion

TRANS	Pattern suggests recent transfusion; clinical correlation is recommended.
HGBS	Hemoglobin S identified.
HGBC	Hemoglobin C identified.

Infant hemoglobinopathies

INFANTS	Hemoglobin S identified, no hemoglobin A detected. Differential includes SS disease or S beta thalassemia zero. Suggest repeat hemoglobin analysis in 6-12 months.
INFANTAS	Hemoglobins A and S identified. Differential includes S trait or S beta thalassemia. Suggest repeat hemoglobin analysis in 6-12 months.
INFANTC	Hemoglobin C identified, no hemoglobin A detected. Differential includes hemoglobin C disease or C beta thalassemia zero. Suggest repeat hemoglobin analysis in 6-12 months.
INFANTAC	Hemoglobins A and C identified. Differential includes C trait or C beta thalassemia. Suggest repeat hemoglobin analysis in 6-12 months.
INFANTF	Hgb F is elevated at birth and decreased toward adult levels over 12-24 months. See age based reference intervals below. Prematurity and hemoglobinopathies can cause elevations. At 1 month: 59-89% At 10 months: 1.7-3.3% At 24 months: 1.3-2.2%
	From Blood 1994;84:3182-8.

Gel Interpretation

PAG	Presence of Hemoglobin __ confirmed by Acid Gel Electrophoresis.
PALG	Presence of Hemoglobin __ confirmed by Alkaline Gel Electrophoresis.
PCAG	Presence of Hemoglobin C confirmed by Acid Gel Electrophoresis.
PCALG	Presence of Hemoglobin C confirmed by Alkaline Gel Electrophoresis.
PSAG	Presence of Hemoglobin S confirmed by Acid Gel Electrophoresis.
PSALG	Presence of Hemoglobin S confirmed by Alkaline Gel Electrophoresis.
PSCAG	Presence of Hgb S and Hgb C confirmed by Acid Gel Electrophoresis.
PSCALG	Presence of Hemoglobin S and Hemoglobin C confirmed by Alkaline Gel Electrophoresis.

SUGGESTED INDICATIONS FOR HEMOGLOBIN DIAGNOSES

Microcytosis, iron studies not performed: MICRO
Microcytosis, iron studies abnormal or previous normal MCV: IRONDEF
Microcytosis, iron studies normal, previous MCV always low: ATHAL
Microcytosis, A2 elevated (>4%): BTHAL
A2 slightly elevated (<4%) without microcytosis: HIGHA2NORM
F elevated in patient with sickle cell disease: HIGHF
F elevated in patient without sickle cell disease: HPFH
Slightly elevated F: HIGHFNORM
S present, no A, A2 normal or slightly elevated: SS
S present, no A, A2 elevated, microcytosis: SBTHALZERO
S 30-45%, A >50%: STRAIT or STRANS
S <30%, A present, no history of transfusion, microcytosis: SATHAL
S >45%, A present, A2 elevated, microcytosis: SBTHAL
S and A present, history of transfusion: TRANS plus diagnosis (e.g. SS, STRAIT, etc., or HGBS)
S present in ambiguous %, A present, possible history of transfusion: STRANS or HGBS plus TRANS
(S can be substituted with other abnormal hemoglobins in the above indications)
Two abnormal hemoglobins in ~same %, no A: SC or similar combined hemoglobinopathy
Infant: INFANT plus hemoglobins present (i.e. INFANTS, INFANTAS, INFANTC, INFANTAC)

CBC “soft” indicators of thalassemia trait vs. iron deficiency for microcytic patients:

	Thalassemia trait	Iron deficiency
MCV	Always low on previous CBCs	May be previously normal
Hgb	May be normal or slightly low	Low
RBC count	Relatively high	Low
RDW	Normal or slightly elevated	High

ALPHA GLOBIN GENE ANALYSIS (Send-Out)

This test detects the number of intact alpha globins and may be used in the diagnosis of alpha thalassemia. It is currently on (molecular) LMR approval, at a list price of >\$500. Often clinical indicators, RBC indices, iron studies, and hemoglobin analysis are enough to diagnose or rule out alpha thalassemia, and those should be recommended before ordering this test. If a patient's MCV is consistently low, iron studies are normal, and hemoglobin analysis rules out beta thalassemia, this test may not be necessary.

It's important to point out that African-American patients with alpha thalassemia trait are almost always homozygous for alleles containing one alpha globin, and thus are not at risk for having children with more severe forms of thalassemia; Southeast Asians, on the other hand, may have alleles with no alpha globin, putting them at risk for having children with thalassemia major (Hgb H disease) or fetal hydrops (Hgb Barts disease).

Anticoagulants

This section covers important laboratory monitoring aspects of anticoagulants. Dosing issues are covered in the BJH Tool Book, which is available on Dorsata (sign up for an account using your WUSTL email).

Heparin (unfractionated heparin, low-molecular-weight heparin, fondaparinux)

Mechanism of action: Binds to antithrombin, allowing more rapid inactivation of factors Xa and IIa (minimal for LMWH and not at all for fondaparinux, a synthetic “mini heparin”).

Administration: Injectable only.

Monitoring: Unfractionated heparin can be monitored by aPTT; therapeutic range is 60-94, or anti-Xa (0.3-0.7 IU/ml). Physicians may order therapeutic heparin continuous infusion that allow nurses to make infusion rate adjustments following either an aPTT or anti-Xa nomogram. Low-molecular-weight heparin (enoxaparin, Lovenox) can be monitored by the anti-factor Xa assay (see above); therapeutic range is 0.6-1.0. If the patient has a lupus anticoagulant resulting in an artificially prolonged aPTT, unfractionated heparin can also be monitored by the anti-factor Xa assay; therapeutic range is 0.3-0.7. BJH anti-factor Xa assay is not calibrated for fondaparinux.

Reversal: Protamine. Low-molecular-weight heparin does not respond as well to protamine as unfractionated heparin.

Heparin resistance: For some patients, the aPTT may be insensitive to heparin, requiring higher than “typical” doses. Major causes of this are heparin-binding proteins (in which increased doses of heparin may be used), elevated FVIII, and sometimes antithrombin deficiency.

Recommend an antithrombin activity assay to differentiate: antithrombin should be <50% (either inherited or acquired). Unfortunately, this situation often occurs in the OR, when it is not feasible to wait for the assay, and the OR team may demand empiric AT concentrate therapy. The core lab performs antithrombin activity assays 24/7.

Warfarin

Mechanism of action: Inhibits vitamin K epoxide reductase (VKOR), resulting in reduced activity of vitamin K-dependent factors (II, VII, IX, and X, protein C, and protein S) due to hypo-gamma carboxylation of selected glutamic acid molecules to provide binding sites for Ca++ that are attracted to negatively charged phospholipid membranes.

Administration: Oral.

Monitoring: The INR is designed to harmonize monitoring of warfarin across different reagent/instrument combinations. Therapeutic goals may be 2-3 or 2.5-3.5 (mechanical mitral valve), depending on indication and treating physician. In the rare case of a PT artifact (e.g. lupus anticoagulant or direct thrombin inhibitors), a chromogenic factor X assay may be helpful, but it is a send-out to Mayo (testing performed M-F).

Reversal: No direct reversal, but oral or I.V. vitamin K will provide reduced vitamin K to resume gamma carboxylation and correction of PT/INR (takes hours to days).

Pharmacy has a 4 factor (X, IX, VII, II) plasma derived concentrate (Kcentra) to reverse coagulopathy in bleeding patients taking warfarin or prior to urgent invasive procedure. See

Prothrombin Complex Concentrate (PCC) section below in coagulation factor section for more details. Plasma is an inefficient, temporary treatment for warfarin induced prolonged INR.

Note: Superwarfarins (*e.g.* brodifacoum, the active ingredient in the rodenticide d-CON) cause severe prolongation of both PT and aPTT when ingested by accident or by suicide attempt. Correction requires protracted treatment with high-dose vitamin K. A toxicology send-out test for brodifacoum exists.

Direct thrombin inhibitors (dabigatran, argatroban, bivalirudin)

Mechanism of action: Bind to thrombin (IIa), causing direct reversible inhibition.

Administration: Dabigatran (Pradaxa) is oral; all others are injectable.

Monitoring: Dabigatran can be monitored by the dilute thrombin time (TT); the regular TT is very sensitive to the presence of the drug, but cannot monitor the therapeutic range. The hematology lab had validated a non-FDA approved dilute thrombin test with dabigatran calibrators. However, in 4 years, we have had < 5 requests, because the routine TT can rule out the presence of dabigatran if normal, and a prolonged aPTT can give us a rough idea about really high concentrations. Therefore the dilute TT was removed from the test menu in 2017. Reversal: Half-life is 30-60 minutes for IV DTIs, and there is no reversal agent for IV DTIs. Dabigatran's half-life is ~12 hours with normal renal function. Praxbind (idarucizumab) is an IV inhibitor for dabigatran. It has been approved by BJC and BJH for the following uses only:

- 1) Known dabigatran exposure with life-threatening bleeding
- 2) Known dabigatran exposure and need for reversal for life-saving intervention

****Idarucizumab is NOT approved for bridging or use for scheduled reversal for a procedure.

****Idarucizumab should NOT be co-administered with 4-factor PCC (Kcentra).

Idarucizumab is stocked in the pharmacy and available in for order entry. Thrombin time is not required but may be helpful if the last dose of dabigatran is not known.

Factor Xa inhibitors (rivaroxaban, apixaban, edoxaban)

Mechanism of action: Reversibly bind to factor Xa, causing reversible inhibition.

Administration: Oral.

Monitoring: The PT is relatively sensitive to these drugs. An anti-factor Xa assay, calibrated with apixaban standards, was recently approved by FDA, but BJH lab does not perform the test. One can estimate the concentration of rivaroxaban and apixaban based on an anti-Xa assay, since it will interfere and give the appearance of heparin in the plasma (see graph in section on hemostasis testing-ant-Xa assay).

Reversal: Half-lives are 7-11 hours with normal renal function. An anti-Xa inhibitor reversal drug andexanet alfa has been developed and is available on the formulary.

Coagulation Factor Concentrates

Coagulation factor concentrates are housed in the pharmacy. As orders for coagulation factors require the physician to document a discussion, and approval of drug/dose/interval, with either a hematology fellow or LMR, you may receive calls on the appropriateness and dosing of factors. Important information to obtain includes the patient's underlying condition

(e.g. hemophilia A) and the present indication (e.g. current bleeding, upcoming surgery). During dosing, advise the clinician to order trough (before infusion) and peak (after transfusion) factor activities, as patients respond differently to factor infusions and may need dosing adjustments. Call the attending on Red service to get confirmation of your advice. Your name will be listed in the Epic order.

Factor VIII (recombinant)

Dosing: 1 U/kg IV will increase activity by ~2%, with a half-life of ~12 hours. With an initial activity of 0% and goal of 100%, use a 50 U/kg loading dose and 25 U/kg q12 hrs maintenance dose.

Note: Monoclonal and recombinant varieties exist, but the pharmacy stocks only recombinant. Several modified rFVIII concentrates with prolonged (>24 hour) half-lives have been FDA-approved since 2015. As of now, BJH only provides one unmodified rFVIII (XYNTHA®).

Factor VIII (recombinant, porcine sequence)

Dosing: 100-200 U/kg initial dose, with subsequent doses every 4-12 hours based on clinical response and FVIII activity levels. Factor VIII activity should be assayed at 30 minutes and 3 hours after the initial dose is administered and 30 minutes after subsequent doses. A target FVIII activity of 100-200% is recommended for major acute bleeding, and 50-100% FVIII activity is recommended for minor/moderate bleeding and after acute bleeding is controlled.

Note: This product (OBIZUR®) is approved for the treatment of acute bleeding episodes in patients with **acquired** hemophilia A. It is NOT indicated for congenital hemophilia A or von Willebrand disease.

Factor IX (recombinant)

Dosing: 1 U/kg IV will increase activity by ~1%, with a half-life of ~24 hours. With an initial activity of 0% and goal of 100%, use a 100 U/kg loading dose and 50 U/kg q24 hrs maintenance dose.

Humate-P (FVIII concentrate with high level of vWF)

Indication: vWD. Do **NOT** use recombinant FVIII concentrates for vWD and be certain the clinician knows which is which when it is ordered. Also, do **NOT** use cryoprecipitate for vWD, as Humate-P is a more efficient source of vWF.

Dosing: Dosing is based on RCo (ristocetin cofactor) units (see below). The box label includes factor VIII activity units, but do **NOT** use these when dosing, except for type 2N.

Note: Plasma-derived and virally inactivated, but still carries a small risk of viral transmission.

Humate-P Dosing Guidelines for Patients with von Willebrand Disease:

(Condensed from HUMATE-P package insert)

VWD Type	Bleeding Severity	Dosing (IU vWF = RCo/kg)
Type 1	Minor, not responding to DDAVP	40 – 50 IU/kg, repeat x 1 after 8 hrs PRN
Type 2A, 2B, 2M, and Type 3	Minor (epistaxis, oral bleeding, menorrhagia)	40 – 50 IU/kg, repeat x 1 after 8 hrs PRN
All Types	Major (GI, CNS, trauma, major surgery)	Load 60-80 IU/kg Maintenance: 40 – 60 IU/Kg q8-12 hr X 3 days; keep nadir RCo > 50% Then 40-60 IU/day x 4 days

Recombinant vWF (Vonvendi): Approved in 2017. This product is not on the BJH formulary

Prothrombin complex concentrate (PCC)

Indication: PCCs may be used for rapid warfarin reversal with life-threatening bleeding. Potential benefits of reversing Vitamin K Antagonists should be weighed against the potential risks of thromboembolic events, especially in patients with history of a thromboembolic event. Kcentra (4 Factor Concentrate): Kcentra PCC is indicated for the urgent reversal of acquired coagulation factor deficiency induced by Vitamin K antagonist (VKA, e.g., warfarin) therapy in adult patients with acute major bleeding or urgent reversal of VKA anticoagulation in patients without acute major bleeding. **Administer Vitamin K concurrently.** Administer reconstituted Kcentra at a rate of 0.12 mL/kg/min (~3 units/kg/min) up to a maximum rate of 8.4 mL/min (~210 units/min.). **Dosing for PCC must be approved by an attending physician. Repeat dosing with Kcentra is not supported by clinical data and is not recommended.**

Pre-treatment INR	2 – < 4	4 – 6	> 6
Dose of Kcentra (units of Factor IX) / kg body weight (not exceeding 100 kg)	25 units/ kg	35 units/ kg	50 units/ kg
Maximum dose‡ (units of Factor IX)	Not to exceed 2500	Not to exceed 3500	Not to exceed 5000

‡ Dose is based on body weight up to but not exceeding 100 kg. Do not exceed stated maximum dose for patients weighing more than 100 kg.

Recombinant activated factor VII (rFVIIa, brand name Novoseven)

Indication: There are only two FDA-cleared indications in the US: emergent bleeding for 1) hemophilia A (or B) patients with inhibitors to FVIII (or FIX) and 2) patients with congenital factor VII deficiency. However, it is much more frequently used off-label for life-threatening, uncontrolled bleeding in any patient, particularly cardiovascular (microvascular surgical bleeding) and neurosurgical (intracranial bleed on an anticoagulant) cases. **Remind ordering physician to use cryo, platelets, and fluid resuscitation first. There is a risk of thrombosis with use of clotting factor concentrates.**

Dosing: Dosed by boxes of 1, 2, or 5 mg each (lyophilized), depending on indication:

- Hemophilia with inhibitors: ~90 µg/kg body weight IV q2 hours until bleeding risk has ceased
- FVII deficiency: ~15–30 µg/kg body weight IV, with future injections based on bleeding risk
- Off-label: No set dose, but we recommend 40 µg/kg body weight IV, with future injections based on bleeding risk.

Off-label uses: Bear in mind that rFVIIa is used to treat *small vessel bleeding*; it is not effective in large vessel bleeding.

Antithrombin Concentrate

Indication: Antithrombin deficiency in the setting of thrombosis or heparin management (heparin requires antithrombin for effective anticoagulation). Although appropriate indication and dosing requires an antithrombin activity measurement, this product is often used by cardiothoracic physicians who suspect heparin resistance (based on the point-of-care ACT [activated clotting time] assay), and are not willing to wait for an activity to be resulted.

Dose: Dosing guidelines: [desired AT* – baseline AT] x weight (kg) divided by 1.4. Dosing interval: q24 hours with 60% of loading dose. Peak and trough monitoring with AT activity is appropriate.

Note: Plasma-derived and virally inactivated, but still carries a small risk of viral transmission. AND desired usually = 100%

Fibrinogen Concentrate (RiaSTAP): A plasma derived lyophilized concentrate (900 mg and 1,300 mg vials) stored at room temperature in pharmacy, and more quickly reconstituted than cryoprecipitate. Approved for acute bleeding in: patients with congenital fibrinogen deficiency. Off-label use at BJH, with approval from critical care physicians, for management of excessive bleeding in labor and delivery, CT-OR, and trauma. Dosing guideline in mg/kg body weight: target fibrinogen (mg/dl)-measured fibrinogen/1.7.

Protocols

Using Cellavision to Review Peripheral Blood Smears

Peripheral blood smears that are referred to the lab for manual morphologic review are stored in Cellavision, a software program that takes photos of individual WBCs and a reviewable area of the smear for RBC and platelet examination. You can use this software remotely to view recent smears. This may be helpful to evaluate leukapheresis requests or urgent cases with abnormal smears (e.g. intracellular bacteria).

To access Cellavision:

1. Log into WUSTL Citrix or ctxremote.wustl.edu
2. Click on the Cellavision icon
3. Log into Cellavision using your username and password received at orientation (should be your wustl key minus punctuation marks, for both). Make sure the "Database" is set to bjh_cellavision_db.

Once in Cellavision, you can search for individual patients to look at their smears. If you see results in **red**, these smears have not been finalized by the lab. Therefore, consider the cell IDs to be preliminary and do **not** release them to other clinical services. Additionally, the smear will be locked from lab review while you view it, so be sure to log out as soon as you're finished reviewing.

Some important buttons to use:



Toggles between patient list and individual smear review.



Toggles between WBC views. Far left button shows all cells in one view, but hides the differential counts.



Toggles between cell lineage views



Corresponds to CBC accession number visible in Epic (ignore the letter at the end).

Lastly, and most importantly: **ALWAYS LOG OUT WHEN YOU'RE DONE!** If you don't, you may lock up a viewing license and prevent the lab from doing its job.

Intracellular Organisms in Peripheral Blood and Body Fluid

Depending on the day of the week, time of the day and the specimen type, the technologist will need to follow a different pathway when an intracellular organism is seen in peripheral blood or body fluid sample.

1. Monday through Friday between the hours of 8am and 5pm.
 - a. Page the Hematology Lab Medicine Resident (LMR) immediately for both peripheral blood smears and body fluids.
 - b. The Hematology LMR will come to the lab to review the microscopy.
 - c. The Hematology LMR will review patient chart for history and simultaneous microbiology orders.
 - d. If the sample in question is a peripheral blood smear, the LMR will discuss the case with the Hematology Laboratory attending.
 - e. If the sample in question is CSF or other body fluid, the LMR will discuss the case with the hematopathology attending covering the consult service.
 - f. If microbes are suspected, the Microbiology LMR will be called by the attending or LMR if needed.
2. After hours and on weekends.
 - a. For **Peripheral blood and CSF**, page the Hematology LMR immediately.
For **all body fluids except CSF**, page the Hematology LMR after 8am.
(Note that after 5pm and on weekends, this pager will connect to the Transfusion LMR).
 - b. The LMR may request the slide to be put in Cellavision.
 - c. The LMR will review the patient chart for history and simultaneous microbiology orders.
 - d. LMR will call the Hematology Laboratory Attending in the following order.
 1. Dr. John Frater 314-484-6369 (cell), 314-836-1184 (pager), 314-925-8383 (home)
 2. Dr. Ron Jackups 314-578-3940
 3. Dr. Charles Eby 314-954-1242
 - e. If microbes are suspected the Microbiology LMR will be called by the Hematology attending or LMR if needed.
 - f. The technologist will be instructed how to report the finding by the attending and/or LMRs involved.

Result Reporting

The following comments could be used as directed by the LMR:

- Intracellular inclusions present
- Intracellular yeast present
- Intracellular bacteria present
- Intracellular organisms present, see microbiology report

Protocol for after hour physician alert values

The alert system for results generated in the hematology lab is in place to ensure that extreme values are reported to the appropriate physician as rapidly as possible (to ensure that a critical value does not sit unseen on the computer). Technologists in the BJH labs handle the vast majority of alert notifications; however, the LMR will occasionally be paged to communicate an alert value. This often happens on outpatients after hours, when it is difficult to reach the clinic or ordering physician.

Remember to get the following information from the lab when you are called about an alert value:

- Patient's name, DOB, and home phone number
- Alert value, including normal range
- Ask if next-of-kin information is available
- Physician's name and phone number
- Ask which provider they have been trying to contact, and what number(s) they have been calling or paging

Inpatient:

- 1) Call/page ordering provider.
- 2) Call floor (look up the patient's floor in Epic, call central page, and ask to be connected to that floor).

Outpatient:

- 1) Ask customer service for the physician's name. Also use your resources to see if this name is accurate, and if there is anyone else who saw the patient that day and would be familiar with the testing ordered. A few resources for this include: lab order form, and recent notes (from that day!!) in Epic. If the physician's name is known, obtain their pager number by:
 - a. Calling Central Page (BJH = 314-362-1242, SLCH = 314-454-6000)
 - b. Use online tools: <http://doclookup/search.aspx>, <http://tfcweb02.carenet.org/ebook>, and <http://smartweb.carenet.org> (you must be on campus or use Citrix as these are intranet resources).
 - c. It may also be useful to email the physician and ask them to call you. You can use send/read receipts to see if the physician received the email, but these should not be used to relay the alert value.
- 2) If the physician's name is not known, or if it is known, and they do not respond to the page within ~15-20 minutes, then determine where the patient was seen. Several clinics/services have a general on-call pager number, e.g. GI Clinic has a GI Fellow on-call and the dialysis center has a nurse on-call. If you do not have a number for that particular clinic, call central page and ask to be connected to that clinic/the on-call resident for that clinic.

- a. If the patient was seen at an off-site clinic and labs were performed at BJH, use Google to find the phone number for that clinic. See if there is an after-hours number, and call that.
- 3) If you still cannot reach a clinician and it was a BJH department of medicine provider that ordered the test in a BJH medicine clinic, call the medicine on call pager (314-393-5578).
- a. Depending on the clinic in which the patient was seen, this resident may be reluctant to take the information. Use your judgment to explain the reason(s) why you are or are not particularly concerned about the lab result in question (there is a difference between hyperkalemia likely due to improper specimen collection/processing and a toxic drug concentration).
- 4) **When you reach a physician or nurse that will accept the alert value, you must ask them to repeat the test name and alert value back to you. You must also record the time and the name of the physician you reported the alert value to, and then call the customer service tech back to let them know to who and when you relayed the alert value.**
- 5) You may find yourself in a situation where you need to phone the patient at home to verify that all is well with them. Call the patient if you feel comfortable doing so and/or call the Chief Fellow or Chief Resident to discuss the situation. If you do phone the patient at home, explain who you are and why you are calling. Ask which doctor they saw earlier that day and encourage them to follow-up with that person the next day. You should notify that physician the next day as well. If the critical value is judged to be accurate it may be appropriate to recommend that the patient present to the local ED.

Policy for CPAP Critical Values- CPAP critical values should be reported to Anesthesia.

Before 5 PM: CPAP main # 454-8134 option 4

5-6:30PM: General Anesthesia Attending #454-8136

6-9 PM and Weekend: Call CPAP Resident pager #360-2727 (360-CPAP)

If no reply to above: Call CPAP Attending directly

Central page can also be used to contact pager/ attending (314-362-1242)

For patients seen at the Primary Care Resident Clinic in COH:

Call the Medicine Ambulatory resident on call 314-215-7788

Miscellaneous

Apt test

The Apt (alkali denaturation) test is offered at SLCH for neonatal body fluid to distinguish neonatal blood (e.g. GI bleed) from maternal blood (usually swallowed blood from delivery or breastfeeding). A bloody sample (e.g. vomitus or stool) is treated with dilute NaOH, and a visual endpoint is observed: Samples that change color from red to brown indicate maternal origin, while samples that remain red indicate fetal origin. This is because fetal hemoglobin is more resistant to NaOH than adult hemoglobin. Note that the sample must contain RED blood in order for the test to be useful. The lab will reject samples without visible red blood, which can sometimes lead to calls from frustrated clinicians.

(Fun fact!): “Apt” is not an acronym; it’s named after the person who developed the test method. Therefore, it is incorrect to use capital letters (APT).

Testing for G6PD deficiency

A qualitative G6PD test can be done in house by a rapid method, while quantitative G6PD testing is sent out to Mayo. The quantitative G6PD test does not require LMR approval.

Glucose-6-phosphate dehydrogenase (G6PD), qualitative

How the assay is performed: Point-of-care device within the BJH lab (BinaxNOW). RBCs (source of G6PD) are lysed and added to a lateral flow test strip. If sufficient G6PD is present, the enzyme will reduce the reagent dye (nitro blue tetrazolium), resulting in a color change. The test is resulted as “normal” (color change) or “deficient” (no color change).

Interpretation: Patients with deficient G6PD activity are at risk of hemolysis when subjected to oxidative stress (favism). The most common appropriate indications for G6PD testing at BJH are prior to administration of the antibiotic dapsone or anti-uremic drug rasburicase, or in neonates with unexplained hemolytic crisis. This test may be falsely “normal” in patients during acute hemolysis or within 3 months of RBC transfusion, since the donor RBCs will contain normal G6PD. Additionally, as G6PD deficiency is X-linked and primarily found in African descent, it is unlikely to be found in patients other than African-American males, though female heterozygotes may be deficient enough to trigger a positive result.

Note: Because anemia and other conditions can cause falsely deficient results, all deficient tests will automatically be sent to Mayo for confirmatory quantitative G6PD testing.

Transfusion Medicine Checklist

*Topic/activity to be covered by Medical Staff

BLOOD BANK/SEROLOGY				
Task	Date	Discussed/ Performed	Instructors initials	Residents Initial
ABO/ Rh determination				
ABO/Rh confirmation				
Retypes (Check Sample)				
Antibody Screens				
Rh phenotypes				
Electronic crossmatch				
Immediate spin/full crossmatch				
Antigen typing				
QC				
DAT				
Antibody identification				
<i>Single</i>				
<i>Multiple</i>				
<i>Cold</i>				
ABO discrepancy				
Prewarm specimen				
Saline replacement				
Elution				
Adsorption				
HSCT specific issues				

QC/QA AND PREVENTIVE MAINTAINCE				
Task	Date	Discussed/ Performed	Instructors initials	Residents Initial
Daily reagent QC				
Daily temperature Monitoring				
PM schedule				
Market withdrawal				
Lookback				
Suspected Post-tx Infection				
Record Retention				

BLOOD PRODUCT INVENTORY MANAGEMENT				
Task	Date	Discussed/ Performed	Instructors initials	Residents Initial
Blood product receipt and storage				
Review available products				
Refrigerator organization				
Freezer organization				
Reagent receipt and storage				
Inventory reconciliation				
Single donor platelets inventory				
Min/Max inventory				
Short date				
Quarantine untested or positive tested units /reissue				
"Release" back into inventory				

PRODUCT PREPARATION AND ISSUE				
Task	Date	Discussed/ Performed	Instructors initials	Residents Initial
Receiving patient specimen				
Mislabeled specimen handling				
Previous Patient history check				
Visual unit checks at time of issue				
Filters				
RBC issue				
Thawing frozen products				
Selection and issue of SDP				
Pooling and issuing cryo				
Issue policy autologous/directed				
Saline washing				
Irradiation of blood products				
Volume reduction / saline washing platelets				
Emergency release/ uncrossmatched				
Box to and from OR				
Sterile docking device				

PRODUCT MANUFACTURING				
Task	Date	Discussed/ Performed	Instructors initials	Residents Initial
Receipt from Apheresis				
Receipt from outside blood center				
Donor Testing*				
Labeling Blood Products				
SDP absolute platelet count				
SDP WBC count				
Bacterial culture-platelets				

APHERESIS				
Task	Date	Discussed/ Performed	Instructors initials	Residents Initial
Orientation to Unit				
Writing Orders *				
Fluid Replacement*				
Anticoagulants*				
Patient Issues*				
Labeling Blood Products				
Preparing to Transport to BB				
Donor Issues				
Apheresis instruments				

LABORATORY MANAGEMENT				
Task	Date	Discussed/ Performed	Instructors initials	Residents Initial
Attend Transfusion Committee				
SOP review				
Review UOR process				
Review prior FDA, AABB CAP audits				
Review internal audits				
Review annual Expiration rates				
SLCH blood bank				

Note: Anyone interested in seeing the cell therapy lab please contact Dr. Thibodeaux.

Suggested Reading

1. Current edition of AABB Standards for Blood Banks and Transfusion Services.
2. Current edition of Blood Transfusion Therapy - A physician's handbook.
3. Current edition of AABB Technical Manual.
4. Title 21, CFR 600s.

Medical Director Review_____

Date_____