BLOOD AND MARROW TRANSPLANT PROGRAM SUPPORTIVE CARE GUIDELINES 3rd EDITION – JULY 2002

Shands at the University of Florida
Gainesville, Florida

Editor: Helen L. Leather B.Pharm, BCPS

Bone Marrow Transplant Program Supportive Care Guidelines; 3rd Edition 2002

INTRODUCTORY REMARKS

Welcome to the 3rd Edition of the Supportive Care Guidelines (SCG) for the Blood and Marrow Program at Shands at the University of Florida.

There have been earlier editions, upon which we have built, resulting in this expanded version. This version of the guidelines has expanded from 80 pages (2nd edition) to 244 pages in the current version. Compilation of the SCG is a multidisciplinary effort, and suggestions for improvement were solicited from all members of the blood and marrow transplant program.

A special thanks to the following contributors to this edition, namely Amy Cheatwood PA-C, Laura Wiggins Pharm.D., Diane Darnell RN, Mary Coons RN, Katarzyna Finiewicz M.D., Vijay Reddy M.D., Jan Moreb M.D., Michelle Sugrue MS, Mark Mogul M.D., KJ Kao M.D., Chris Meyer PA-C, Shelley Doran RN, John Wingard M.D., Vivian Cozatt RN, Paula Kinchen RN, David Roque, Marc Zumburg M.D., Ken Klinker Pharm.D., Amy Serrano Pharm.D., and Richard Lottenberg M.D. These contributors went out of their way to make recommendations for inclusion in this version, review collated documents, or researched an area and created tables or text that comprise some sections of this handbook.

I would also like to thank everyone who spent time at the numerous SCG review meetings to discuss all the changes put forward by the many members of our program.

Any book like this will inevitably overlook some aspects of HSCT patient care. As you read, feel free to forward your suggestions for other topics you think would add to the care of patients in our program for inclusion in the next edition.

A final note, that the purpose of the SCG is to be a guide to the management of HSCT and leukemia patients. Healthcare professionals have the sole responsibility to be fully aware of current practices and standards, to avoid use of outdated regimens and recommendations, to employ good clinical judgement in selecting therapeutic regimens/ calculating doses for individual patients. The editor of this book accepts no responsibility for any damage caused following the use of the recommendations outlined in this manual.

Helen Leather, B.Pharm, BCPS
Clinical Pharmacy Specialist BMT/Leukemia
Department of Pharmacy
Shands at the University of Florida

PHONE NUMBERS

Person/Department	Phone Number	Beeper
Admissions	5-0236	
Apheresis	4-7011	
Bed Control	5-0233; FAX 5-0269	
Blood Bank	Phone: 5-0377; FAX: 5-0320	
BMT laboratory		
Diane Fisk	4-6269	1-877-364-0336
Michelle Medei	5-0232	
Cheryl Roberts	5-0232	
Emma Rosenau	5-0232	
Michele Sugrue	5-0232	
Traci Pena	5-0232	
FAX for stem cell lab	338-9817	1-877-364-0335
On-call Pager		
Cancer Center		
Adults	5-0725	
Pediatrics	5-8208	
Cardiology	5-0725	
MUGA	5-0116	
Echo	5-0047	
CDC	5-0493	
Chaplain	5-0123	
Civitan	334-1000	
Clinical Laboratory		
Direct	4-7740	
Processing	4-4868	
Hematology	4-4857	
Chemistry	4-4869	
Microbiology	5-0165	
Virology	4-4778	
Stat Lab	5-0199	
Clinic (BMT) – main line	5-0062	
Nursing station	4-6266	
Triage Room	4-3837	
Apheresis	4-7011	
Clinic (BMT)	FAX: 5-0525	
Computer Support	5-0526	
Coordinators		
Becky Gaa	4-6272	727-6732
Jan Luzins	4-6629	2492
Margaret Youngblood	4-6626	2981
Phyllis Pumphrey	4-5507	727-6847
Catherine (Cathy) Stegall	4-3373	727-4029

Person/Department	Phone Number	Beeper
Clerks		
BMT clinic – front desk	4-6276	
BMT clinic – back desk	4-6261	
Clinical Psychology	Adult – 250-0313 Pediatrics 392-3641	1-877-206-7621
CT scan		
Phone	4-6068	
FAX	338-9820	
Body results	4-6068	
Neuro results	4-4296	
ENT results	5-8989	
Cytogenetics	5-0071	
Cytology	955-5877	
Data Managers		
John Hopkins	8-6511	1-877-206-7670
David Roque	4-5246	727-6731
Dermatology	5-6804	
Employee Lounge (clinic)	4-6263	
Eye Center	392-3111	
Family Room	4-6646	
Fellows		
Cogle		1-877-214-3217
George		1-877-216-3545
Gordan		1-877-216-3495
Gorman		727-5012
Hagler		1-877-206-8652
Helner		1-877-214-3347
Larson		727-4284
McGrath		727-4178
Mehta		727-4917
Redinger		727-5770
Financial Counselors		
Kathy Henderson	5-0359	
Joanne Brown	4-4588	
FAX for above	338-9852	
Financial Specialist	4-7015	
FAX	265-0562	
FISH results	955-5877	
GI Lab	5-0048	
Heart Station	5-0047	
Heme Path	4-5338	
HLA Laboratory	4-7289	
Homecare	5-0789	
Hospital Stores		
Phone	5-0261	
Fax	338-9876	
Infection Control	5-0284	

Person/Department	Phone Number	Beeper
Infectious disease	392-4058	
Information Services	5-7979	
Maintenance	265-0059	2580
Medical Records	5-0131	
MRI	5-0106	
Nuclear Medicine	5-0105	
Nursing		
Mary Coons	4-5436	727-6733
Suzette Martin	4-3632	727-6725
Pamela Roberts (assistant)	5-0419	1-877-206-3438
Helen Welsh	5-0247	727-6734
Oral Oncology	392-4399	
Outpatient Pharmacy	5-0405 (Direct 4-7332)	
Outpatient registration	5-0256	
Pentamidine treatment		
Phone	5-0078	
FAX	338-9891	
Pharmacists		
Helen Leather	4-5839	1-877-364-1029
Melissa Johnson	4-4716	1-877-364-1070
Masha Lam	4-7019	
Laura Wiggins	4-4683	1-877-364-1042
Pharmacy		
Cancer Center/SMP	5-0720	
Medical Plaza	5-8270	
Outpatient	5-0405/ direct 4-7332	
Satellite (4th floor)	4-4051	
Stores	5-0407	
Physical Therapy	5-0295	
Physicians – ADULT BMT		
Finiewicz	2-4925	1-877-206-9656
Khan	2-2303	1-877-214-6482
May	6-1144	727-4763
Moreb	2-3875	1-877-214-6421
Reddy	2-7346	1-877-206-7395
Wingard	846-1846	1-877-364-0442
Physicians – HEME/ONC	392-3000	
Kitchens	2-6016	413-5809
Lottenberg	2-2976	1-877-214-9463
Lynch	2-5110	1-877-206-7620
Marsh	2-2976	1-877-214-6430
Richardson	58-7301	1-877-214-6413
Riggs	5-8419	1-877-206-7664
Shea	2-2995	1-877-214-6429
Zumberg	2-2976	1-877-214-6424

Person/Department	Phone Number	Beeper
Physicians – IMMUNOLOGY		
Sleasman	392-2962	1-877-332-9442
Skoda-Smith	392-2961	1-877-214-3259
Physicians – PEDIATRIC		
John Graham-Pole	2-1532	1-877-206-9565
Stephen Hunger	2-6452	1-877-206-7676
Amos Kedar	2-0656	1-877-206-7671
Mark Mogul	2-8724	1-877-206-9564
Bill Slayton	2-0214	1-877-206-7677
Physician Assistants (PA's)		
Tammy Briar	392-6412	1-877-216-3330
Sharon Fielding	2-1535	1-877-206-9566
Debbie Givens	4-4923	3126
Samantha Greene	4-4454	1-877-214-6425
Jeremy Heinerich	4-4923	3136
Jerry Janicec	2-1535	1-877-206-7669
Chris Meyer	4-6256	727-4877
Neet Patel		1-877-330-4862
Amy Pazzalia	4-4769	1-877-364-6414
Warren Reed	4-4769	1-877-214-6487
Raiza Rodriguez		1-877-330-4857
Lily Schlenz		1-877-214-2060
Kate Vellis	8-7853	1-877-216-3307
Aya Yamazaki		1-877-330-4860
PICC		727-4217
Program Assistants		
Atha Ellerker	4-5921	
Sally Brown	4-6271	
Amy Weber	4-5261	
Psychology	See Clinical Psychology	
Pulmonary Laboratory	5-0275	
Radiation Therapy	4-3924	
Radiology Scheduling	5-0104	
FAX (Special Procedures)	265-7547	
Radiology Centralized Testing	4—7203	
FAX	5-0544	
Radiology (invasive/specials)		
Phone	5-0116	
FAX	5-0544	
Radiology Transport	4-4285	
Research Nurses		
Renee Boyette	4-4110	3133
Sidney Lasley	4-6646	0306
Susan Lybarger	4-7437	0135
Joanne Malles	4-4110	1-877-206-8664
Christine Nejame	4-4110	0134

Person/Department	Phone Number	Pager
Research Nurses Cont'd Joe Stokes	 4-7437	 4-7437
Respiratory Supervisor	5-0078	1148 2709
Ronald McDonald House	374-4404	
Rush Lake Motel	373-5000	
Secretaries – Adult MD's Dr Wingard's – Connie Dr Reddy/Dr Finiewicz - Heather	 846-2814	
Secretaries – Pediatric MD's Dr Hunger's – Cathy Dr Hunger's – Kitty Dr Graham-Pole's – Joyce	 2-4732 2-4470 2-5665	
Security (Shands) General Stat	 5-0109 41	
Shands Home Care	5-0789	4757
Social Work – Gale Smith	4-6630	727-4089
STR's (Blood Bank)	5-0377	265-0320
Surgical Pathology	5-0208	
TPN	4-4248	
Transcription	4-4816	
Ultrasound Phone FAX	 4-4363 1-888-678-4013	
Wound	265-0262	1841

DAILY ROUTINE INPATIENT SERVICE

0900 – 0930:	Pediatric Rounds
0930 - 1100:	Adult Rounds
1200 - 1300:	Noon conference (see weekly meeting schedule)
1630 – 1730:	Afternoon rounds

WEEKLY MEETING SCHEDULE

Monday:	Nil
Tuesday:	0800 – 0930: BMT Referral Meeting R4-265 1200 – 1300: BMT Conference R4-265
Wednesday	0800 – 0900: Fellows Conference Library ARB 0830 – 0930: 2nd Wednesday of the month is Research and Data Trends; 3rd Wednesday of the month is Quality Assurance R4-265 1200- 1300: Heme/Onc Grand Rounds R4-265
Thursday	0800 – 0900: Pediatric Issues Meeting (PAR room in BMT clinic) – every other week 1100 – 1200: Medicine Grand Rounds (Communicore Buildings)
Friday	1200 – 1300: Heme/Onc Grand Rounds R4-265

PRE-TRANSPLANT CONSIDERATIONS

SCREENING LUMBAR PUNCTURES IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES WHO ARE TO RECEIVE CONVENTIONAL CHEMOTHERAPY

Perform a lumbar puncture to look for CNS involvement in the following malignancies upon presentation to the Shands BMT/leukemia program:

1. Non-Hodgkin's Lymphoma

   a. Aggressive large cell NHL (diffuse large cell lymphoma and follicular lymphoma grade 3) patients with an elevated LDH and > 1 extranodal site of disease
   b. All patients with testicular and paranasal sinus involvement
   c. All patients with very aggressive (lymphoblastic lymphoma, Burkitt's and Burkitt's-like's lymphoma). It is a part of treatment regimens for these diseases.

* Aggressive = intermediate grade
** Very aggressive = high grade

2. Acute Myeloid Leukemia (AML): patients with AML-M4 and AML M5

3. Acute Lymphoblastic Leukemia (ALL): part of treatment protocol

NEED FOR LUMBAR PUNCTURES IN PATIENTS BEING WORKED UP FOR TRANSPLANT (PART OF PRE- BMT EVALUATION)

1. Patients with aggressive lymphoma [DLCL and FC grade 3 with increased LDH and > 1 extranodal site) who should have had a LP and treatment as part of the conventional chemotherapy regimen, BUT it was never done should have a LP performed within 30 days of transplant
2. Patients with very aggressive lymphoma (lymphoblastic, Burkitt's and Burkitt's like lymphoma)
3. All patients with acute leukemia (AML and ALL)

These LP's should be performed in the routine work-up for patients undergoing transplantation, within 30 days of transplant.

SHANDS

at the University of Florida
Gainesville Florida 32610

Patient Name: MR#:

Physician's Orders

Date/Time		**Admission Orders: Bone Marrow Transplant (Page 1 of 3)**
		(All orders with a □ must be checked to be activated)
		1. Admit to BMTU LAF room. Diagnosis: _____
		2. Allergies: _____ If yes, explain _____
		3. VS q4h
		4. Regular diet unless/until ANC < 500 then neutropenic diet
		5. Activity as tolerated in BMTU
		6. Compromised Host precautions
		7. Physical Therapy consult for evaluation and recommendations.
		8. EKG & CXR (give reason)
		9. CBC with diff, RDB, LFTs now. CBC with diff & RDB q day; LFTs q MWF
		10. Culture any suspected infection sites
		11. On admission, please send stool culture (or perirectal swab if stool sample not available) for VRE
		On any patient who has not had a screen within 30 days.
		12. PRN medications:
		□ a. Tylenol _____mg q_____ hours for temperature ≥ 38.5.
		□ b. Zolpidem 5 – 10mg PO q HS PRN insomnia
		□ c. Oxycodone 5 – 10mg PO 14-6 hrs PRN pain
		□ d. Maalox TC 30cc PO q 4hrs PRN dyspepsia
		□ e. TPA lines 1mg/ml prn.
		□ f. Benadryl 25 – 50mg PO q 4hrs PRN pruritus
		□ g. Phenergan 12.5 – 25mg PO q6h PRN nausea/ vomiting
		13. Pre-med for blood products, only if history of prior reactions
		a. Tylenol _____ mg PO
		b. Benadryl _____ mg PO/IV.
		14. Transfusion parameters. Irradiate all blood products. Check post platelet count.
		CMV negative □ Yes □ No
		Filtered □ Yes □ No
		For Hct. ≤ _____, transfuse with _____ units PRBC over _____.
		For Plts. ≤ _____, transfuse with _____ units, □ RDP □ SP □ HLA ***(check)***
		(continued on next page)

SHANDS

at the University of Florida
Gainesville Florida 32610

Patient Name: MR#:

Physician's Orders

Date/Time		Admission Orders: Bone Marrow Transplant (Page 2 of 3)
		(All orders with a □ must be checked to be activated)
		15. For initial fever with neutropenia:
		a. Obtain urinalysis and urine cultures
		b. Obtain 2 sets of blood cultures
		c. CXR to evaluate for infiltrate; if after 1700, obtain CXR the following AM.
		16. All patients on antibiotics who continue to be febrile (Temp ≥ 38.5): Obtain 1 set of bacterial blood
		Cultures from CVL daily (every 24 hours). Day starts at 2400.
		17. GERD prophylaxis (choose one): □ Axid _____mg PO BID □ Protonix 40mg PO QD
		18. Electrolyte Bolus Orders: **only if plasma creatinine < 2.0**; if ≥ 2.0, call HO for orders.
		a. For corrected Ca ≤ 8.0, give 4 gms Ca Gluconate IV in 100cc D_5W or NS over 2 hours.
		b. For Magnesium level: Recheck plasma Mg within one hour completing IV boluses.
		• 1.5 – 1.7, give MagTab SR 2 tablets po with next dose of oral meds, if pt able to tolerate.
		If unable to tolerate, give 4 gms $MgSO_4$ IV in 100cc D_5W or NS over 2 hours.
		• 1.1 – 1.4, give 4 gms $MgSO_4$ IV in 100cc D_5W or NS over 2 hours.
		• <1.1, give 8 gms $MgSO_4$ IV in 100cc D_5W or NS over 4 hours.
		c. For Potassium Level: **Recheck** plasma K within one hour of completing IV boluses.
		• 3.0 – 3.2, give 40 mEq KCl PO with next dose of oral meds, if pt able to tolerate.
		If unable to tolerate, give 40 mEq KCl IV in 100cc D_5W or NS over 2 hours.
		• 2.7 – 2.9, give 40 mEq KCl IV in 100cc D_5W or NS over 2 hours. .
		• < 2.7, give 80 mEq KCl IV in 100cc D_5W or NS over 4 hours.
		d. For inorganic phosphorus level < 2.5, give sodium phosphate 15 mmol IV over 4 – 6 hours, unless
		Na > 140. If Na > 140, call HO with low phosphorus level.
		(continued on next page)

SHANDS

at the University of Florida
Gainesville, Florida 32610

Patient Name: MR#:

Physician's Orders

		Admission Orders: Bone Marrow Transplant (*Page 3 of 3*)
		(All orders with a □ must be checked to be activated)
		19. Prophylactic antimicrobials beginning (circle one): day 0 (date _____)/ANC < 500
		Adult Autologous □ Gatifloxacin 400mg po QD □ Fluconazole 100 mg po QD □ Valtrex 500 mg po QD (if HSV +) □ _____ □ _____ Adult Allogeneic □ Gatifloxacin 400mg po QD □ Fluconazole 200 mg po QD □ Valtrex 500 mg po QD (if HSV +) □ _____ □ _____
		Adult Chemo Only □ Gatifloxacin 400mg po QD □ Fluconazole 100 mg po QD □ Valtrex 500 mg po QD (if HSV +) □ _____ □ _____ Adult Chemomobilization □ Gatifloxacin 400mg po QD **(to start day 6: date _____)** □ _____ □ _____
		20. Surveillance Cultures a. Allogeneic, MUD, Cord Blood, & Mismatched: Weekly CMV antigen every Monday beginning day +17 or ANC >500, through day +100 or until off GVHD therapy. b. Chronic GVHD: Weekly CMV antigen every Monday. Start when GVHD treatment starts and continue until off therapy. c. If pt has a positive blood culture, please send daily blood cultures (one set) with AM labs until cultures are negative x 3 consecutive days
		MD Signature_____ MD # _____ Beeper # _____
		Orders transcribed by_____ Date/Time _____
		Orders verified by _____ Date/Time _____

GROWTH FACTORS

Growth Factors – Guidelines for ADULTS		
Transplant Type	**Mobilization**	**Post-Infusion***
Autologous – Bone Marrow	N/A	GCSF - Start day +6 unless specified otherwise by protocol. Discontinue when the ANC is > 500/mm^3 x 3 days and increasing or > 1500 x 1 (whichever is sooner)
Autologous – PBSC	GCSF	GCSF - Start day +6 unless specified otherwise by protocol. Discontinue when the ANC is > 500/mm^3 x 3 days and increasing or > 1500 x 1 (whichever is sooner)
Allogeneic – Bone Marrow	-	No Growth Factor
Allogeneic – PBSC	GCSF	No Growth Factor
Matched Unrelated Donor – PBSC and BM	-	No Growth Factor
Umbilical Cord Blood	-	GCSF – Start Day +6 unless specified otherwise by protocol. If delayed engraftment (defined as > 30 days), then may increase growth factors to 5mcg/kg SQ BID.

* If $CD34^+$ counts > 4.5 x 10^6/kg, do not give post-infusion growth factors to minimize risk of engraftment syndrome.

Peripheral Stem Cell Mobilization: (G-CSF only)

Autologous:

1. Mobilization with G-CSF only:
   G-CSF 10 mcg/kg subcutaneous QD. First leukapheresis on Day +5
2. Mobilization with Chemotherapy + G-CSF [chemotherapy to be dosed on IBW, unless TBW is < IBW, then use TBW]:
   a. If using salvage disease-specific regimen: Last dose of induction chemotherapy and then G-CSF 5 mcg/kg IBW (if patient is coming to the clinic daily, please prescribe exact doses, if patient having doses at home, round to nearest vial/syringe size) SQ starting Day +4 after chemotherapy. First leukapheresis between day 10 - 14 post chemotherapy.
   b. Cyclophosphamide (Cytoxan®) 4 g/m^2 day 1 and Etoposide 200 mg/m^2 IV QD days 1-3 and then G-CSF 5 mcg/kg IBW SQ starting Day +4 (first day of chemotherapy is day 1). First leukapheresis between day 10-14 post chemotherapy. Reference: FHCRC and Searle Protocol (since closed)
   c. Cytoxan 2 g/m^2 IV (when WBC > 1.0/mm^3). Give as outpatient therapy with hydration, followed with G-CSF as above in (b). Recommended IV hydration: NS + 20mEq KCL/L @ 250 ml/hr for 2 hours before and 8 hours after. Give mesna 500mg/m^2 IV, 30 minutes before Cytoxan and then 3 and 6 hours after Cytoxan.

NOTES:

1. When the patient's WBC is $\geq$ 1000, the patient will report to the outpatient clinic the following day and daily thereafter for laboratory draws or apheresis procedures. Labs will be sent for WBC and $CD34^+$ flow analysis.

2. Apheresis will usually begin when the peripheral blood $CD34^+$ absolute number is > 5 cells/ul and the WBC is greater than $1000/mm^3$.

3. Begin Gatifloxacin 400mg PO QD on day 4 and continue through day 14 or recovery of ANC whichever comes first.

Allogeneic:

1. Mobilization with G-CSF
   G-CSF 10 mcg/kg (IBW) subcutaneously QD. First leukapheresis on Day +5

Timing of Stem Cell Collection by Apheresis after GCSF Administration:

Recent studies demonstrate that the yield of $CD34^+$ cells after GCSF administration peaks at 18 hours. Growth factor doses should be administered 12 – 16 hours prior to apheresis.

Scheduling of BID growth factors:

Patients who are scheduled to receive BID growth factors, do not need to return to the clinic exactly 12 hours after the first injection. The second daily dose can be administered early, to facilitate early discharge if this is more convenient for the patient and the inpatient staffing load. However, on the day prior to apheresis the second daily dose of growth factor must be scheduled 12 – 16 hours prior to apheresis to maximize yield.

CONSIDERATIONS FOR "HARD TO MOBILIZE" PATIENTS

I. Definition:

A. General: A patient who, after repeated apheresis (3-4), does not reach an ideal cell dose of $\geq 5 \times 10^6$ CD 34^+ cells/kg ideal body weight (IBW).

B. Practical: A patient who, after 2 large volume apheresis procedures does not achieve $\geq 1 \times 10^6$ CD 34^+ cells/kg IBW. Stop at this point and implement another mobilization strategy. Situations where continuation of apheresis can be considered despite a low yield include when collecting backup marrow, and in those patients where the $CD34^+$ counts are still rising.

II. Guidance for Adequate Cell Dose:

1. A dose of $< 1 \times 10^6$ $CD34^+$ cells/kg is not adequate for transplantation unless CFU-GM $\geq 1 \times 10^5$/kg.

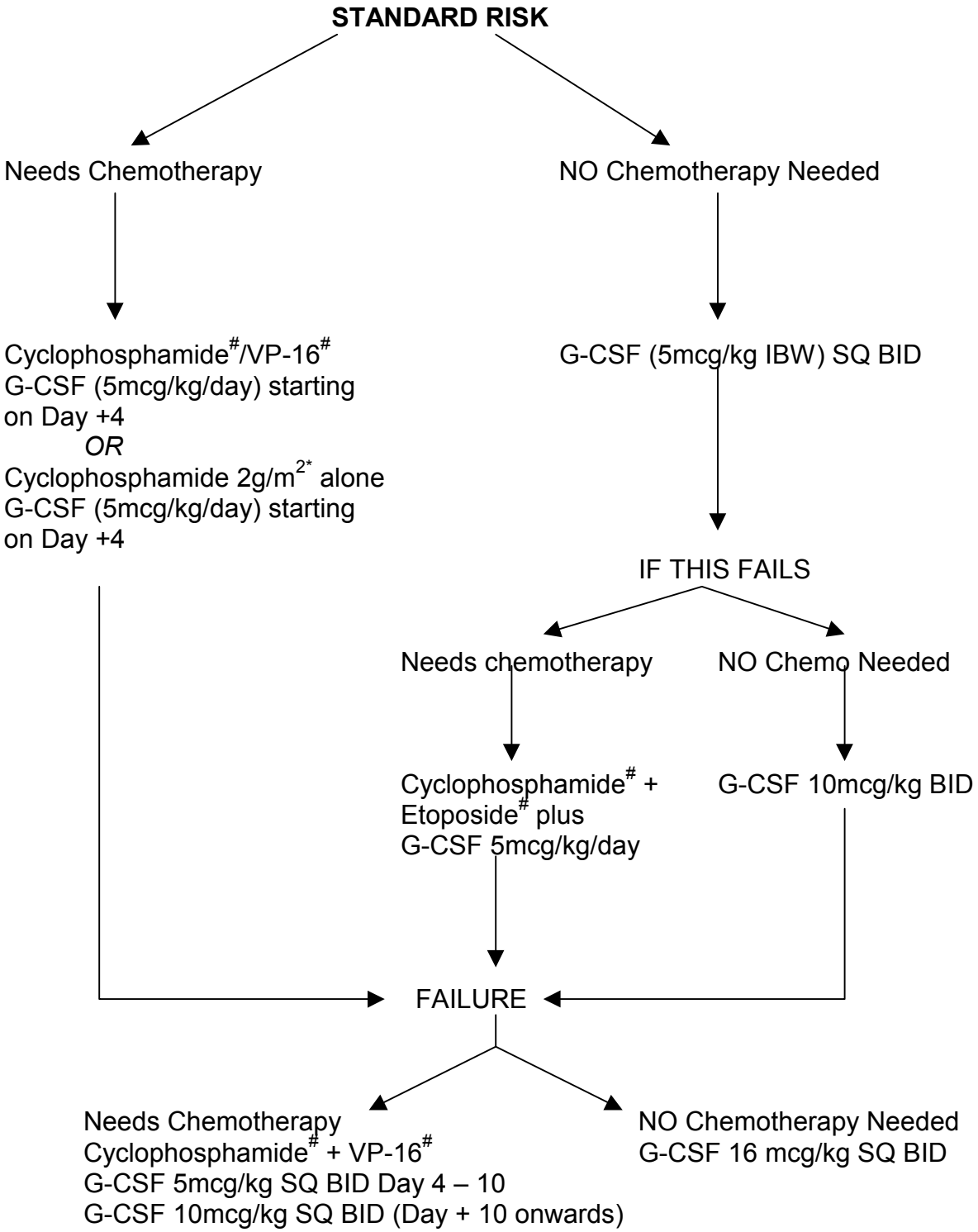
2. A dose of $\geq 1 \times 10^6$ $CD34^+$ cells/kg IBW (all doses on the lesser of IBW or actual body weight) is acceptable for transplantation. Delayed platelet recovery may occur.

3. In order to shorten time to platelet engraftment and reduce platelet transfusions, a dose of $\geq 5 \times 10^6$/kg IBW is preferred.

III. High Risk Patients for Mobilization:

1. > 3 prior therapies OR
2. Prior radiation therapy OR
3. $\geq$ 6 months alkylating agents
4. Bone marrow involvement with disease, older age, prior fludarabine, prolonged prior chemotherapy, and cytokine only mobilization

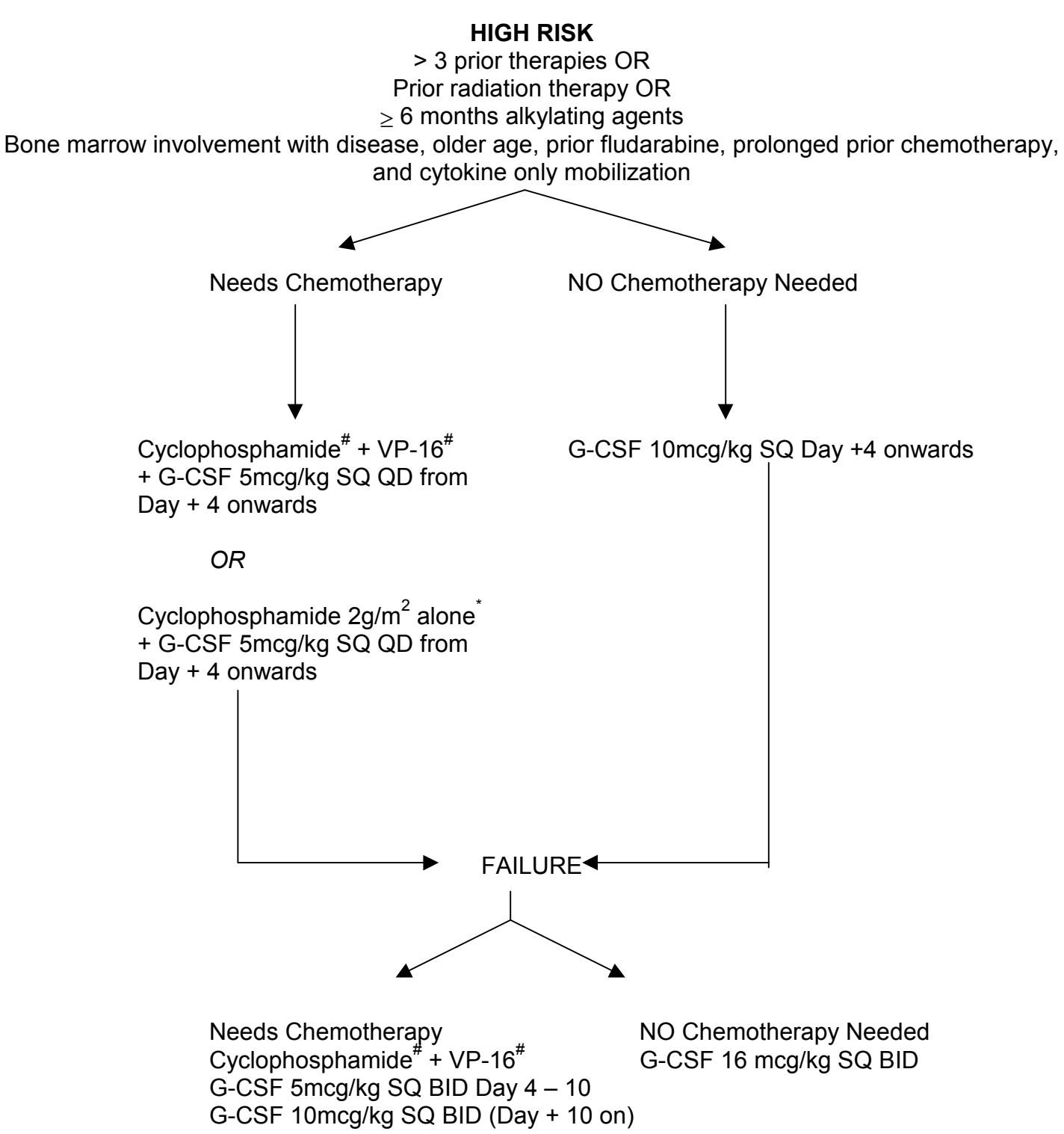
AUTOLOGOUS STEM CELL MOBILIZATION
INITIAL MOBILIZATION



Doses: Cyclophosphamide 4g/m^2 IV Day 1; Etoposide 200mg/m^2 IV Day 1 – 3.

* Typical dose is 2g/m^2, but doses may be increased to 4g/m^2 in non-elderly patients who require continued antitumor effect

AUTOLOGOUS STEM CELL MOBILIZATION
INITIAL MOBILIZATION



Doses: Cyclophosphamide 4g/m^2 IV Day 1; Etoposide 200mg/m2 IV Day 1 – 3.
* Typical dose is 2g/m^2, but doses may be increased to 4g/m^2 in non-elderly patients who require continued antitumor effect

CALCIUM REPLACEMENT PROTOCOL - PBSC COLLECTIONS

Rationale:
Anticoagulation of whole blood for the collection of cellular components is an essential element in any procedure using blood cell separation devices. The most commonly used method is extracorporeal anticoagulation using citrate, which interferes with the clotting cascade by binding with ionized calcium. As the citrate molecules bind the ionized calcium in the blood, hypocalcemia occurs. As a result, patients undergoing large volume Peripheral Blood Stem Cell Collections (PBSCC) may require calcium replacement.

I. Considerations pre-collection:

A. Advise patients to take Tums® 3 tabs PO QID prior to procedure
(Pediatric Dosing: 45-65 mg/kg/day divided QID; Tums® = 500mg/tab and
Tums EX® = 750mg/tab)

B. Draw pre-collection ionized calcium

II. Criteria for a Calcium Drip during PBSC Collections:

A. Patients chemotherapy-mobilized within two weeks of PBSC collection or whose counts are beginning to nadir. These patients often have abnormal electrolytes, secondary to chemotherapy treatment, and may have difficulty tolerating the citrate used for anticoagulation.

B. Patients undergoing large volume PBSC collections.

C. Any patient experiencing difficulty tolerating the anticoagulant, during the procedure, despite appropriate measures to manage side effects.

II. Guidelines for Administration of Calcium Gluconate:

A. If a patient is experiencing citrate sensitivity (e.g. perioral or acral paresthesia), increase the Inlet: AC Ratio or decrease the Inlet flow rate.
- If symptoms subside, continue with procedure.
- If symptoms persist, repeat ionized calcium and give calcium gluconate as follows:
  Ionized Ca^{++} 1.00 to 1.05, infuse 2 grams (50 mg/kg for Pediatrics) Ca Gluconate
  Ionized Ca^{++} 0.75 to 1.00, infuse 4 grams (100 mg/kg for Pediatrics) Ca Gluconate
  Ionized Ca^{++} < 0.75, page attending physician

B. All drips must be hung by a RN and recorded on the PBSC flowsheet.

C. All drips must be run on an infusion pump. All continuous calcium drips must be run into a separate IV. DO NOT PIGGYBACK INTO THE RETURN LINE.

D. The infusion rate for the calcium drip will vary with the flow rate of the procedure. The initial infusion rate should be at least 50 ml/hr. The rate may be increased if the patient becomes/remains symptomatic.

BMT CONDITIONING REGIMENS

IRB 102-00 CYCLOPHOSPHAMIDE (AUTOIMMUNE)

Day –6, -5	Cyclophosphamide 60mg/kg IV QD
Day –6, -5, -4	ATGAM 30mg/kg IV qd OR thymoglobulin 3mg/kg IV QD
Day –6, -5, -4	Methylprednisolone 500mg IV QD

IRB 141-96 CYCLOPHOSPHAMIDE/TBI OR BUSULFAN/CYCLOPHOSPHAMIDE OR BUSULFAN/CYCLOPHOSPHAMIDE/ATGAM

Days –6 and –5	Cyclophosphamide 60mg/kg IV QD
Days –4 to –1	TBI BID
Day 0	TBI QD
	OR
Days –9 to –6	Busulfan 0.75mg/kg/dose PO q6 x 16 doses
Days –5, -4, -3	Cyclophosphamide 50mg/kg IV QD
Days –4, -3, –2	ATGAM 30mg/kg IV QD
	OR
Day –6 to –3	Cyclophosphamide 10mg/kg IV QD
Day –6 to –2	ATGAM 12.5mg/kg IV QD
Day –1	Total Body Irradiation 500 rads

IRB 213-94 CYCLOPHOSPHAMIDE/THIOTEPA/CARBOPLATIN

Days –7 to –4	Cyclophosphamide 750mg/m^2 IV q12 CIVI x 8 doses
Days –7 to –4	Thiotepa 62.5mg/m^2 IV q12 CIVI x 8 doses
Days –7 to –4	Carboplatin 100mg/m^2 IV q12 CIVI x 8 doses

NOTE: doses administered as a continuous infusion.

IRB 252-00 CYCLOPHOSPHAMIDE WITH NO STEM CELL RESCUE

Day 1, 2, 3, 4	Cyclophosphamide 50mg/kg IV QD
Day 10	Filgrastim 5mcg/kg SQ QD

IRB 257-97 MULTIPLE CONDITIONING REGIMENS

(A) TBI + MELPHALAN + ATG

Day –9 to –5	TBI 1350 cGy in 9 fractions of 1.5 Gy
Day –4 to –2	Melphalan 45mg/m^2 IV QD
Day –3 to –1	ATGAM 30mg/kg IV QD

(B) BUSULFAN + MELPHALAN + ATG

Day –8 to –5	Busulfan x 16 doses (dosing based on patients age – see protocol)
Day –4 to –2	Melphalan 45mg/m^2 IV QD
Day –3 to –1	ATGAM 30mg/kg IV QD

(C) BUSULFAN + CYCLOPHOSPHAMIDE + ATGAM – WISCOTT ALDRICH SYNDROME, OSTEOPETROSIS, WHITE CELL DISORDERS, INBORN ERRORS OF METABOLISM OR INHERITED HEMATOPOIETIC DISORDERS

Day –9 to –6 Busulfan x 16 doses (dosing based on patients age – see protocol)
Day –5 to –2 Cyclophosphamide 50mg/kg IV QD
Day –3 to –1 ATGAM 30mg/kg IV QD

(D) BUSULFAN+ CYCLOPHOSPHAMIDE + ATGAM – SCID PATIENTS

Day –7 to –4 Busulfan x 16 doses (dosing based on patients age – see protocol)
Day –3 to –2 Cyclophosphamide 50mg/kg IV QD
Day –3 to –1 ATGAM 30mg/kg IV QD

(E) CYCLOPHOSPHAMIDE + ATGAM + TLI – APLASTIC ANEMIA, BM FAILURE, MDS

Day – 5 to –2Cyclophosphamide 50mg/kg IV QD
Day –4 to –2 ATGAM 30mg/kg IV QD
Day –1 TLI 750 rads

(F) CYCLOPHOSPHAMIDE + ATGAM + THORACOABDOMINAL RADIATION – FANCONI'S ANEMIA PATIENTS

Day –6 to –3 Cyclophosphamide 10mg/kg IV QD
Day –6 to –3 ATGAM 12.5mg/kg IV QD
Day –1 Thoracoabdominal irradiation 500 rads

(G) FLUDARABINE + MELPHALAN + ATGAM – REJECTED CORD AND BEING RETRANSPLANTED

Day –9 to –5 Fludarabine 25mg/m^2 IV QD
Day –4 to –2 Melphalan 45mg/m^2 IV QD
Day –3 to –1 ATGAM 30mg/kg IV QD

(H) CYCLOPHOSPHAMIDE + ATG – PATIENTS WHO FAIL TO ENGRAFT FOLLOWING INITIAL TRANSPLANT

Day –3 and –2 Cyclophosphamide 30mg/kg IV QD
Day –3 to –1 ATGAM 30mg/kg IV QD
Day +2, +5 ATGAM 10mg/kg IV QD

IRB 281-00 MINI-ALLOGENEIC TRANSPLANTATION

Version 1: If backup marrow: Fludarabine/ATGAM/Busulfan

Days –7 to –2 Fludarabine 30mg/m^2 IV QD
Days –6 to –3 ATGAM 10mg/kg IV QD
Days –4 and –3 Busulfan 1mg/kg/dose PO Q6H

Version 2: If no backup marrow: Fludarabine/TBI

Day –4, -3, -2 Fludarabine 30mg/m^2 IV QD
Day 0 Total Body Irradiation 200cGy

IRB 281-02 [COG A5962] Note: has a special dosing weight requirement.

Day –9 to -2	Methylprednisolone 0.25mg/kg IV Q6H
Day –8 to –6	Carmustine 100mg/m^2/day IV over 3 hours QD [total dose 300mg/m^2]
Day –8 to –6	Etoposide 800mg/m^2/day CIVI QD [total dose 2400mg/m^2 over 72 hours]
Day –5 to –2	Cyclophosphamide 1500mg/m^2/day IV over 1 hour QD
Day –5 to –2	Mesna 20mg/kg over 15 minutes pre each Cytoxan® then at 3, 6, 9, and 12 hours after start of Cytoxan®
Day –1	Begin MP taper (refer to protocol)
Day 0	PBSC infusion; Begin G-CSF 5mcg/kg 2 hours after last PBSC infusion [continue until ANC > 2000/μL for 3 days]

IRB 304-99 [POG 9407]

Day –8	Ara-C 100mg/kg/dose IV x 1 [administer at 8pm]
Day –7	Ara-C 100mg/kg/dose IV Q12H [8am and 8pm] Cyclophosphamide 45mg/kg/dose IV [at 2pm]
Day –6	Ara-C 100mg/kg/dose Q12H IV [8am and 8pm] Cyclophosphamide 45mg/kg/dose IV [at 2pm]
Day –5	Ara-C 100mg/kg/dose IV x 1 [at 8am]
Day –4	Rest [begin IVIG]
Day –3	TBI#
Day –2	TBI# Methylprednisolone 33mg/kg IV QD [administer at midnight]
Day –1	TBI# Methylprednisolone 33mg/kg IV BID [administer at noon and midnight]
Day 0	TBI# Methylprednisolone 33mg/kg IV x 1 dose [administer at noon] *plus* Methylprednisolone 6.6mg/kg IV 90 minutes prior to marrow infusion and 3.3mg/kg IV 8 and 16 hours after marrow infusion, then discontinue.

#TBI 1200 cGy administered in 8 fractions over 4 days

IRB 311-02 [COBLT PROTOCOL]

A. FOR PATIENTS WITH MALIGNANT DISEASE OR SEVERE APLASTIC ANEMIA

Day –8	TBI 150 cGy x 1
Day –7 to –4	TBI 150cGy x 2
Day –3, -2	Cyclophosphamide 60mg/kg/day IV QD
Day –3 to –1	Methylprednisolone 2 – 2.5mg/kg/day IV (in ddd) = premed for ATG
Day –3 to –1	Antithymocyte globulin (HORSE) 15mg/kg IV BID (total 30mg/kg/day)
Day 0	Methylprednisolone 2mg/kg/day in ddd, with 1mg/kg IV given prior to stem cell infusion Cord transplant

NOTE: If ATGAM (Horse) is not tolerated, thymoglobulin at a dose of 3mg/kg/day can be substituted. If neither form is tolerated, substitute methylprednsiolone (MP) at a dose of 1g/m^2/day (ddd).

B. FOR PATIENTS WITH FANCONI'S ANEMIA

Day –6	TBI 450 cGy
Day –5 to –2	Cyclophosphamide 10mg/kg/day IV
Day –5 to –2	Fludarabine 35mg/m^2/day IV
Day –5 to –1	Antithymocyte globulin (horse) 30mg/kg/day IV
Day –5 to –1	Methylprednisolone 2mg/kg/day IV
Day 0	Cord blood transplant
Day +1	Filgrastim 5mcg/kg/day IV until ANC $\geq$ 2.5 x 10^9/L

C. INBORN ERRORS OF METABOLISM

Day –9 to –6	Busulfan (IV or oral – note dosing differences between products). Refer to protocol for doses
Day –5 to –2	Cyclophosphamide 50mg/kg/day IV
Day –3 to -1	Methylprednisolone 2 – 2.5 mg/kg/day (in divided doses) IV
Day –3 to –1	Antithymocyte globulin (Horse) 30mg/kg/day IV
Day 0	Antithymocyte globulin 2mg/kg/day (in divided doses with 1mg/kg of the total dose given just prior to infusion) Cord transplant

D. NON-MALIGNANT DISEASES

Day –9 to –6	Busulfan (IV or oral – note dosing differences between these products, refer to protocol for doses
Day –5 to –2	Cyclophosphamide 50mg/kg/day IV
Day –3 to –1	Methylprednisolone 2 – 2.5 mg/kg/day (in divided doses) IV
Day –3 to –1	Antithymocyte globulin (Horse) 30mg/kg/day IV
Day 0	Antithymocyte globulin 2mg/kg/day (in divided doses with 1mg/kg of the total dose given just prior to infusion) Cord transplant

E. NON-TBI CONTAINING REGIMEN FOR PATIENTS WITH MALIGNANT DISEASE

Day –8 to –5	Busulfan (IV or PO – note differences in dosing between products)
Day –4 to –2	Melphalan 45mg/m^2/day IV
Day –3 to –1	Methylprednisolone 2 – 2.5mg/kg/day IV (ddd)
Day –3 to –1	Antithymocyte globulin 30mg/kg/day IV QD
Day 0	Methylprednisolone 2mg/kg IV in divided doses with 1mg/kg of the total given just prior to infusion Cord transplant

IRB 469-96 BUSULFAN/ETOPOSIDE/CYCLOPHOSPHAMIDE

Days –8 thru –5	Busulfan 0.75mg/kg/dose PO Q6H
Days –4, -3, -2	Etoposide 10mg/kg IV QD*
Days –3, -2	Cyclophosphamide 60mg/kg IV QD**

* Etoposide omitted from preparative regimens in those patients' $\geq$ 65 years.

** Mesna added with h/o pelvic XRT, etc.

IRB 482-01 [COG A3973]

Day –7, -6, -5, -4	Carboplatin 425mg/m^2/d (14.2mg/kg if $\leq$ 12kg) as a CIVI (24 hour)
Day –7, -6, -5, -4	Etoposide 338mg/m^2/d (11.3mg/kg if $\leq$ 12kg) as a CIVI (24 hour)
Day –5, -6, -5	Melphalan 70mg/m^2/d (2.3mg/kg if $\leq$ 12kg) IV bolus
Day –3 to –1	Rest
Day 0	Stem cells, start G-CSF 4 hours post cells at 5mcg/kg/day IV over 2 hrs

NOTE: IF patients creatinine clearance is < 100mL/min/1.73m^2, please refer to main protocol for dosage modification.

IRB 499-00 IV BUSULFAN

Multiple cohorts and schedules, refer to protocol

IRB 522-97 THIOTEPA/CYCLOPHOSPHAMIDE/ATGAM

Day –6 only	Thiotepa 5mg/kg IV x 1 dose
Days –5, -4	Cyclophosphamide 60mg/kg IV QD
Days –4 and –2	ATGAM 15mg/kg IV QD

IRB 533-97 BUSULFAN/CYCLOPHOSPHAMIDE/ATGAM

Day –9 to –6	Busulfan 1mg/kg Q6H
Day –5 to –2	Cyclophosphamide 50mg/kg IV QD
Day –4 to –2	ATGAM 30mg/kg IV QD

IRB 544-00 MELPHALAN (HALIFAX PROTOCOL)

Day –2	Melphalan 100mg/m^2 IV x 1
Day 0	Stem cell infusion

Patients will have 2 cycles of melphalan 100mg/m^2 administered followed by stem cell rescue.

IRB 589-95 BUSULFAN/CYCLOPHOSPHAMIDE (CLOSED 2001 – SEE TREATMENT PLAN 123)

Day –9 to –6	Busulfan 1mg/kg q6h PO x 16 doses (total dose 16mg/kg)
Day –5, -4, -3, -2	Cyclophosphamide 50mg/kg IV QD

IRB 589-94 CYTOXAN ALONE VERSUS CYTOXAN/ATG (APLASTIC ANEMIA IBMTR RANDOMIZED PROTOCOL) – CLOSED 2002 – see treatment plan 121

<u>Cyclophosphamide alone:</u>

Day –5 to –2 Cyclophosphamide 50mg/kg IV QD

Mesna 5mg/kg IV, 30 minutes pre cyclophosphamide then IV Q4H ATC until 24 hours post cyclophosphamide

Cyclophosphamide plus ATG:

Day –5 to –2	Cyclophosphamide 50mg/kg IV QD
	Mesna IV as above
Day –5, -4, -3	ATGAM 30mg/kg IV QD

IRB 660-00 (TANDEM TRANSPLANT – MULTIPLE MYELOMA)

Transplant 1:

Day –8 to –5	Busulfan 0.75mg/kg PO Q6H x 16 doses (12mg/kg total dose)
Day –4, -3, -2	Etoposide 10mg/kg IV QD
Day –3, -2	Cyclophosphamide 60mg/kg IV QD

Transplant 2:

Day –7 to –4	Cyclophosphamide 1500 mg/m^2/day CIVI
Day –2, -1	Total Body Irradiation (150 rads BID on Day –2 and –1 = total 600 rads)

If patient unable to tolerate TBI due to previous radiation therapy, then Melphalan will be substituted at a dose of 140mg/m^2 on Day –2.

SICKLE CELL ANEMIA PROTOCOL [IRB NUMBER NOT ALLOCATED AT TIME OF PRESS]

Day –4, -3, -2	Fludarabine 30mg/m^2 IV QD
Day 0	TBI 200 cGy

NOTE: this protocol has specific mandates about GVHD – different to SCG see protocol.

IRB NUMBER NOT ALLOCATED AT TIME OF PRINTING [AAML0122]

Day –7	TBI [150 cGy BID]
Day –6	TBI [150 cGy BID]
Day –5	TBI [150 cGy BID]
Day –4	TBI [150 cGy BID]
Day –3	Cyclophosphamide 60mg/kg/day
	ATGAM (horse) 15mg/kg IV Q12H*
	Methylprednisolone 1mg/kg IV Q12H [premedication]
Day –2	Cyclophosphamide 60mg/kg/day IV
	ATGAM (horse) 15mg/kg IV Q12H*
	Methylprednisolone 1mg/kg IV Q12H [premedication]
Day –1	ATGAM (horse) 15mg/kg IV Q12H*
	Methylprednisolone 1mg/kg IV Q12H [premedication]

* ATG may be deleted if donor is HLA-genotype-identical

TREATMENT PLANS

TREATMENT PLAN 101 CYCLOPHOSPHAMIDE/CARBOPLATIN/MITOXANTRONE

Day –8 to –5	Carboplatin 375mg/m^2/day CIVI
Day –8 to –5	Cyclophosphamide 30mg/kg/day CIVI
Day –8 to –5	Mitoxantrone 18.75mg/m^2/day IV

TREATMENT PLAN 102 MELPHALAN/MITOXANTRONE

Day –5 and –4	Melphalan 70mg/m^2/day IV
Day –5 and –4	Mitoxantrone 22.5mg/m^2/day IV

TREATMENT PLAN 103 (IRB 545-95) CARBOPLATIN/ETOPOSIDE/CYCLOPHOSPHAMIDE

Day –5 to –3	Carboplatin 600mg/m^2 IV QD
Day –5 to –3	Etoposide 600mg/m^2 IV QD
Day –5 to –3	Cyclophosphamide 50mg/kg IV QD

TREATMENT PLAN 104 ETOPOSIDE/CARBOPLATIN/CYCLOPHOSPHAMIDE/MESNA

Day –6, -5, -4	Etoposide 800mg/m^2/day CIVI
Day –6, -5, -4	Carboplatin 667mg/m^2/day IV
Day –3, -2	Cyclophosphamide 60mg/kg/day IV
Day –3, -2	Mesna 12mg/kg IV at time 0, 3 and 6 hours
Day +3	Filgrastim 10mcg/kg/day IV/SQ until ANC > 1000 x 2 days

TREATMENT PLAN 105 (IRB 244-94) ETOPOSIDE/TBI

Days –6 to –4	TBI TID (150 cGy/fraction x 9 fractions)
Day –3	Etoposide 60mg/kg IV

TREATMENT PLAN 106 (064-94) TBI/ETOPOSIDE/CYCLOPHOSPHAMIDE - CLOSED

Day –8 to –6	TBI 150 cGy/fraction TID (total 9 fractions)
Day –5 to –2	Etoposide 250mg/m^2 IV CIVI Q12H (administer each dose over 11 hr)
Day –5 to –2	Cyclophosphamide 500mg/m^2 IV BID (administer over 1 hours)

TREATMENT PLAN 107 (IRB 059-95) BUSULFAN/CYCLOPHOSPHAMIDE [ADULTS ONLY, SEE TREATMENT PLAN 124 FOR PEDIATRICS]

Day –7 to –4	Busulfan 0.75mg/kg PO Q6H x 16 doses (total dose 12mg/kg)
Day –3, -2	Cyclophosphamide 60mg/kg/day IV QD

TREATMENT PLAN 108 CYCLOPHOSPHAMIDE/THIOTEPA/CARBOPLATIN

Day –7 to –4	Cyclophosphamide 1500mg/m^2/day CIVI
Day –7 to –4	Thiotepa 125mg/m^2/day CIVI
Day –7 to –4	Carboplatin 200mg/m^2/day CIVI

TREATMENT PLAN 109 (IRB 92-94) CYTARABINE/CYCLOPHOSPHAMIDE

Days –9 to –5	Cytarabine 100mg/m^2 IV QD CI
Days –4 and –3	Cyclophosphamide 60mg/kg IV QD
Day 0	Total Body Irradiation 550 rads in AM

NOTE: if the patient has CML and has not had a splenectomy, the patient will received splenic irradiation at a cumulative dose of 500 rads to be delivered in 100 rad fractions over 5 days preceding TBI.

TREATMENT PLAN 111 CYCLOPHOSPHAMIDE/THIOTEPA/CARBOPLATIN/MESNA

Day –7 to –3	Cyclophosphamide 1500mg/m^2/day CIVI
Day –7 to –3	Thiotepa 125mg/m^2/day CIVI
Day –7 to –3	Carboplatin 200mg/m^2/day CIVI
Day –7 to –2	Mesna 1500mg/m^2/day CIVI
Day 0 – 4	GM-CSF 250mcg/m^2 SQ QD
Day +5 onwards	G-CSF 5mcg/kg SQ QD (until ANC > 1500 x 2 days)

TREATMENT PLAN 112 BUSULFAN/MELPHALAN (HEMATOLOGICAL MALIGNANCIES)

Day –6 to –3	Busulfan 0.75mg/kg PO Q6H x 16 doses (total dose = 12mg)
Day –2	Melphalan 140mg/m^2 IV

TREATMENT PLAN 114 CYCLOPHOSPHAMIDE (NON-TRANSPLANT)

Day 1 – 4	Cyclophosphamide 50mg/kg IV QD
Day 10	Filgrastim 5mcg/kg SQ QD

TREATMENT PLAN 117 MELPHALAN (AMYLOIDOSIS) – [Ref: *Blood* 1998; 91:3662 – 70]

Day –4, -3	Melphalan 100mg/m^2 IV QD

TREATMENT PLAN 118 CYCLOPHOSPHAMIDE [Reference: *BMT* 1993; 11:459 – 64].

Day –5 to –2	Cyclophosphamide 50mg/kg IV QD

TREATMENT PLAN 119 BUSULFAN/CYCLOPHOSPHAMIDE/ETOPOSIDE

Day –8 to –5	Busulfan 0.75mg/kg PO Q6H (total 16 doses)
Day –4 to –2	Etoposide 10mg/kg IV QD*
Day –3 and –2	Cyclophosphamide 60mg/kg IV QD

* Omit VP-16 in patients $\geq$ 65 years of age

TREATMENT PLAN 120 CISPLATIN/VINCRISTINE/CYCLOPHOSPHAMIDE/MESNA

Day –4	Cisplatin 75mg/m^2 IV x 1 dose
Day –4	Vincristine 1.5mg/m^2 IV x 1 dose
Day –3 and –2	Cyclophosphamide 2000mg/m^2 IV QD
Day –3 to –1	Mesna 2000mg/m^2 CIVI QD
Day +1	Filgrastim
Day +6	Vincristine 1.5mg/m^2 IV x 1 dose

TREATMENT PLAN 121 CYCLOPHOSPHAMIDE

Day –5 to –2	Cyclophosphamide 50mg/kg IV QD

TREATMENT PLAN 122 CYCLOPHOSPHAMIDE/ETOPOSIDE/MESNA/TBI

Day –5 and –4	Cyclophosphamide 1800mg/m^2 IV QD
Day –5 and –4	Etoposide 900mg/m^2 IV QD
Day –5 and –4	Mesna 360mg/m^2 IV at time 0, 3, 6, and 9 hours
Day –3 to –1	TBI 200 cGy per fraction BID

TREATMENT PLAN 123 BUSULFAN/CYCLOPHOSPHAMIDE [ADULTS > 12 YEARS]

Day –9 to –6	Busulfan 1mg/kg q6h PO x 16 doses (total dose 16mg/kg)
Day –5, -4, -3, -2	Cyclophosphamide 50mg/kg IV QD

TREATMENT PLAN 124 [PEDIATRIC PATIENTS ≤ 12 YEARS]

Day –9 to –5	Busulfan (refer to treatment plan for dose and dose form i.e., IV vs. PO)
Day –5 to –2	Cyclophosphamide 50mg/kg IV QD

TREATMENT PLAN 125 [PEDIATRIC PATIENTS ≤ 21 YEARS]

Day –6 to –4	Etoposide 800mg/m^2 QD CIVI [total dose 2400mg/m^2]
Day –6 to –4	Carboplatin 667mg/m^2/day IV over 1 hour QD
Day –3 and –2	Cyclophosphamide 1800mg/m^2/day IV QD
Day +5 onwards	Filgrastim 5mcg/kg SQ/IV until ANC > 2000

MOBILIZATION ORDERS

Day 1	Cyclophosphamide 4000mg/m^2 IV
Day 1, 2, and 3	Etoposide 200mg/m^2 IV QD
Day 4	Filgrastim 5mcg/kg SQ QD

Day 1	Cyclophosphamide 2g/m^2 IV
Day 2	Filgrastim 5mcg/kg SQ QD

WEIGHT ISSUES – DRY WEIGHT

Patients are to be weighed within 7 days of admission. A dry weight is to be established on admission, and patients aggressively diuresed with 10 – 40mg furosemide (Lasix) to maintain that dry weight during the conditioning regimen and in the immediate post-transplant period. Fluid balance should be checked every shift and if the patient is greater than their dry weight should be administered Lasix to achieve that dry weight.

PEDIATRICS

NOTE: Dosing of antineoplastic therapy for pediatrics is age and weight dependent. If a patient is < 2 year old and/or weighs 8 – 12kg, dosing should be on a mg/kg basis, NOT a mg/m^2 basis. Refer to a pediatric hematologist/oncologist if protocols not written accordingly. To calculate mg/kg from mg/m^2, divide the mg/m^2 dose by 30.

IRB APPROVED CONDITIONING PROTOCOLS, DISEASE ELIGIBILITY AND STEM CELL SOURCE

IRB Number	Transplant type eligible	Eligible Diseases
102-00	Autologous	Rheumatoid arthritis SLE Systemic Sclerosis
141-96	MUD CORD	Advanced MDS: see protocol for exact inclusion criteria ALL: see protocol for exact inclusion criteria AML: see protocol for exact inclusion criteria Chronic Lymphocytic Leukemia CML CP or AP Hereditary + acquired disorders of hematopoiesis or immunity or inborn errors of metabolism HL, NHL Multiple Myeloma
213-94	Autologous	Breast cancer: Stage II with $\geq$ 7 lymph nodes; Stage III (T3b, T4, N2, or N3, M0) inflammatory breast cancer; Stage IV chemotherapy sensitive breast cancer
257-97	CORD (primarily pediatrics)	ALL AML Aplastic or Fanconi's anemia CML Congenital immune deficiency syndromes Inborn errors of metabolism MDS with adverse risk factors Relapsed, recurrent or high risk solid tumors
281-00	Allogeneic/ MUD	Acute leukemia Advanced malignant melanoma Advanced renal cell carcinoma Aplastic anemia not controlled by immunosuppression CLL CML Lymphoproliferative disorders not eligible for auto BMT MDS Multiple Myeloma
281-02 [COG A5962]	Autologous PBSC	Refractory Hodgkin's and Non Hodgkin's lymphoma
304-99 [POG 9407]	Allogeneic	Children < 1 year with previously untreated ALL or AUL
469-96	Autologous	Chronic Lymphocytic leukemia Lymphoma (HD or NHL) Multiple Myeloma

482-01 [COG A3973]	Autologous	Neuroblastoma [NOTE: 6 cycles of chemotherapy followed by autologous HSCT]
499-00 (IV Busulfan)	Allogeneic Autologous	ALL: see protocol for exact inclusion criteria AML: see protocol for exact inclusion criteria CLL: see protocol for exact inclusion criteria CML in CP, AP, or BC HD or NHL: see protocol for exact inclusion criteria MDS: see protocol for exact inclusion criteria MM: see protocol for exact inclusion criteria
533-97	Allogeneic Haploidentical MUD/ CORD	Severe combined immunodeficiency syndrome: refer to protocol for complete subtype inclusion
544-00 (Halifax)	Autologous	Multiple myeloma
589-95	Autologous	AML – CLOSED see TP 123
660-0	Autologous	Multiple Myeloma
Not IRB approved at time of printing [AAML0122]	Allogeneic	JMML patients

TREATMENT PLANS, DISEASE ELIGIBILITY AND STEM CELL SOURCE

Treatment Plan Number	Eligible Diseases	Transplant type eligible
101	Ovarian cancer	Autologous
103	Germ cell tumors	Autologous
104	Neuroblastoma	Autologous
105	Leukemia Lymphoma Multiple Myeloma	Allogeneic
105A	Leukemia Lymphoma Multiple Myeloma	Autologous
106	Small round cell sarcoma of bone or soft tissue	Autologous (purged) OR Allogeneic
107	AML Hematologic malignancies or disorders in 1st or subsequent remissions, relapse or PRD	Allogeneic
108	Breast cancer	Autologous
109	CML CP or AP MDS	Allogeneic
111	Lymphoma	Autologous
112	Multiple Myeloma	Autologous
114	Autoimmune hematologic disease: AIHA or ITP (see protocol for exact inclusion criteria) Autoimmune neutropenia: Felty's syndrome or disorders of large granular lymphocytes with recurrent infections or an absolute ANC of < 200/mm^3	NON-TRANSPLANT
115	CD 34+ selection protocol, not a conditioning regimen	
116	Granulocyte collection protocol, not a conditioning regimen	
117	Amyloidosis	Autologous
118	Severe aplastic anemia	Allogeneic
119	Lymphoma Multiple myeloma	Autologous
120	Medulloblastoma Supratentorial primitive neuroectodermal tumors (PNET)	Autologous
121	Severe aplastic anemia	Allogeneic
122	PNET Sarcomas	Autologous
123 [ADULTS]	AML	Autologous
124 [PEDIATRICS]	AML	Allogeneic
125	Neroblastoma/Sarcoma	Autologous

PRD = primary refractory disease

CHEMOTHERAPY DILUENT AND RATE GUIDE

Agent	Diluent	Admin Rate	Comments
Asparaginase*	D5W or NS (50ml)	IV over ≥ 30 min	Skin test prior to first dose or if > 1 week between doses (2 units ID). IM too.
Arsenic trioxide	D5W or NS (100-250mL)	IV over 1 – 2 hours	Can administer over 4 hours if acute vasomotor reactions seen. Have antidote avail
Bleomycin*	NS (50ml)	IV over 15 min	Test dose of 1 unit IM or SQ. Wait 1 hr for reaction. Monitor lifetime doses.
Busulfan	D5W or NS (0.5mg/ml)	2hr	Oral form usually used. IV form new.
Carboplatin	D5W preferred or NS (500ml)	30-60 min	Can concentrate if necessary.
Carmustine	D5W or NS (250ml)	2 hr	Irritant. Monitor lifetime doses.
Cisplatin	NS (500ml)	1-2hr *Not IV push*	Hydration/Lasix
Cladribine	NS (500ml)	Varies	Usually given as 7 day CI.
Cyclophosphamide*	D5W or NS (250ml)	1hr but varies	Oral form available
Cytarabine*	D5W or NS (250ml)	2hr-24hr CI	Can be given IV, SQ, IT. For HiDAC-signature sheet and dexamethasone eye drops.
Dacarbazine	D5W or NS (250ml)	30min	Irritant
Dactinomycin*	D5W preferred	IV Push 15min	Vesicant
Daunorubicin*	D5W or NS (100ml)	30min but varies IV push to CI	Vesicant. Monitor lifetime doses.
Docetaxel	D5W or NS (250ml)	1hr	Premeds
Doxorubicin*	NS (100ml)	30min but varies IV push or CI	Vesicant. Mix with vincristine in VAD regimen. Monitor lifetime doses.
Etoposide	D5W or NS (500ml)	At least 1hr	Oral form available
Fludarabine*	D5W or NS (100ml)	30min	
Fluorouracil*	D5W or NS (CI 1000ml)	Varies IV push to CI	Irritant
Gemcitabine*	NS (100ml)	30min	
Gemtuzumab	NS (100mL)	2 hours	Infusional side effects will occur; premedicate
Idarubicin*	D5W or NS (50ml)	At least 15min	Vesicant
Ifosfamide	D5W or NS (250ml)	1hr	Give MESNA with Ifosfamide
Irinotecan	D5W preferred or NS (500ml)	30-90min	
Mechlorethamine*	D5W or NS	IV push over 3-5 min	Vesicant. Unstable-begins to decompose immediately.
Melphalan	NS (0.1 -0.45mg/ml)	15min	Vesicant. Stable for 1hr. Oral form available.
Methotrexate*	D5W or NS (250ml)	Varies IV push to CI	Can be given IV, IM, IT, PO
Mitomycin*	D5W or NS	IV push	Vesicant. Short inf in 100ml can be done.
Mitoxantrone*	D5W or NS (50ml)	30min	? Vesicant
Paclitaxel	D5W or NS (0.5-1L	3 or 24hr	Premeds
PEG-asparaginase	If IV D5W or NS 100ml	1hr	IM route preferred
Rituximab	D5W or NS (1-4mg/ml)	Begin first infusion at 50mg/hr	Round down to nearest 100mg. Premeds
Teniposide	D5W or NS (100ml)	30min	Irritant
Thiotepa	NS only (for CI 100ml)	IV push or CI	Can be given IT
Topotecan*	D5W pref or NS (50ml)	30min	
Trastuzumab	NS (250ml)	Load 90min, maintenance 30min	Premeds
Vinblastine*	D5W or NS (bolus 100ml or CI 1000ml)	IV push over 1min, 30min bolus, CI	Vesicant
Vincristine*	D5W or NS (for CI)	IV push or CI	Vesicant. Mix with doxorubicin in VAD
Vinorelbine	D5W or NS (50ml)	IV push or 30min inf	Vesicant

Infused vesicants require central venous access; *Agents that may be ordered undiluted and dispensed in a syringe at the Ca Center

ANTIDOTES FOR VESICANT/IRRITANT AGENTS

Drug	Antidote Preparation	Method of Administration
Mechlorethamine Mitomycin	10% sodium thiosulfate: mix 4 ml of 10% sodium thiosulfate with 6 ml of sterile water for injection (1/6 molar solution results).	1. Inject 5-6 ml IV through the existing line* and subcutaneously into the extravasated site with multiple injections. 2. Repeat dosing subcutaneously over the next several hours. 3. Apply <u>cold</u> compresses. 4. No total dose established.
Vinblastine Vincristine Vinorelbine Teniposide Etoposide	Hyaluronidase (Wydase) 150 u/ml: Add 1 ml U.S.P. NaCl (150 u/ml results)[#] **Note**: Corticosteroids and topical cooling appear to worsen toxicity.	1. Inject 1-6 ml subcutaneously into the extravasated site with multiple injections. 2. Repeat dosing subcutaneously over the next several hours. 3. Apply <u>warm</u> compresses. 4. No total dose established.
Daunorubicin Doxorubicin Idarubicin	Topical cooling	1. Cooling of site to patient tolerance for 24 hours. 2. Elevate and rest extremity for 24-48 hours, then resume normal activity as tolerated. 3. If pain, erythema and/or swelling persist beyond 48 hours discuss the need for surgery consult.
Paclitaxel	Topical heating	1. Heating of the site to patient tolerance for 24 hours.

* If unable to aspirate residual agent from the IV tubing DO NOT instill the antidote through the needle.

NOTE: Hyaluronidase is no longer commercially available.

Adapted from Cancer Chemotherapy Guidelines Recommendations for the Management of Extravasation and Anaphylaxis, Oncology Nursing Society, 1988.

PHENYTOIN PROPHYAXIS FOR BUSULFAN CONTAINING PROTOCOLS

ALL patients receiving high dose busulfan containing conditioning regimens should receive phenytoin (Dilantin®) as seizure prophylaxis throughout busulfan therapy (unless the patient is already on anticonvulsant therapy in which case they will continue with their prescribed antiepileptic therapy).

1) Phenytoin load the day prior to initiation of busulfan by one of the following methods:

A) Oral Load (preferred):

Phenytoin 15 - 20 mg/kg (total body weight) as total loading dose. This should be divided into increments of no greater than 400mg administered at 2 hourly intervals (minimum interval) until full dose administered.

B) IV Bolus Load:

Phenytoin 15-20 mg/kg (total body weight) as total load given slowly (Mix in NS only; given over 2-3 hours)

2) Begin maintenance dose of Phenytoin 5 mg/kg/day (total body weight) as a single oral dose within 24 hours of loading dose. For doses > 400mg please fractionate the dose into a BID dosing schedule to maximize absorption.

3) Check phenytoin level at 10am, prior to the second maintenance dose.
   a) If albumin $\geq$ 3, draw total phenytoin level (goal: 10 - 20 mcg/ml)
   b) If albumin < 3, draw unbound (free) phenytoin level (goal: 1 - 2 mcg/ml)

4) If the phenytoin trough level returns lower than the normal therapeutic range, reload the patient based on dose calculated utilizing the following equation:

   IV dose (mg/kg) = 0.7 x (plasma $C_{desired}$ – plasma $C_{observed}$)

   Oral dose (mg/kg) = IV dose (mg/kg) +10%

5) Last dose of phenytoin due at 10am the day following cessation of Busulfan.

Adjustment of serum concentrations in patients with low serum albumin

[LexiComp; 10th edition, page 1080]

Measured Total Phenytoin Concentration (mcg/mL)	**Patients Serum Albumin (g/dL)**			
	3.5	3	2.5	2
	Adjusted Total Phenytoin Concentration (mcg/mL)			
5	6	7	8	10
10	13	14	17	20
15	19	21	25	30

Adjusted concentration = measured total concentration ÷ [(0.2 x albumin) + 0.1]

Re-dosing of Busulfan if Emesis Occurs:

Since Busulfan is given by mouth, there is a chance that the dose may be inadequate if a patient vomits shortly after receiving a dose. The procedure for re-dosing Busulfan is as follows:

1. If the patient vomits within ½ hour of administration and has tablets and/or tablet fragments in vomitus, repeat the entire dose of Busulfan.
2. If the patient vomits within ½ hour of administration, has not tablets or fragments in vomitus, repeat 50% of the dose.
3. If the patient vomits ½ to 1 hour after administration, repeat 50% of the dose.

Note: Measurement of busulfan plasma levels is currently unavailable at the University of Florida; an empiric 25% reduction in dose of busulfan will be made for several busulfan containing protocols (i.e. 0.75mg/kg/day) [IRB 281-00 dosed at 1mg/kg, treatment plan 123 dosed at 1mg/kg]

ANTIEMETICS IN BMT – GUIDELINES FOR ADULTS

Chemo/TBI	Antiemetic Regimen	Comments
Parenteral Chemotherapy	**Ondansetron (Zofran®)** 8 mg PO q12h **starting 30 minutes prior to chemotherapy** and ending 24 hours after the end of chemotherapy. (If the patient is unable to take PO then Ondansetron 8mg IV may be given q12h). **Dexamethasone (Decadron®)** 8 mg PO/IV q12h from start of chemotherapy, and ending 24 hours after the end of chemotherapy.	See information below regarding breakthrough or delayed emesis.
Oral Busulfan High Dose Busulfan ($\geq$ 0.75 mg/kg/dose)	**Prochlorperazine (Compazine®)** 10 mg PO q6h prior to each dose of busulfan.	If significant emesis occurs, consider PO ondansetron.
TBI	**Ondansetron** 8-mg PO 30 minutes prior to each TBI fraction PLUS dexamethasone 4 - 8mg PO 30 minutes prior to each fraction (dose of dexamethasone depends on the # fractions. BID use 8mg, TID use 4mg).	May also consider addition of Lorazepam 1mg PO/SL/IV prior to each TBI if the ondansetron is insufficient.
Breakthrough/Delayed Emesis **NOTE:** Serotonin antagonists should **NOT** be used for longer than 24 hours post chemotherapy. If required then ondansetron oral should be used whenever possible; if IV route required then the dose is 8mg IV up to a maximum of q8h	**Lorazepam (Ativan®)** 1 - 2 mg PO/SL/IV every 4-6 hours prn (dose dependent upon weight: $\leq$ 60kg use 1mg; > 60kg may use 2mg dose) **Promethazine (Phenergan®)** 12.5 - 25 mg PO/IV every 4-6 hours prn **Prochlorperazine (Compazine®)** 10 mg PO/IV every 6 hours prn **Metoclopramide (Reglan®)** 10 – 20mg PO/IV every 6 hours when required) **<u>Motion related sickness:</u>** **Meclizine: Antivert®, Dramamine II®** 12.5 – 25mg PO q6h prn	Breakthrough emesis should be treated with other antiemetics besides serotonin antagonists and dexamethasone. If lorazepam is used, the oral route should be tried first. If unable to take PO, then try **sublingual.** If unable to take PO or SL, then use IV route. If > 3 emetic episodes, use IV route. Prescribe diphenhydramine prn (Benadryl®) to prevent extrapyramidal side effects.

NOTE: patients with a past history of significant nausea and vomiting may have the dose of ondansetron changed to 24mg PO QD plus dexamethasone 20mg PO QD.

GUIDELINES FOR ANTIEMETIC USE

EMETOGENIC POTENTIAL OF CHEMOTHERAPEUTIC AGENTS AND REGIMENS

One of the most common classification systems for the emetogenicity of a particular chemotherapeutic agent is the Hesketh model. Agents are categorized into 5 levels: level 1 (< 10% patients experience acute [$\leq$ 24 hours after chemotherapy] emesis without antiemetic prophylaxis); level 2 (10 – 30%); level 3 (30 – 60%); level 4 (60 – 90%); and level 5 (> 90%).

For combinations the emetogenic level is determined by identifying the most emetogenic agent in the combination and then assessing the relative contribution of the other agents. Rules that apply:

(1) Level one agents do not contribute to the emetogenic level of a combination

(2) Adding $\geq$ one level 2 agents increases the emetogenicity of the combination by one level greater than the most emetogenic agent in the combination; and

(3) Adding level 3 or 4 agents increases the emetogenicity of the combination by one level per agent

LEVEL 5 AGENTS

Carmustine > 250mg/m^2
Cisplatin $\geq$ 50mg/m^2
Cyclophosphamide > 1500mg/m^2
Dacarbazine
Lomustine (oral)
Methchloramine
Pentostatin
Streptozocin

LEVEL 4 AGENTS

Carboplatin
Carmustine $\leq$ 250mg/m^2
Cisplatin < 50mg/m^2
Cyclophosphamide > 750mg/m^2 and $\leq$ 1500mg/m^2
Cytarabine > 1000mg/m^2
Doxorubicin > 60mg/m^2
Methotrexate > 1000mg/m^2
Procarbazine (oral)

LEVEL 3 AGENTS

Carboplatin < 1000mg/m^2
Cyclophosphamide $\leq$ 750mg/m^2
Cyclophosphamide (oral)
Cytarabine > 250mg/m^2, but < 1000mg/m^2
Dactinomycin $\leq$ 1.5mg/m^2
Doxorubicin 20 – 60mg/m^2
Epirubicin $\leq$ 90mg/m^2
Hexamethylmelamine (oral)
Idarubicin
Ifosfamide $\leq$ 2000mg/m^2
Irinotecan
Methotrexate 250 – 1000mg/m^2
Mitoxantrone < 15mg/m^2

LEVEL 2 AGENTS

Asparaginase
Cytarabine 100mg/m^2 to < 1000mg/m^2
Docetaxel
Doxorubicin < 20mg/m^2
Etoposide
Fluorouracil < 1000mg/m^2
Gemcitabine
Methotrexate > 50mg/m^2 and < 250mg/m^2
Mitomycin C
Paclitaxel
Teniposide
Thiotepa
Topotecan

LEVEL 1 AGENTS

Bleomycin
Busulfan
Chlorambucil (oral)
2-Chlorodeoxyadenosine
Fludarabine
Hydroxyurea
Methotrexate $\leq$ 50mg/m^2
Thioguanine (oral)
Vinblastine
Vincristine
Vinorelbine

HIGH EMETOGENIC POTENTIAL

Agents with emetogenic potential from 60 to > 90%

- ***Hesketh Levels 3, 4, 5 (see above)***

Extensive pre-chemotherapy education and alleviation of patient fears are critical in order to minimize or eliminate potential difficulties with nausea and/or vomiting.
For prevention of acute N/V (0-24 hours after chemotherapy) options include: (begin 30 minutes prior to chemo)

Ondansetron 24 mg PO* or 8-32 mg IV (over 15 mins), x 1 dose +
Dexamethasone 20 mg PO or IV

OR

Granisetron 2 mg PO x 1 dose, or 1 mg PO BID x 2 doses, or 10 mcg/kg IV **(NON FORMULARY, NOT AVAILABLE)** x 1 dose +
Dexamethasone 20 mg PO or IV

OR

Dolasetron 100-200 mg PO, or 1.8 mg/kg IV or 100 mg IV, or x 1 dose **(NON FORMULARY, NOT AVAILABLE)** +
Dexamethasone 20 mg PO or IV

* Shands HealthCare we use ondansetron 8 – 24mg/day. A common regimen is 8mg, 30 minutes prior to emetogenic chemotherapy. Granisetron and dolasetron are non-formulary and not available at Shands.

INTERMEDIATE EMETOGENIC POTENTIAL

Agents with emetogenic potential from 10 to 30%

- ***Hesketh Level 2***

Extensive pre-chemotherapy education and alleviation of patient fears are critical in order to minimize or eliminate potential difficulties with nausea and/or vomiting.

For each day of chemotherapy (start before chemotherapy), options include:

1) Dexamethasone 4-8 mg PO or IV x 1 dose

AND/OR

2) Prochlorperazine 10 mg IV or 10 mg regular or 15 mg Spansule PO x 1 dose

OR

3) Metoclopramide 20 mg IVP or PO x 1 dose
4) No treatment for some of these agents is an option

LOW EMETOGENIC POTENTIAL

Agents with emetogenic potential <10%
Hesketh Level 1 (see page 3 of guideline)

Antiemetics are not routinely administered prior to chemotherapy

DELAYED NAUSEA AND VOMITING

Prophylactic treatment for delayed N/V associated with highly emetogenic antineoplastic agents should begin 24 hours after the last dose of chemotherapy

Agents most commonly associated with delayed nausea and vomiting include:

Cisplatin	Cyclophosphamide
Carboplatin	Doxorubicin
Dacarbazine	

For prevention of delayed N/V (>24 hours post-chemo) treatment with one or more of the following should be initiated ***(agents are listed in order of preference for delayed therapy):***

1) Metoclopramide 30-40 mg or 0.5 mg/kg PO QID, with Diphenhydramine 25-50 mg IV PO q4-6H and Dexamethasone 8 mg PO/IV BID x 2-4 days
   Note: the use of metoclopramide should be avoided in patients experiencing diarrhea as its use may exacerbate the problem
2) Lorazepam 1-2 PO/SL/IV q6H (as an adjunctive agent)
3) Haloperidol 0.5 - 1 mg q6H
4) Ondansetron 8 mg PO/IV BID +
   Dexamethasone 8 mg PO/IV BID x 2-4 Days

   OR

   Dolasetron 100 mg PO/IV QD + **(NON FORMULARY, NOT AVAILABLE)**
   Dexamethasone 8 mg PO/IV BID x 2-4 Days

OR

Granisetron 2 mg PO or 10 mcg/kg IV QD + **(NON FORMULARY, NOT AVAILABLE)**
Dexamethasone 8 mg PO/IV BID x 2-4 Days

Note: There is little evidence to support the use of $5HT_3$ antagonists in the delayed treatment setting, but their use is an option once other agents have failed.

ANTICIPATORY NAUSEA AND VOMITING

- Extensive pre-chemotherapy education and alleviation of patient fears are critical in order to minimize or eliminate potential difficulties with nausea and/or vomiting.
- Optimum prevention/treatment of acute N/V is imperative in the prevention of anticipatory nausea/vomiting
- Lorazepam 1-2 mg PO at bedtime, and 1-2 mg PO/SL/IV upon arrival to the office

or

- Alprazolam 0.5-2 mg PO at bedtime and upon arrival to office prior to chemotherapy administration

RADIATION INDUCED

High Risk

Total body irradiation

1) If XRT is given only once daily, pretreat with:
   Ondansetron 8 mg IV/PO x 1
   Granisetron 10 mcg/kg IV or 1 mg PO x 1 **(NON FORMULARY, NOT AVAILABLE)** or
   Dolasetron 1.8 mg/kg IV or 100 mg IV or 100-200 mg PO x 1 **(NON FORMULARY, NOT AVAILABLE)**
   +/-
   Dexamethasone 20 mg PO x 1

2) If XRT fractionation is BID or TID, use
   Ondansetron 8 mg + Dexamethasone 8 mg PO/IV prior to each fraction

Intermediate Risk

Hemibody radiation ;Upper abdominal radiation; Abdominal/pelvic radiation; Mantle radiation
Cranio-spinal radiation; Cranium (radio-surgery)

1) Ondansetron 8 mg IV or 8 mg PO x 1 *
   Dolasetron 1.8 mg/kg IV or 100 mg IV or 100-200 mg PO x 1* **(NON FORMULARY, NOT AVAILABLE)** or
   Granisetron 10 mcg/kg IV or 2 mg PO x 1 * **(NON FORMULARY, NOT AVAILABLE)**
   +/-
   Dexamethasone 20 mg PO x 1

* Give 1 dose before each fraction

2) Metoclopramide 20 mg PO or 0.5 mg/kg PO/IV x 1
3) Prochlorperazine 10-20 mg PO/IV or 25 mg PR

Low Risk

Breast; Extremity; Head and Neck; Pelvis; Thorax; Cranium only

Treatment should be reserved for patients who experience nausea and vomiting

HEMORRHAGIC CYSTITIS MANAGEMENT GUIDELINES

Patients presenting with hemorrhagic cystitis should be routinely worked up as follows:

1. Urine should be sent for urinalysis
2. Send the urine culture for the following viruses:
   - Adenovirus
   - CMV
3. Urine for Cytology for BK virus, immunofluorescence for CMV
4. Check platelet count to maintain count > 50,000 if possible
5. Check coagulation parameters

Medication treatment options for symptomatic hemorrhagic cystitis:

Fluids

Antispasmodics:

- Oxybutinin 5 – 10mg PO QID prn
- Phenazopyridine (Pyridium®) 100 – 200mg QID

To decrease urinary frequency:

- Oxybutinin (Ditropan®) 5 – 10mg PO QID prn

Morphine sulfate q1h prn pain

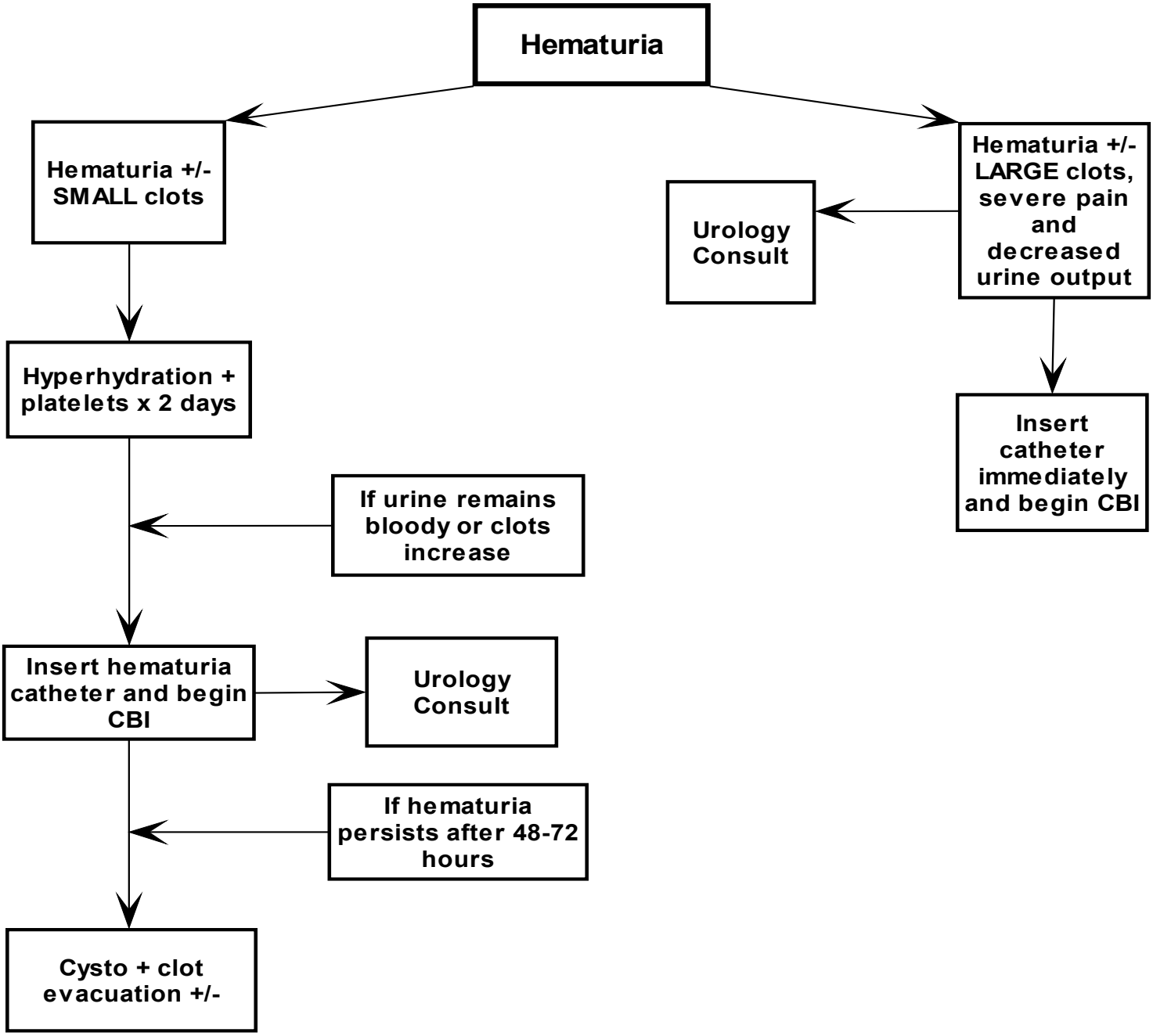
For Continuous Bladder Irrigation if needed:

- Insert 3-way hematuria catheter
- Begin CBI and run to keep urine clear

Laboratory Tests:

- Regular platelet counts
- Weekly urine culture (if positive)
- PT, PTT twice a week
- SCr QD

ALGORITHM FOR HEMORRHAGIC CYSTITIS



Shands BMTU Hyperhydration Guidelines

Prehydration:
At 2200 the evening prior to cyclophosphamide administration, begin hydration with Normal Saline plus 20 mEq/Liter KCl at 4 mL/kg/hour. The hydration dosing weight will be the same as the chemotherapy dosing weight. Foley, Texas or straight catheters will not be used prophylactically.

Bolus Cyclophosphamide:
Beginning when each dose of cyclophosphamide is hung, measure urine output every hour for 12 hours, then every 2 hours for 12 hours. **Only urine volume need be measured** and may be stopped 24 hours after cyclophosphamide is completed. Dipstick for hemoglobin only once daily, beginning 24 hours from the start of cyclophosphamide and finishing 24 hours after cyclophosphamide is completed..

Mesna may be used in patients with a history of previous radiation therapy or other urologic disorders, marginal cardiac function (EF < 50%) and pulmonary compromise (FEV_1, FVC, DLCO < 60%). Decrease hydration to maintenance when mesna is used

Continous Infusion Cyclophosphamide:
Beginning when each dose of cyclophosphamide is hung, measure urine volume every 4 hours. **Only urine volume need be measured,** and may be stopped 24 hours after cyclophosphamide is completed. Dipstick for hemoglobin only once daily, beginning 24 hours from the start of cyclophosphamide and finishing 24 hours after cyclophosphamide is completed..

Maintain UOP of at least 3 mL/kg/hour

A. If UOP < 3 mL/kg/hour, increase hydration to 5 mL/kg/hour

A. If UOP ≥ 3 mL/kg/hour, continue current rate

B. If UOP < 3 mL/kg/hr continues, then give furosemide 40 mg IV and maintain hydration at 5 mL/kg/hr. For patients under age 12, use furosemide dose of 0.5 to 1 mg/kg/dose.

C. If UOP ≥ 3 mL/kg/hr x 1 hour, then falls below 3 mL/kg/hr, repeat step **B.**

Completion of Hydration:
Continue hydration at last rate until 24 hours after last cyclophosphamide dose is completed

CONSCIOUS SEDATION

Definition:*A state of depressed level of consciousness in which a patient is able to maintain a patent airway independently and can be aroused by physical stimuli. Patients are unable to hold a conversation, but respond to commands by appropriate action or brief verbalization.*

Equipment, Monitoring, Documentation

*** See Conscious Sedation Policy****

Pharmacology of Conscious Sedation

Ideal:

- Reliable and rapid onset of action
- Predictable level of sedation
- Desired amnesic effect
- Well-defined dose-effect relationship
- Minimal side effects
- Return to baseline quickly

Clinical Pearls of Drug Dosing:

- IV analgesic sedatives should be administered in small repeated doses and titrated to clinical effect.
- Wait until drug has achieved maximal effect prior to initiating procedure or repeating dose.
- **If a sedative (midazolam, lorazepam) is given with an opioid analgesic (fentanyl, hydromorphone (Dilaudid®), meperidine or morphine) the initial dose of each should be reduced by 50%.**
- If patient is obese, use Calculated Idea Body Weight.

SPECIFIC AGENTS

BENZODIAZEPINES:

Pharmacology: Produce CNS depression. All benzodiazepines are capable of producing anxiolytic, sedative, skeletal muscle relaxant, and anticonvulsant effects.

Midazolam (Versed®)

Intravenous Route:
Dose: 0.07 – 0.2 mg/kg/dose IV given slowly over 10 min. and titrated to desired effect. Max IV dose: 8 mg.

Pharmacokinetics:

Onset: Within 1 – 5 minutes
Duration: 2 hours mean, up to 6 hours

Lorazepam (Ativan®)

Intravenous / PO Route
Dose: 0.05 – 0.1 mg/kg/dose not exceed 4mg as a single dose. If given PO administer 15-20 minutes prior to procedure.
Pharmacokinetics:
Onset: Within 1 – 5 minutes
Duration: 12 – 24 hours (half-life: 10 hours in children)

Administration: IV not to exceed 2mg/minute or 0.05 mg/kg over 2 – 5 minutes.

REVERSIBLE AGENTS

Flumazenil (Romazicon®)

- Flumazenil is used to reverse sedative effects of benzodiazepines (NOTE: it does not antagonize the CNS effects of the other GABA agonists and does NOT reverse sedative effects of narcotics)..
- Most common adverse effects are dizziness, nausea and vomiting.

Adult dose for the reversal of conscious sedation:

Initial dose: 0.2 mg IV over 15 seconds.
Repeat doses: 0.2 mg IV at 1-minute intervals until desired level of consciousness is achieved.
Max dose: 1 mg (most patients respond to 0-6 to 1 mg). ***Note: this is a CUMULATIVE DOSE***

Pediatric dose for reversal of conscious sedation (Children up to 40 kg):
Initial dose: 0.01 mg/kg IV over 15 seconds (maximum dose of 0.2 mg).
Repeat doses: 0.005 – 0.01mg/kg at 1minute intervals (maximum dose 0.2 mg).
Max total dose: 1 mg (***Note: this is a CUMULATIVE DOSE)***

Children > 40 kg; use adult dosages.

Pharmacokinetics:
Onset: 1- 3 minutes (80% respond within 3 minutes)
Duration: resedation occurs usually within 1 hour; duration is related to the dose given and benzodiazepine blood concentrations; reversal effects of flumazenil may wear off before the effects of the benzodiazepine.

Key Points:

- Flumazenil will only reverse benzodiazepine-induced sedation.
- Risk of resedation: duration flumazenil activity is related to dose given and benzodiazepine plasma concentrations. Reversal effects may wear off before effects of benzodiazepine.
- Risk of seizures in patient's who have been on long term benzodiazepine therapy.
- Flumazenil does **NOT** fully reverse respiratory depression / hypoventilation or cardiac depression.
- **Any administration of Flumazenil at Shands Hospital is considered an Adverse Drug Reaction (ADR) and should be reported to ADR Hotline.**

OPIATES

Pharmacology: Opiates are centrally acting analgesics. Opiates increase pain threshold, alter pain perception and inhibit ascending pain pathways.

Adverse effects: CNS depression, drowsiness, sedation, hypotension, bradycardia or respiratory depression. The most common reports of adverse effects associated with conscious sedation have occurred in patient's receiving an opiate plus another agent from a different class e.g. benzodiazepines.

Morphine

Intravenous Route
Dose: 0.05 – 0.1 mg/kg dose slow IV push 5 minutes prior to procedure.

Pharmacokinetics:

Onset: 5 –10 minutes; peak at 20 minutes
Duration: 4-5 hours; half-life of 2 – 40; may have analgesic effect out to 7 hours.

Meperidine (Demerol®)

Intravenous Route
Dose: 1 - 2mg/kg/dose IV slow push (Max 100 mg/dose)

Pharmacokinetics
Onset: 5 minutes
Duration: 2 - 4 hours

Fentanyl (Sublimaze®)

Intravenous Route
Dose: 0.5 - 1 mcg/kg IV titrated slowly over 10 minutes until desired effect.

Pharmacokinetics:
Onset: 1 - 5 minutes
Duration: 30 – 60 minutes

REVERSAL AGENTS

Naloxone (Narcan®)

Naloxone is used to reverse CNS and respiratory depression from overdose of opiates only (will not reverse over sedation with benzodiazepines).

Adverse Effects: Sweating, hypertension, hypotension, tachycardia, ventricular arrhythmia's.

Intravenous Dose:
0.1 – 0.2mg IV at 2 – 3 minute intervals to desired degree of reversal based on response (maximum dose 2mg).

Pharmacokinetics:
Onset: 1 – 2 minutes
Duration: 20 – 60 minutes

RECOMMENDED COMBINATION (70 kg ADULT)

Midazolam (Versed®)
Initial Dose: 2 mg IV
Repeat Dosage: every 5 minutes until desired effect (Max: 8 mg)

Meperidine (Demerol®)
Initial Dose: 50 mg IV.
Repeat Dosage: 25 mg Q 10 minutes (Max: 100 mg)

SUPPORTIVE DATA: Core Policy and Procedure CP2.22; Hospital Guidelines CP2.22g; Cardiovascular Protocol: 03 Telemetry Monitoring in Non ICU Areas (AN3E1B)

PAIN MANAGEMENT

Guidelines for patient-controlled (PCA) intravenous opioid administration for adults with acute pain

Drug	Usual Starting Dose After Loading	Usual Dose Range	Usual Starting Lockout (minutes)	Usual Lockout Range (minutes)
Morphine (1mg/mL)	1mg	0.5 – 2.5mg	8	5 – 10
Hydromorphone [Dilaudid] (0.2mg/mL)	0.2	0.05 – 0.4mg	8	5 – 10
Fentanyl (50mcg/mL)	10mcg	10 – 50 mcg	6	5 - 8

Narcotic Dose Comparison

	Adult		Pediatric				
DRUG	**PO**	**IV/IM**	**PO**	**IV/IM**	**Available Oral Products**	**Dosing Frequency**	**Comments**
Morphine	30 mg	10 mg	0.3 mg/kg	0.1 mg/kg	IR: Morphine tabs 15 mg, 30 mg *Morphine elixir 2 mg/ml Morphine elixir (Roxanol) 20 mg/ml SR: MS Contin 15, 30, 60, 100, and 200 mg *Oramorph SR 15, 30, 60, 100 mg	IR: Q3-4H prn SR: Q8H or Q12H	
Oxycodone	20 mg	N/A	0.3 mg/kg	N/A	IR: *Oxycodone 5 mg tabs, 5mg/5 ml solution OxyFast 20 mg/ml solution Percocet: APAP 325mg/Oxycodone 5mg† *Tylox: APAP 500 mg/Oxycodone 5 mg SR: *Oxycontin 10, 20, 40, 80 mg tablets	IR: Q3-4H prn SR: Q12H	
Hydromorphone	7.5 mg	1.5 mg	0.06 mg/kg	0.01 mg/kg	IR: *Dilaudid 2, 4, 8 mg SR: Not available	IR: Q3-4H prn	Duration of effect generally shorter than for morphine

Abbreviations: IR = Immediate release, SR = sustained release, APAP = acetaminophen

* Formulary products at Shands at the University of Florida

† Percocet available in community pharmacies in other strengths (APAP/oxycodone): 325mg/2.5mg, 500mg/7.5mg, 650mg/10mg

CONVERSION FROM OTHER OPIOID ANALGESICS TO MORPHINE SUSTAINED RELEASE

Approximate opioid equivalents:

Drug (A)	Conversion Factor (B)
Hydromorphone (oral)	X 20
Hydromorphone (parenteral)	X 4
Oxycodone	X 1
Methadone[1]	[+]
Meperidine (oral)	X 1/8
Morphine (parenteral)	X 3
Codeine	X 1/10

1. Gourlay GK, Cherry DA. A comparative study of the efficacy and pharmacokinetics or oral methadone and morphine in the treatment of severe pain in patients with cancer. *Pain* 1986; 25:297 – 312.

[+] There is no reliable equipotent dose comparing methadone used clinically with morphine due to PK variations. It is a suggested a conversion of 1 be used to start therapy and titrate up if necessary.

EQUIANALGESIC DOSES FOR CONVERTING MORPHINE TO TRANSDERMAL FENTANYL

Oral 24-hour Morphine (mg/day)	IM 24-hour Morphine (mg/day)	Duragesic® Dose (mcg/hour)
45 -134	8-22	25
135 – 224	23 – 37	50
225 – 314	38 – 52	75
315 – 404	53 – 67	100
405 – 494	68 – 82	125
495 – 584	83 – 97	150
585 – 674	98 – 112	175
675 – 764	113 – 127	200
765 – 854	128 – 142	225
855 – 944	143 – 157	250
945 – 1034	158 – 172	275
1035 – 1124	173 – 187	300

Reference: Guidelines for treatment of cancer pain; The Revised Pocket Edition of the Final Report of the Texas Cancer Council's Workgroup on Pain Control in Cancer Patients, 1997

GUIDELINES FOR EVALUATING AND TREATING SEIZURES IN TRANSPLANT PATIENTS

Potential causes include hypo- or hypernatremia, hypomagnesemia, hypo- or hyperglycemia, hypo- or hypercalcemia, FK506 or CSA toxicity, hypertension, hypoxia, fever, infection, CNS mass or hemorrhage, hepatic encephalopathy, alcohol or drug withdrawal, iatrogenic.

1. Isolated or short-duration seizure management:
   - For the actively seizing patient, see #2 below.
   - Check vital signs (if unstable, see #2 below).
   - Send electrolyte panel to assess Na, Ca, Mg, and glucose, and CBC if the platelet count or white count is unknown.
   - Use bedside glucometer to assess blood sugar. If low, administer one amp of 50% glucose solution IV.
   - Check FK506 or CSA level if applicable.
   - **If IV FK506 or CSA is actively infusing, stop the infusion.** Hold these and other infusions until patient is stable and has been fully evaluated. (See list of commonly used seizure-causing medication on next page)
   - Once the patient is stable, obtain a head CT without contrast to evaluate for intracranial hemorrhage, mass, infarct, leukoencephalopathy, infectious changes.
   - Consult neurology and obtain an EEG.

2. For patients with continuing convulsive activity, status epilepticus, or unstable vital signs:
   - Secure airway.
   - Start continuous cardiac and respiratory monitoring for hypotension or respiratory depression.
   - Check metabolic panel and CBC; consider ABG if respiratory status is compromised.
   - Use bedside glucometer to assess blood sugar. If low, administer one amp of 50% glucose solution.
   - Check FK506 or CSA level if applicable.
   - **If IV FK506 or CSA is actively infusing, stop the infusion.** Hold these and other infusions until patient is stable and has been fully evaluated. (See list of commonly used seizure-causing medication on next page)
   - Consider emptying gastric contents via NG tube if aspiration is a risk.
   - Perform a neuro exam to confirm seizure type/classification.
   - Administer IV lorazepam according to the dosing chart below.
   - Administer fosphenytoin (even if seizure abates) according to the dosing chart below; monitor pt closely during infusion for heart block or hypotension.
   - Patient may require intubation and general anesthesia with neuroblockade if seizures persist for > 30 min.
   - Once the patient is stable, obtain a head CT without contrast to evaluate for intracranial hemorrhage, mass, infarct, leukoencephalopathy, infectious changes.
   - Consult neurology and obtain an EEG.

Treatment of Status Epilepticus

Drug	Adult Dose	Pediatric Dose	Infusion Rate	Repeat Doses
Lorazepam	4mg IV over 2-5min. **MAX: 8mg**	0.1mg/kg IV over 2-5min. **MAX: 4mg/dose**	Over 2-5min	q10-15min prn
Fosphenytoin	15-20mg PE/kg IV	15-20mg PE/kg IV	100 – 150 PE/minute	Serum level: 10-20mg/L 2hr after dose

PE = phenytoin equivalents

Medications commonly used in BMT patients that may cause seizures:

- ◊ FK506 (tacrolimus)
- ◊ Cyclosporine
- ◊ Imipenem (Primaxin®)
- ◊ Demerol (meperidine)
- ◊ Busulfan
- ◊ Tricyclic antidepressants
- ◊ Phenothiazines
- ◊ Phenergan
- ◊ Opiates
- ◊ Clozapine
- ◊ Bupropion
- ◊ Venlafaxine (overdose doses)

Reading materials: Delanty N, et al. Medical causes of seizures. *Lancet* 1998; 352:383 – 90.

H_2 ANTAGONIST/PROTON PUMP INHIBITOR GUIDELINES

I. Begin H_2 antagonist at initiation of chemotherapy (if patient admitted on a proton pump inhibitor continue therapy with this medication, all other patients to be started on a H_2-antagonist)

Products are therapeutically interchangeable (based on formulary selection):

PO Options	IV Options
Axid® (Nizatidine) 150mg PO BID**	Pepcid® 20mg IV q12h
Zantac® (Ranitidine) 150mg PO BID	**Zantac® 50mg IV q8h****
Pepcid®(Famotidine) 20mg PO BID	

**** = Current formulary products at Shands HealthCare**

If a patient is not responding to the initial dose of the agent then increase to maximal doses before considering the change to a proton pump inhibitor e.g. nizatidine 300mg PO BID.

II. Consider proton pump inhibitors only in those patients who fail to respond to 7 – 10 days of H_2 antagonist therapy (unless recommended by gastroenterology).

PO Options	IV Options
Prilosec® (Omeprazole) 20mg PO QD	None
Prevacid® (Lansoprazole) 30mg PO QD	None
Protonix® (Pantoprazole) 40mg PO QD**	**Pantoprazole IV 40mg IV QD****

**** = Current formulary product at Shands HealthCare**

THROMBOCYTOPENIC/HYPERTENSIVE PATIENT GUIDELINES

In an attempt to standardize the approach to thrombocytopenic patients who are also moderately hypertensive (diastolic blood pressure greater than 110 we recommend the following guidelines:

1. Assess pain control (which can transiently increase blood pressure). If pain is not well controlled then manage with morphine or other narcotic equivalent $\pm$ tranquilizers.
2. Assess fluid/salt status. If I's > O's by 1,000 mL for patients whose body weight exceeds 40kg, give furosemide 20mg x serum creatinine or a dose that has been found to be effective in the past. For smaller patients, use a dose of 0.5-1 mg/kg/dose. If urine output is less than 500mL over the next 30 minutes, the physician staff should be consulted.
3. If the diastolic blood pressure continues to be greater than 110mHg, clonidine 0.2mg PO x 1 dose followed by 0.1mg/hour PO up to a maximum of 0.8mg PO if necessary. Blood pressure should drop within 45 – 60 minutes (alternatives are: minoxidil 20mg x 1 dose followed by 10-20mg PO q4-6h prn, a response should be seen within 30 minutes; captopril 25mg x 1 dose and repeated hourly as necessary, a response should be seen within 30 minutes). A more gradual reduction of BP is desirable.
4. The blood pressure should be repeated 20 minutes later. If it is still elevated, then follow guidelines in item 3.
5. If the diastolic BP still exceeds 110mmHg, nursing staff should confer with the physician staff.
6. If the diastolic BP persists above 110, then we suggest (a) using IV bolus doses of medications and if this fails, or if there is (b) signs of end organ damage, transferring the patient to the MICU for IV infusion administration of drips of antihypertensives such as nitroprusside.
7. If it appears that hypertension is something other than a transient phenomenon, then oral therapy with a longer acting calcium channel blocker, ACE inhibitor, or beta-blocker should be commenced concomitant with the oral or intravenous therapy.
8. For patients aged less than 12, assess adequacy of pain control, assess fluid/salt status on an individual basis, and confer with physicians regarding parameters for each patient. Use table of blood pressures indicating hypertension (defined as BP exceeding the 90th percentile) as a guide for therapy in the pediatric section of this book.

The primary focus should be on controlling the blood pressure. We strongly recommend that the temptation to give platelet transfusion be avoided since there are no data suggesting that increasing the platelet transfusion threshold above the typical thresholds ordinarily used for platelet transfusion prophylaxis is warranted for mild to moderate hypertension.

HYPERTENSIVE URGENCY TREATMENT OPTIONS – ADULTS

Drug	Dose	Time to Onset of Action	Comments
Oral Options			
Clonidine	0.2mg PO Q1 – 2 hours	30 – 45 minutes	
Captopril	25mg PO Q1 –2 hours prn	30 – 45 minutes	
Labetalol	200 – 400mg PO Q2 – 3 hours	30 – 60 minutes	
Minoxidil	20mg Loading dose, THEN 5 – 10mg PO Q4 – 6 hr prn		Should be a last line agent due to reflex tachycardia and fluid accumulation side-effects
Prazosin	1 – 2mg PO Q1 hour	60 minutes	Tachyphylaxis associated with long term use.
Intravenous Options			
Labetalol	20mg IV Q1 – 4 hours prn	20 – 30 minutes	Boluses can be increased to 80mg.
Enalaprilat	0.625 – 1.25mg IV Q4 – 8 hours	30 minutes	May increase dose to 5mg if necessary
Hydralazine	10mg IV Q 4 – 6 hours [dose may be titrated to 10 – 40mg each dose]	10 minutes	
Metoprolol	5mg IV Q 1 – 2 hours		Maximal response seen within 20 minutes Length of response short: 1 – 2 minutes

OCCLUDED CATHETER

1. Attempt to gently flush catheter with 1-3 cc normal saline. Do not push against resistance.

2. For peripheral IV: discontinue current site, restart.
   For central line: notify MD

3. Nurses may instill Alteplase (tPA) into the occluded central catheters.

Alteplase (tPA) Use for Catheter Occlusion:

1. Alteplase (tPA) (1 syringe = 1mg/mL) (MD order in admission orders).

2. Verify loss of patency or withdrawal occlusion by attempting to flush with saline and attempting blood aspiration after changing patient position.

3. If no blood return is obtained, then use Alteplase (tPA) to aid in gaining access to the line.

4. Cleanse the diaphragm of male adapter or directly access the line.

5. Attempt to slowly inject Alteplase (tPA). If the Alteplase (tPA) will not infuse, attempt to withdraw then inject using gentle pressure multiple times (push-pull action). Wait at least 60 minutes following instillation of Alteplase (tPA).

6. Attempt to withdraw Alteplase (tPA) and aspirate 2.5 - 3 ml of blood. Clamp catheter. Remove blood-filled syringe and discard. Flush line with saline and restart infusion or **heparin flush**. [If no blood can be aspirated, attempt to infuse more Alteplase (tPA) (if all had not be infused in step 5). Wait another 60 minutes and repeat step 6.

NOTE: Examine PICC or CVL for integrity. Frequently lines are damaged when forceful attempts to clear occlusion are employed. If line is damaged contact MD, IV nurse therapists, nurses from oncology units, or nutrition support nurse.

If the catheter does not open within 2 hours, a second injection of Alteplase (tPA) may be needed. Contact the physician for a repeat Alteplase (tPA) order.

Adapted from: Shands Hospital at the University of Florida Department of Nursing and Patient Services. IV/Medications Procedures: 04A, page 5-6.

MANAGEMENT OF DEPRESSION

Agents typically used include:
Fluoxetine (Prozac®); dose 20 – 80mg PO QD
Paroxetine (Paxil®); dose 20 – 60mg PO QD
Sertraline (Zoloft®); dose 50 – 100mg PO QD
Venlafaxine (Effexor®); dose 75 – 375mg PO QD

Notes:

1. Fluoxetine causes:
   weight loss in > 5%, occurred in 10 – 15% patients
   insomnia in > 10%
2. Paroxetine causes:
   Anorexia 1 – 10%
   Sedation > 10%
3. Sertraline causes:
   weight gain
   somnolence

Selected SSRIs Adverse Reactions % (in ≥ 1% of Patients)				
Adverse Reaction		**Fluoxetine**	**Paroxetine**	**Sertraline**
Cardiovascular	Palpitations	2	2-3	≥ 1
	Vasodilatation	3	3-4	--
CNS	Insomnia	20	13-24	16-28
	Somnolence	13	19-24	13-15
	Nervousness	13	6-9	6
	Dizziness	10	12-14	13
	Tremor	10	8-11	5-11
	Decreased libido	4	3-9	1-11
	Myoclonus	0.1-1	3	0.1-1
	Abnormal Dreams	5	4	0.1-1
Dermatological	Sweating (excessive)	8	9-14	5-8
GI	Nausea	23	23-26	26-30
	Diarrhea/loose stools	12	10-12	18-24
	Dry mouth	10	18	15
	Anorexia	11	6 (1-10)	3-11
	Increased appetite	≥ 1	2-4	≥ 1
GU	Sexual dysfunction/impotence	--	5-8	≥ 1
	Abnormal ejaculation	--	21-23	7-19
	Urination disorder/retention	0.1-1	3	0.1-1
Musculoskeletal	Myalgia	5	2	≥ 1
Miscellaneous	Headache	21	18	26
	Asthenia	12	14-22	≥ 1
	Flu syndrome	5	--	--
	Weight loss	2 (may be as high as 10-15%)	≥ 1	0.1-1
	Weight gain	≥ 1	≥ 1	≥ 1 (may be higher)

Selected adverse reactions. Ref: Facts and Comparisons. Note that data are from different studies and not necessarily comparable.

THERAPEUTIC DRUG MONITORING

PHARMACOKINETIC GUIDELINES FOR DRUG MONITORING

Test#	Tube	Drug	Peak	When to draw peak	Trough	When to draw	Comments
3069	Purple	**Cyclosporine A**	NA	Not applicable	150-450 ng/ml	Immediately prior to next dose	Samples processed twice daily M-F and once Sat/Sun.
2517	Red	**Digoxin**		6-8hrs after last dose	1-2 mcg/ml	Immediately prior to next dose	Trough levels provide the most useful information
	Red	**Itraconazole**	0.1 – 2.2μg/mL	90 minutes post oral dose			Send Out. MRL Labs 1 800 445 4032 (California)
2520 2521	Red	**Gentamicin** **Tobramycin**					Samples processed around the clock.
		Conventional Dosing	8-12 mcg/ml	30 min. after a 30 min. infusion	< 2 mcg/ml	Immediately prior to next dose	If renal function normal, levels should be drawn **after** 4th dose
		Once daily dosing**	***	***	***	***	Once daily dosing is monitored by obtaining a level 10 hours following the dose. The 10-hour level should be < 5mcg/ml. Consult Pharm.D. for assistance in adjusting dose.
2529	Red	**Phenobarbital**	NA	NA	15-40 mcg/ml	Immediately prior to next dose	
2531	SS tube 1ml blood	**Phenytoin (Dilantin®)**	NA	NA	10-20 mcg/ml	Immediately prior to next dose	Consider unbound phenytoin levels in patients with altered protein binding. This includes renal failure, hypoalbuminemia, malnutrition and hyperbilirubinemia.
2532	2ml blood (1ml serum)	**Phenytoin (unbound)**	NA	NA	1-2 mcg/ml		
2539	Purple	**Tacrolimus (FK506 or Prograf®)**			10-20 ng/ml	Immediately prior to next dose	Random levels can be drawn at any time while on CIVI. Samples processed daily
2546	Red	**Vancomycin**	25-40 mcg/ml	1 hr after infusion is complete	5-10 mcg/ml	Immediately prior to next dose	If renal function normal, check trough only after 4 doses (if therapy continued beyond 48h). Will accept trough up to 15
	Red	**Mycophenolic acid** **Mycophenolic acid glucuronide (MPAG)**		NA	1 – 3.5μg/mL 35 - 100μg/mL	Immediately prior to next dose	Send Out: Mayo Medical Labs; 200 SW 1st St; Rochester, MN 55905 1-800-533-1710; fax 507-284-1759

*Consult your unit pharmacist on frequency and timing of checking levels for patients with renal dysfunction, renal failure, and patients on dialysis.
**Pharm.D. may order drug levels as necessary. Consult Pharm.D. for interpretation of drug levels.

CYCLOSPORIN AND TACROLIMUS LEVELS
LABORATORY SCHEDULE

CYCLOSPORINE levels are run as follows:

MONDAY – FRIDAY*

7.30am cut-off; 8.30am reported
9.30am cut-off; 11.00am reported
12.30pm cut-off; 2.30pm reported

SATURDAY + SUNDAY

9am cut-off

TACROLIMUS levels are run as follows:

MONDAY – FRIDAY

9am cut-off; 11am reported
11am cut-off; 1.00pm reported

SATURDAY + SUNDAY

11am cut-off; 1.00pm reported

* NOTE: there is a renal clinic on Monday, Wednesday, Thursday and Friday. On these days the 3 runs will be processed. If there are not sufficient samples, then there is one run at 12.30pm.

Information provided by laboratory services 4/25/02; received by H.Leather

GUIDELINES FOR WHEN TO DRAW SERUM DRUG CONCENTRATIONS

Updated 01-08-02

(Consult a pharmacist for any questions)

Drug Name	Start Date/Time	Comments
Acetaminophen (Tylenol®)	**Routine or Timed Draw**	Repeat levels no less than 4 hours apart.
Amikacin	**Peak** –schedule 30 minutes after a 30 minute infusion ***(Timed or Nurse Draw Only)*** **NOTE- Peak drug levels should never be drawn earlier than scheduled time without consulting a Pharmacist.** **Random**—can be ordered for defined time by prescriber ***(if prescriber orders level for specific time, it should be placed as a "Timed" or "Nurse Draw". If no time specified, order as "Routine")*** **Trough**-- schedule 30 minutes prior to next scheduled dose. ***(Timed or Nurse Draw Only)***†	Peak and Trough usually drawn around the 3rd or 4th dose of starting a new regimen. Random levels are usually done as part of a high dose (5-7 mg/kg once daily) regimen where the level should be drawn 8 - 12 hours (not > 14 hours) after the dose or as part of a pharmacokinetic evaluation. † If next scheduled dose is delayed, continue to draw trough at scheduled time.
Carbamazepine (Tegretol® Tegretol XR®* Carbatrol®*)	***Timed (preferred)--***order 30 minutes prior to next scheduled dose† ***Routine (alternate)--see comments***	† If next scheduled dose is delayed, continue to draw trough at scheduled time. For slow release products (Tegretol XR®), may draw level a minimum of 6 hours after a dose.
Cyclosporine (Sandimmune® Neoral® Gengraf®)	**Oral dosage form**: ***Timed draw*** (order 30 minutes prior to next scheduled dose) † **Continuous Infusion:** may be ordered as ***Routine***	† If next scheduled dose is delayed, continue to draw trough at scheduled time.
Digoxin (Lanoxin®)	***Timed (preferred)--***order 30 minutes prior to next scheduled dose† ***Routine (alternate)--see comments***	† If next scheduled dose is delayed, continue to draw trough at scheduled time. Digoxin levels should generally not be drawn less than 8 hours after a dose.
Ethosuximide	***Timed (preferred)--***order 30 minutes prior to next scheduled dose†	† If next scheduled dose is delayed, continue to draw trough at scheduled time.

Drug Name	Start Date/Time	Comments
Gentamicin	**Peak** --30 minutes after a 30 minute infusion ***(Timed or Nurse Draw Only)*** **NOTE- Peak drug levels should never be drawn earlier than scheduled time without consulting a Pharmacist.** **Random**—can be ordered for defined time by prescriber **(*if prescriber orders level for specific time, it should be placed as a "Timed" or "Nurse Draw". If no time specified, order as "Routine")*** **Trough**-- Schedule 30 minutes prior to next scheduled dose† ***(Timed or Nurse Draw Only)***	Peak and Trough usually drawn around the 3rd or 4th dose of starting a new regimen. Random levels are usually done as part of a high dose (5-7 mg/kg once daily) regimen where the level should be drawn 8 - 12 hours (not > 14 hours) after the dose or as part of a pharmacokinetic evaluation. † If next scheduled dose is delayed, continue to draw trough at scheduled time.
Methotrexate	For high dose chemotherapy, order at times specified in chemotherapy orders. ***(Timed or Nurse Draw Only)***	
Lidocaine	**Routine**	
Lithium	***Timed (preferred)--***order 30 minutes prior to next scheduled dose†	† If next scheduled dose is delayed, continue to draw trough at scheduled time.
Phenobarbital	***Timed (preferred)--***order 30 minutes prior to next scheduled dose† ***Routine (alternate)--***may be ordered as routine due to long elimination half-life	† If next scheduled dose is delayed, continue to draw trough at scheduled time.
Phenytoin (Dilantin® Cerebyx®)	***Timed (preferred)--***order 30 minutes prior to next scheduled dose† If loading dose was given, ***random*** level may be drawn 2 hours after the last loading dose.	† If next scheduled dose is delayed, continue to draw trough at scheduled time. **Can be ordered as total or free/unbound. If "free or unbound" is not indicated on MD order, place order as total.**
Primidone	***Timed (preferred)--***order 30 minutes prior to next scheduled dose†	† If next scheduled dose is delayed, continue to draw trough at scheduled time.

Drug Name	Start Date/Time	Comments
Procainimide (+NAPA) (Procan SR® Pronestyl®)	***Timed (preferred)--***order 30 minutes prior to next scheduled dose†	† If next scheduled dose is delayed, continue to draw trough at scheduled time. For slow release products (Procan SR®), peak to trough variation is minimal therefore, may draw level as soon as the midpoint of the dosing interval
Quinidine	***Timed (preferred)--***order 30 minutes prior to next scheduled dose†	† If next scheduled dose is delayed, continue to draw trough at scheduled time.
Salicylate (Aspirin)	***Timed (preferred)--***order 30 minutes prior to next scheduled dose†	† If next scheduled dose is delayed, continue to draw trough at scheduled time.
Sirolimus (Rapamune®)	***Timed (preferred)--***order 30 minutes prior to next scheduled dose†	† If next scheduled dose is delayed, continue to draw trough at scheduled time.
Tacrolimus (FK 506, Prograf®)	**Oral dosage form**: ***Timed (preferred)--***order 30 minutes prior to next scheduled dose† **Continuous Infusion:** may be ordered as ***Random or Routine***	† If next scheduled dose is delayed, continue to draw trough at scheduled time.
Theophylline (SloBid® TheoDur® Unidur® Slo-Phyllin® Aminophylline)	**Slow release products** **Peak** (*Children only*)--schedule 4 hours after dose. ***(Timed or Nurse Draw Only)*** **NOTE- Peak drug levels should never be drawn earlier than scheduled time without consulting a Pharmacist.** **Trough** (*Adults only*)-- schedule for 30 minutes prior to next scheduled dose. † ***(Timed or Nurse Draw Only)*** **Continuous Infusion** ***Routine*** or ***timed*** levels may be ordered Intermittent IV infusions, Regular absorption oral products, and Liquids **Peak**--schedule 1 hour after dose. ***(Timed or Nurse Draw Only)*** **Trough**--schedule 30 minutes prior to next scheduled dose.† ***(Timed or Nurse Draw Only)***	**Slow release products** include SloBid® TheoDur®, Unidur®, Slo-Phyllin®. † If next scheduled dose is delayed, continue to draw trough at scheduled time. **Continuous and intermittent infusions** utilize aminophylline. **Liquids** are prescribed as theophylline liquid.
Drug Name	**Start Date/Time**	**Comments**

Tobramycin	**Peak** –schedule 30 minutes after a 30 minute infusion ***(Timed or Nurse Draw Only)*** **NOTE- Peak drug levels should never be drawn earlier than scheduled time without consulting a Pharmacist.** **Random**—can be ordered for defined time by prescriber **(*if prescriber orders level for specific time, it should be placed as a "Timed" or "Nurse Draw". If no time specified, order as "Routine")*** **Trough**-- schedule 30 minutes prior to next scheduled dose.† ***(Timed or Nurse Draw Only)***	Peak and Trough usually drawn around the 3rd or 4th dose of starting a new regimen. Random levels are usually done as part of a high dose (5-7 mg/kg once daily) regimen where the level should be drawn 8 - 12 hours (not > 14 hours) after the dose or as part of a pharmacokinetic evaluation. † If next scheduled dose is delayed, continue to draw trough at scheduled time.
Valproic Acid (Depakote®, Depakene®)	***Timed (preferred)--***order 30 minutes prior to next scheduled dose†	† If next scheduled dose is delayed, continue to draw trough at scheduled time. **Can be ordered as total or free/unbound. If "free or unbound" is not indicated on MD order, place order as total.**
Vancomycin	**Random**—can be ordered for defined time by prescriber **(*if prescriber orders level for specific time, it should be placed as a "Timed" or "Nurse Draw". If no time specified, order as "Routine")*** **Trough**-- Schedule 30 minutes prior to next scheduled dose† ***(Timed or Nurse Draw Only)***	Peak levels are generally not indicated except for certain CNS infections. If ordered, draw Peak 1 hour following completion of vancomycin infusion. Peak (if indicated) and Trough are usually drawn around the 3rd or 4th dose of a new regimen. † If next scheduled dose is delayed, continue to draw trough at scheduled time.

DOSE MODIFICATIONS

Adult Dosage Guidelines for Renal Insufficiency

DRUG	CREATININE CLEARANCE (mL/min)			
	≥ 80	**50-79**	**10-49**	**< 10**
Acyclovir	250-500 mg/m^2 q8h	250-500 mg/m^2 q8h	250-500 mg/m^2 q12-24h	250 mg/m^2 q24h
Aztreonam	2g q8h	2g q8h	2g q12h	2g q24h
Cefepime	2 g q8h	2 g q12h (30-60)	2 g q24h (11-29)	1 g q24h
Ciprofloxacin	500 mg PO q12h OR 400mg IV q12h	500 mg PO q12h OR 400mg IV q12h	500 mg PO q18h OR 400 mg IV q18-24 (CrCl < 30)	500 mg PO q18h OR 400 mg IV q18-24 (CrCl < 30)
Fluconazole	100-400 mg q24h	100-400 mg q24h	100-400 mg q48h	100-400 mg q72h
Foscarnet	60 mg/kg q8h	Dose based on CrCl in ml/min/kg – See nomogram in these guidelines		
Ganciclovir	5 mg/kg q12h	2.5 mg/kg q12h (CrCl 50-69)	2.5 mg/kg q24h (CrCl 25-49)	1.25 mg/kg q24h (CrCl < 25)
Gatifloxacin	400mg QD (po or IV)	400mg QD (po/IV)	< 40mL/minute 400mg x 1, then 200mg QD	Hemodialysis/PD: as for < 40mL/min
Imipenem	500 mg q6h	500mg q6-8h (30-70)	500 mg q8-12h (20-30)	250-500 mg q12h (5-20)
Pentamidine	4mg/kg IV q24h	4mg/kg q24h	4mg/kg q24 – 36 h	4mg/kg q48h
TMP/SMX (PCP dosing)	15 – 20mg/kg/day (DDD)	15-20mg/kg/day (DDD)	Q12-24h	q24h
Valganciclovir	900mg BID (CrCl ≥ 60) - I 900mg QD (CrCl ≥ 60) - M	450mg BID (CrCl 40-59) I 450mg QD (CrCl 40-59) M	450mg QD (CrCL 25-39) I 450mg QOD (CrCl 25-39) M	450mg QOD (CrCl 10-24) 450mg 2x/wk (CrCl 10-24)
Vancomycin	15mg/kg q 12 h	See nomogram on page **		

I = induction; M = maintenance

GUIDELINES AND RECOMMENDATIONS FOR DOSING CHEMOTHERAPEUTIC AGENTS IN RENAL FAILURE

Chemotherapeutic Agent	Adjustment for Renal Failure i.e., % dose that should be administered			
	GFR (mL/min)			
	> 60	**30-60 mL/min**	**10 – 30 mL/min**	**< 10 mL/min**
Bleomycin*	100%	50%	OMIT	OMIT
Carboplatin (if NOT AUC dosing)	> 60mL/min: 100%			16 – 40mL/min: 200mg/m^2 < 15mL/min: no data
Carboplatin*	Dose determined by "Calvert formula"			
Cisplatin*	100%	50%	OMIT	OMIT
Cyclophosphamide*	100%	100%	100%	50%
Cytarabine	100%	50%	OMIT	OMIT
Dacarbazine*	100%	75%	50%	OMIT
Etoposide*	100%	100%	100%	50%
Fludarabine*	100%	75%	50%	OMIT
Hydroxyurea*	100%	75%	75%	50%
Ifosfamide*	100%	75%	50%	OMIT
Melphalan*	100%	75%	75%	50%
Methotrexate*	100%	50%	OMIT	OMIT
Mitomycin **	100%	75%	50%	OMIT
Nitrosoureas*	100%	OMIT	OMIT	OMIT
Paclitaxel	100%	100%	100%	100%
Pentostatin*	100%	50%	OMIT	OMIT
Procarbazine	No recommendation, monitor closely in renal failure			
Streptozocin	100%			
Thiotepa	No recommendation, monitor closely as 85% renally eliminated			
Topotecan*	100%	75%	50%	OMIT

References:

* Patterson WP, Reams GP. Renal and electrolyte abnormalities due to chemotherapy (Chapter 41). In: Perry MC, ed. The Chemotherapy Sourcebook, 3rd edition. Philadelphia: Lippincott Williams & Wilkins, 2001:494 – 504.

GUIDELINES AND RECOMMENDATIONS FOR DOSING CHEMOTHERAPEUTIC AGENTS WITH HEPATIC DYSFUNCTION

Chemotherapeutic Agent	Adjustment for Hepatic Dysfunction i.e., give the following % of drug						
	T Bili < 1.5	**SGOT < 60**	**T.Bili 1.5 – 3**	**SGOT 60 – 180**	**T Bili 3.1 – 5**	**SGOT > 180**	**T.Bili > 5**
Cyclophosphamide[*]	100%		100%		75%		OMIT
Cytarabine[#]	50% dose						
Dacarbazine	Unknown, carefully monitor in liver impairment						
Daunorubicin	100%		85%		50%		OMIT
Doxorubicin	< 1.2mg/dL – 100%		1.2 – 3.0 mg/dL – 50%		> 3mg/dL – 25%		_
Doxorubicin[*]	100%		50%		25%		OMIT
Etoposide[*]	100%		50%		OMIT		OMIT
Fluorouracil[*]	100%		100%		100%		OMIT
Idarubicin[**]	_		≥ 2.5mg/dL – 50%		_		OMIT
Melphalan	No dose reduction						
Methotrexate	100%		100%		75%		OMIT
Mitoxantrone	100%		50%		25%		_
Navelbine	< 2mg/dL 30mg/m^2		2.1 – 3 mg/dL 15mg/m^2		> 3mg/dL 7.5mg/m^2		_
Paclitaxel[#]	≤ 1.5mg/dL 75%		1.6 – 2.9mg/dL – 40%		≥ 3mg/dL – 25%		_
Vinblastine	100%		50%		50%		OMIT
Vinblastine[*]	100%		50% > 3mg/dL		OMIT		OMIT
Vincristine	100%		100%		50% >3mg/dL		-
Vincristine[*]	100%		50%		OMIT		OMIT

References:

[*] King PD, Perry MC. Hepatotoxicity of Chemotherapeutic Agents (Chapter 40). In: Perry MC, ed. The Chemotherapy Sourcebook, 3rd edition. Philadelphia: Lippincott Williams & Wilkins, 2001:483 – 93.

[#] King PD, Perry MC. Hepatotoxicity of Chemotherapy. *The Oncologist* 2001; 6:162 – 76.

[**] Dorr R. Handbook of Chemotherapy. 2nd Edition.

Table 8.6.9. Common drugs in BMT that need dosage adjustment

Drug	CrCl (ml/min/70 kg)				
	> 80	50-80	20-50	< 20	Dialyzed
Acyclovir	5 mg/kg q8°	same	q12-24°	2.5 mg/kg q24°	Yes
Allopurinol	300 mg/d	75%	50%	25%	Yes
Aminoglycosides'	100% (q8-12°)	60-90% (q12°)	30-60%(q12-24°)	10-30% (q24-48°)	Yes
Amphotericin	0.5-1.0 mg/kg/d	same	same	q36-48°	No
Ampicillin	0.5-2 g q4-6°	same	75%	50%	Yes
Azathioprine	0.5-3 mg/kg/d	same	75%	50%	Yes
Aztreonam	1-2 g q8°	same	0.5-1g q12°	0.5g q12°	Yes
Cefazolin	1-2 g q8°	q8°	0.5-1g q12°	0.5g q24°	Yes
Cefaperazone	1-2 g q12°	same	same	same	No
Cefotaxime	1 g q6°	q6°	q8-12°	q24°	Yes
Cefoxitin	1-2 g q6-8°	q8°	q12°	q24°	Yes
Ceftazidime	1-2 g q8°	q8-12°	1g q12-24°	0.5g q24°	Yes
Ceftizoxime	1-2 g q6-8°	q8-12°	1g q12-24°	0.5g q24°	Yes
Ceftriaxone	0.5-1 g q12-24°	same	same	same-q24°	No
Clindamycin	600-900 mg q8°	same	same	same	No
Cimetidine	400 mg q12°	same	50%	25%	Yes
Ciprofloxocin	250-750 mg q12°	same	50-75%	50%	No
Compazine	5-10 mg q6°	same	same	same	NA
Cyclosporine*	3-10 mg/kg/day	same	same	same	No
Clarithromycin	500 mg q12°	same	75%	50%	Yes
Erythromycin	250-750 mg q6°	same	same	50-75%	No
Ethambutol	15 mg/kg/d	same	same	q48°	Yes
Famotidine	20-40 mg q24°	same	50%	25%	No
Fluconazole	200-400 mg/d	same	50-100 mg/day	50 mg/day	Yes
FK 506*	0.1-0.5 mg/kg/day	same	same	same	No
Ganciclovir	5 mg/kg q12°	same	25-50%	12%	Yes
Imipenim/Cilastin	0.25-1 g q6°	same	50%	< 25%	Yes
Isoniazide	300 mg/d	same	same	50%	Yes
Itraconazole	100-200 mg q12°	same	same	same	No
Methotrexate	up to 12 g/m²	same	50%	?	No
Metoclopramide	10-40 mg QID	same	75%	50%	No
Metronidazole	250-750 mg q8°	same	same	50%	Yes
Norfloxacin	400 mg q12°	q12-24°	q24°	avoid	No
Odansetron	0.15-0.45 mg/kg	same	same	same	No
Omeprazole	20 mg/d	none	none	none	No
Pentamidine	4 mg/kg/d	same	q36°	q48°	No
Piperacillin	3-4 g q4-6°	same	75%	50%	Yes
Ranitidine	300 mg/d PO	75%	50%	25%	Yes
Ticarcillin	3-4 g q4-6°	same	50%	25%	Yes
Trimethoprim-sulfamethoxazole	5-20 mg/kg/d of TMP	same	50-75%	25%	Yes
Ursodeoxy-cholic acid	300-600 mg PO BID-TID	same	same	same	No
Vancomycin'	15 mg/kg q12°	15 mg/kg q24-36°	15 mg/kg q36-48°	15 mg/kg q3-7 days	No

*Some centers adjust FK 506 and cyclosporine dose on renal function—refer to GVHD chapter
'Refer to drug-specific dosing information ° = hour

INFECTION

Cultures

Cultures for Initial Spike

PATIENT TYPE	CULTURE	COMMENT
All Patients (Initial Spike)	Obtain 2 sets (2 x anaerobic and 2 x aerobic) of bacterial **blood** cultures and one **urine** culture. Obtain **CVL** cultures through each port and label exact source of cultures in the computer system.	Obtain prior to initiation of antibiotic therapy. NOTE: If the patient is unable to produce urine, do not hold antibiotics. Administer antibiotics and perform a UA and culture as soon as possible.

Surveillance Cultures

Allogeneic [HLA-matched siblings, MUD's and cords]	Weekly CMV antigenemia assay every Monday (ALL patients, including D/R CMV -/- status)	Begin the first Monday after Day +17 (ANC must be > 500) or when the ANC > 500 and continue up to Day +100 or until off aGVHD therapy
All patients on antibiotics who continue to be febrile (Temp $\geq 38.5^{o}C$)	Obtain bacterial blood cultures from CVL daily (every 24 hours)	Day starts at 2400
Patients with diarrhea of 10cc/kg/24hours	*Clostridium difficile* (*C.Diff*) stool QD x 3 separate stool samples	Do not do cultures if diarrhea is within 24hrs of chemotherapy or patient not on broad spectrum antibiotics recently
Chronic GVHD	Weekly CMV antigenemia assay every Monday/or upon return clinic visit	Start when GVHD treatment starts

Ongoing Monitoring

Positive Blood Cultures	Daily Blood Cultures from CVL until advised by the attending physician	Continue with daily blood cultures in patients with positive cultures even if the patient is afebrile. Need to document clearance of infection. Please draw 1 repeat set after completion of treatment course.
All	Heme positive urine	Send urine for urinalysis.

**Other cultures as clinically indicated (e.g., sputum, wound, CSF, etc.)

Adult Allogeneic BMTU Antimicrobial Prophylaxis

Patient Type	*Start Date*	*Drug*	*Dose/Route/Frequency*	*Stop Date*
All Allogeneic Patients	Day 0	GATIFLOXACIN (Tequin®)	400mg PO/IV QD	Temperature spike OR ANC > 250
All Allogeneic Patients	Day 0	FLUCONAZOLE (Diflucan®)	200mg PO/IV	When ANC > 250 OR when Amphotericin B started
All non-myeloablative patients (mini's)	ANC < 500	GATIFLOXACIN FLUCONAZOLE	400mg PO/IV QD 200mg PO/IV	Temperature spike OR ANC > 250
Allogeneic patients with GVHD on steroids	When steroids start	FLUCONAZOLE (Diflucan®)	100mg PO daily	When steroids stop
All Patients(unless sulfa-Allergic)	Begin weekend following engraftment	TRIMETHOPRIM/ SULFAMETHOXAZOLE (Septra®)	1 Double Strength Tab given QD on Sat/Sun/Mon	Day +180
Sulfa-Allergic Patients	Begin the weekend following engraftment	ATOVAQUONE DAPSONE or PENTAMIDINE	1500mg three times/week 100 mg PO QD Pent: 300mg inhalation qmonth	Day +180
HSV positive	Day 0	VALACYCLOVIR (Valtrex®)	500mg PO daily	ANC > 250 OR when unable to tolerate oral medications
HSV positive	When unable to tolerate oral meds	ACYCLOVIR (Zovirax®)	250mg IV q12h	ANC > 250 OR when patients able to tolerate oral medication
VZV positive	Engraftment	ACYCLOVIR VALACYCLOVIR	800mg PO BID 500mg PO QD	12 months from start date

Adult Autologous BMTU Antimicrobial Prophylaxis

Patient Type	*Start Date*	*Drug*	*Dose/Route/Frequency*	*Stop Date*
ALL	Day 0	GATIFLOXACIN (Tequin®)	400mg PO/IV QD	Temperature spike OR ANC > 250
ALL	Day 0	FLUCONAZOLE (Diflucan®)	100mg PO/IV QD	ANC > 250 OR when Amphotericin B starts
All Patients (Unless sulfa-allergic)	Begin weekend following engraftment	TRIMETHOPRIM/ SULFAMETHOXAZOLE (Septra®)	1 Double Strength Tab QD on Sat/Sun/Mon	Day +180
Sulfa-Allergic Patients	Begin weekend following engraftment	ATOVAQUONE* Or DAPSONE or PENTAMIDINE	1500mg three times/wk 100 mg PO QD Pent: 300mg inh qmonth	Day +180
HSV positive patients	Day 0	VALACYCLOVIR (Valtrex®)	500mg PO daily	ANC > 250 OR when patient unable to tolerate oral medication
HSV positive Patients	Day 0	ACYCLOVIR (Zovirax®)	250mgIV q12h	ANC > 250 OR when patient able to tolerate oral medications
VZV positive pts	Engraftment	ACYCLOVIR VALACYCLOVIR	800mg PO BID 500mg PO QD	12 months from start date

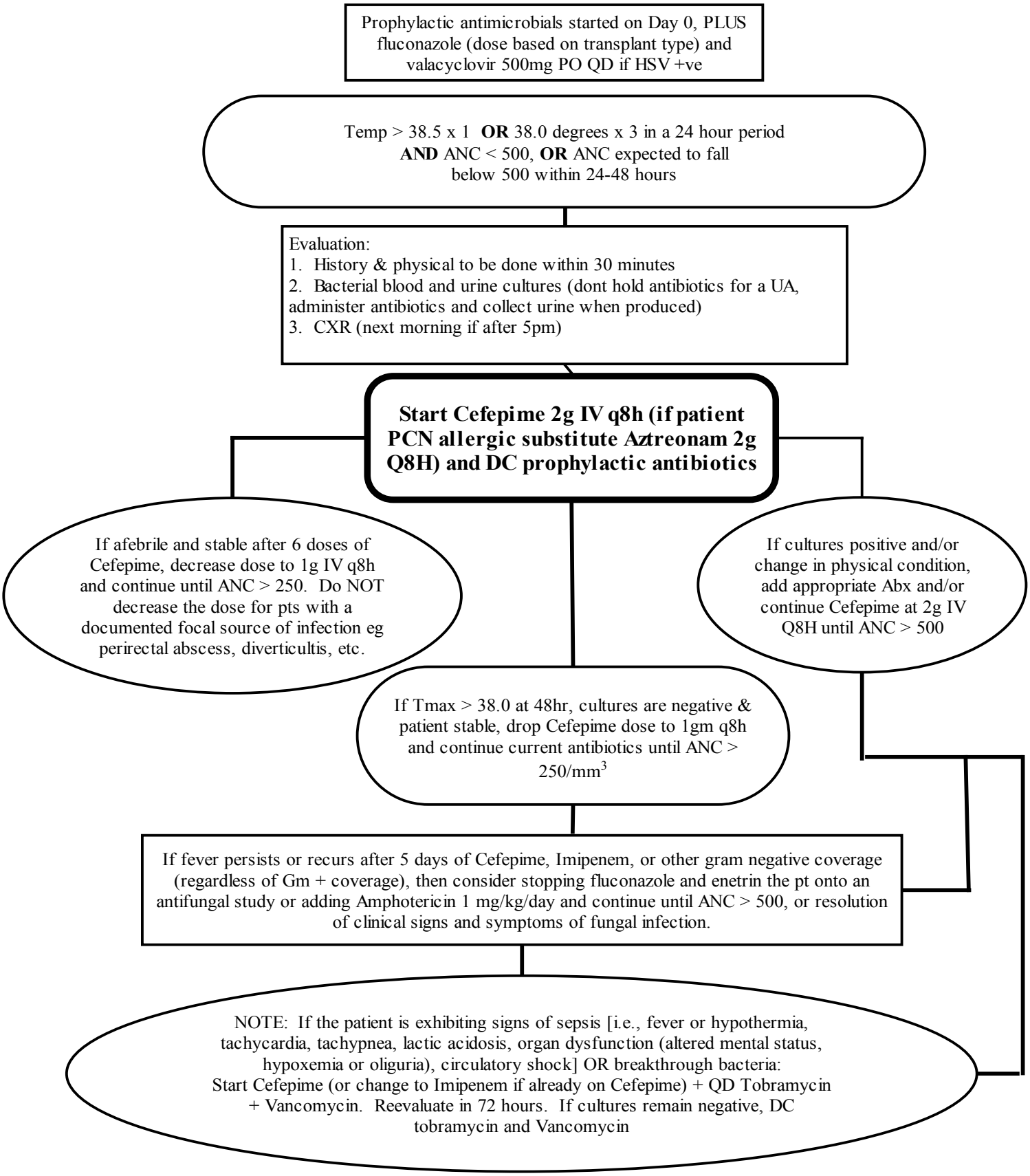
* Reference: Colby C, et al. *BMT* 1999; 24:897 – 902.

Adult Leukemia Antimicrobial Prophylaxis

Patient Type	*Start Date*	*Drug*	*Dose/Route/Frequency*	*Stop/Change Date*
All Adult	When ANC < 500	GATIFLOXACIN (Tequin®)	400mg PO/IV QD	Temperature spike OR ANC > 250
All Patients	When ANC < 500	FLUCONAZOLE (Diflucan®)	100mg PO/IV QD*	When ANC > 250 on recovery OR when Amphotericin B started
HSV positive patients	When ANC < 500	VALACICLOVIR (Valtrex®)	500mg PO daily	When unable to tolerate oral medications OR ANC > 250 OR develops an active herpes infection (simplex or zoster)
HSV positive Patients	When unable to tolerate oral medication	ACYCLOVIR (Zovirax®)	250mg IV q12h	ANC > 250 OR when patient able to tolerate oral medications OR when patient develops an active herpes infection

*Fluconazole 100mg to be used for 7-3, FLAG or HIDAC protocols

ADULT FEBRILE NEUTROPENIA ALGORITHM



1. If using aztreonam it is NOT necessary to add vancomycin empirically unless there is a definite suspicion of a gram-positive infection. There are no data to support dose reduction of aztreonam, and therefore the dose must remain at 2g Q8H throughout.

2. If the pt becomes afebrile on CEF 1g Q8H, then respikes, only increase the CEF dose if there are signs of sepsis/signs of infection i.e. perirectal abscess. If the patient is stable, continue at 1g.

STANDARD INPATIENT NEUTROPENIC NEW FEVER ORDERS

(1) Vitals including orthostatic blood pressure and pulse, oxygen saturation, and respiratory rate

(2) Call PA/MD if:
- Mental status changes evident,
- Orthostatic,
- Systolic pressure < 90mmHg,
- Respiratory rate > 30,
- Oxygen saturation < 90%

(3) Laboratory: blood cultures x 2 sets (i.e., 4 bottles); urine culture.

(4) Radiology: portable chest, evaluate for infiltrate (schedule in AM if after 5pm)

(5) Antibiotic:

After asking about allergies start antibiotic orders

Cefepime 2g every 8 hours IV (if penicillin allergic administer aztreonam 2g every 8 hours)

Call PA/MD if antibiotic not running within one hour of initial fever

If Systolic pressure < 90mmHg

- Add Vancomycin 15mg/kg IV q12hr (dose assuming normal renal function). If elevated SCr contact clinical pharmacist for a dosing recommendation (see nomogram)
- Add Tobramycin or Gentamicin 7 mg/kg Ideal body weight IV QD. For those patients > 20% over IBW, dose based on an adjusted body weight
  (Adjusted Body Wt = IBW + 0.4 (TBW-IBW). Note if the patient's serum creatinine is not within normal limits then the dose should be modified. Contact the clinical pharmacist by pager.
- Send random serum Tobramycin/Gentamicin level 10 hours after first Tobramycin/Gentamicin dose
- D/C Vancomycin after 48 hours if blood cultures negative (even if fever does not resolve)
- D/C Tobramycin after 72 hours if blood cultures negative

Stress Dose Steroids:

For patients that have received steroids for greater than one month duration within the previous three months consider stress dose steroids during an acute illness, injury, or perioperative period.

Adults:

Hydrocortisone 50mg IV q8h x 48 hour's then taper dose over next three days to prior maintenance dose.

VANCOMYCIN USAGE

Situations in which the use of vancomycin is appropriate or acceptable:

1. For treatment of serious infections caused by beta-lactam- resistant gram-positive microorganisms. Vancomycin may be less rapidly bactericidal than are beta-lactam agents for beta-lactam- susceptible staphylococci.
2. For treatment of infections caused by gram-positive microorganisms in patients who have serious allergies to beta-lactam antimicrobials.
3. When antibiotic-associated colitis fails to respond to metronidazole therapy or is severe and potentially life threatening.
4. Prophylaxis, as recommended by the American Heart Association, for endocarditis following certain procedures in patients at high risk for endocarditis
5. Prophylaxis for major surgical procedures involving implantation of prosthetic materials or devices (e.g., cardiac and vascular procedures and total hip replacement) at institutions that have a high rate of infections caused by MRSA or methicillin-resistant *S. epidermidis*. A single dose of vancomycin administered immediately before surgery is sufficient unless the procedure lasts greater than 6 hours, in which case the dose should be repeated. Prophylaxis should be discontinued after a maximum of two doses.

Situations in which the use of vancomycin should be discouraged:

1. Routine surgical prophylaxis other than in a patient who has a life-threatening allergy to beta-lactam antibiotics.
2. Empiric antimicrobial therapy for a febrile neutropenic patient unless initial evidence indicates that the patient has an infection caused by gram-positive microorganisms (e.g., at an inflamed exit site of Hickman catheter) and the prevalence of infections caused by MRSA in the hospital is substantial.
3. Treatment in response to a single blood culture positive for coagulase-negative staphylococcus, if other blood cultures taken during the same time frame are negative (i.e., if contamination of the blood culture is likely). Because contamination of blood cultures with skin flora (e.g., *S. epidermidis*) could result in inappropriate administration of vancomycin, phlebotomists and other personnel who obtain blood cultures should be trained to minimize microbial contamination of specimens.
4. Continued empiric use for presumed infections in patients whose cultures are negative for beta-lactam-resistant gram-positive microorganisms.
5. Systemic or local (e.g., antibiotic lock) prophylaxis for infection or colonization of indwelling central or peripheral intravascular catheters.
6. Selective decontamination of the digestive tract.
7. Eradication of MRSA colonization.
8. Primary treatment of antibiotic-associated colitis.
9. Routine prophylaxis for very low-birthweight infants (i.e., infants who weigh less than 1,500 g.
10. Routine prophylaxis for patients on continuous ambulatory peritoneal dialysis or hemodialysis.
11. Treatment (chosen for dosing convenience) of infections caused by beta-lactam-sensitive gram-positive microorganisms in patients who have renal failure.
12. Use of vancomycin solution for topical application or irrigation

Reference: Recommendations for Preventing the Spread of Vancomycin Resistance Recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC). *MMWR* 1995; 44(RR12): 1-13

VANCOMYCIN DOSE MODIFICATION NOMOGRAM

Emory University Hospital Nomogram

Total body weight (kg)	CrCl 80-120 mL/min Q12H	CrCl 60-79 mL/min Q24H	CrCl 40-59 mL/min Q24H	CrCl 20-39 mL/min Q48H	
40-49	500mg	1000mg	750mg	1000mg	Consult Kinetics Service
50-59	750mg				
60-69	1000mg	1250mg	1000mg	1250-1500mg	
70-79		1500mg	1250mg	1500mg	
80-89	1250mg	1500-1750mg	1500mg	1500-1750mg	
90-100	1250-1500mg	1750mg		2000mg	

Creatinine clearance is estimated using the Cockcroft-Gault Equation (SCr is rounded up to 1 mg/dL for patients > 60 years old). No serum concentrations are obtained unless the duration of therapy is > 7 days in which case troughs are obtained weekly for the duration of therapy. If CNS penetration is needed or an *Enterococcal* infection is suspected, a trough is obtained on Day 5.

Dosing Adjustments for Vancomycin Troughs	
5-15 mcg/mL	Continue
< 5 mcg/mL	Increase dose by 250 mg
16-19 mcg/mL	Decrease dose by 250 mg
20-25 mcg/mL	Widen interval by 12 hours
> 25 mcg/mL	Hold dose, consult kinetics service

Source: Emory University Hospital, Department of Pharmacy

Cockcroft and Gault Formula:

$$CrCl = \frac{[140 - \text{Age (years)}] \times \text{IBW (Kg)}}{72 \times \text{SCr (mg/dL)}}$$

Females: 0.85 x above

PULSE-DOSE AMINOGLYCOSIDES

Dose:

7mg/kg for gentamicin/tobramycin
15mg/kg for amikacin

Dosing Weight:

Ideal Body Weight (kg), UNLESS patients are > 20% over their ideal body weight in which case an adjusted weight should be used

Formulas for Ideal Body Weight:

Male = 50kg + 2.3 (number of inches > 60)
Female = 45.5kg + 2.3(number of inches > 60)
Adjusted Weight = 0.4 [actual weight (kg) – ideal weight (kg)] + Ideal weight

Dosing Interval (initial):

CrCl (mL/min)	Interval
> 60	Q 24 hours
40 – 59	Q 36 hours
20 – 39	Q 48 hours

$$\text{CrCl} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{SCr (mg/dL)} \times 72}$$

Females = multiply above equation by 0.85

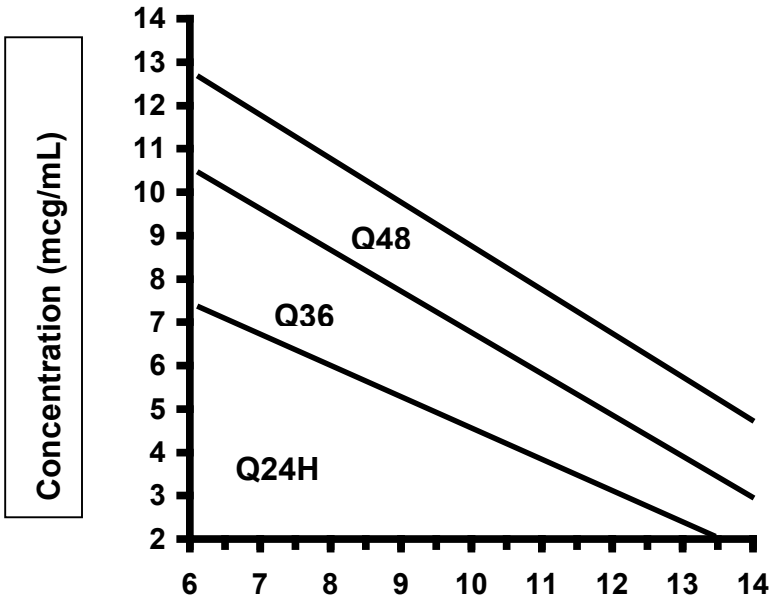
Exclusion Criteria for Pulse-Dosing:

Ascites; > 20% burn; cystic fibrosis; end stage renal disease; *Enterococcal* endocarditis; hypermetabolic state; pregnancy; pediatric patients

Laboratory Recommendations:

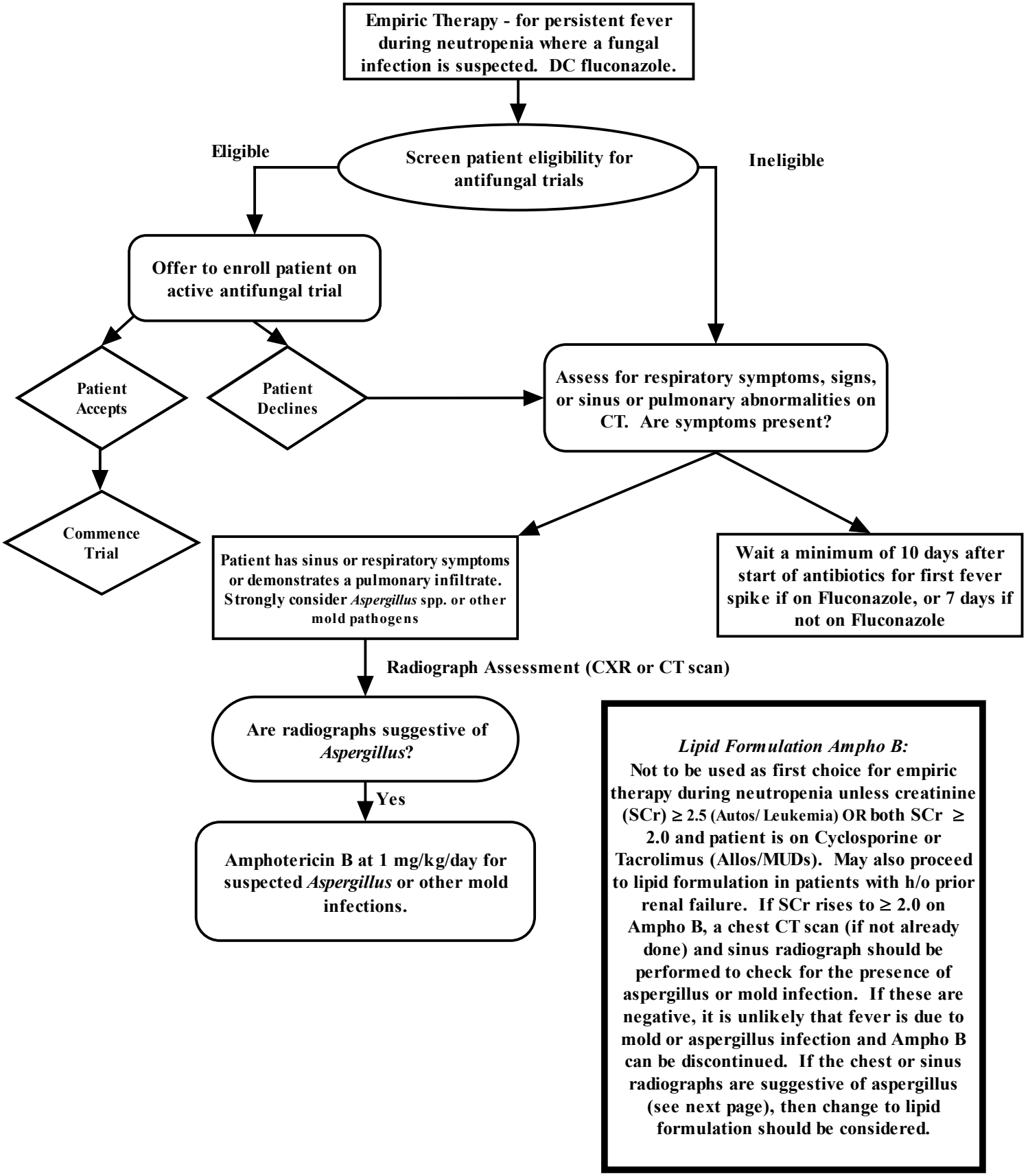
Day 1: baseline SCr, RANDOM level 8 – 12 hours post—infusion
Day 3: SCr
Day 5: SCr and repeat RANDOM level 8 – 12 hours post-infusion

NOTE: In patients with elevated SCr, the random level is not a reliable indicator of aminoglycoside clearance, and in these circumstances as true TROUGH level (i.e., immediately prior to the next dose) should be drawn and should be < 0.4mg/dL. Please consult your clinical pharmacist for further advice on the dose and dosing interval.

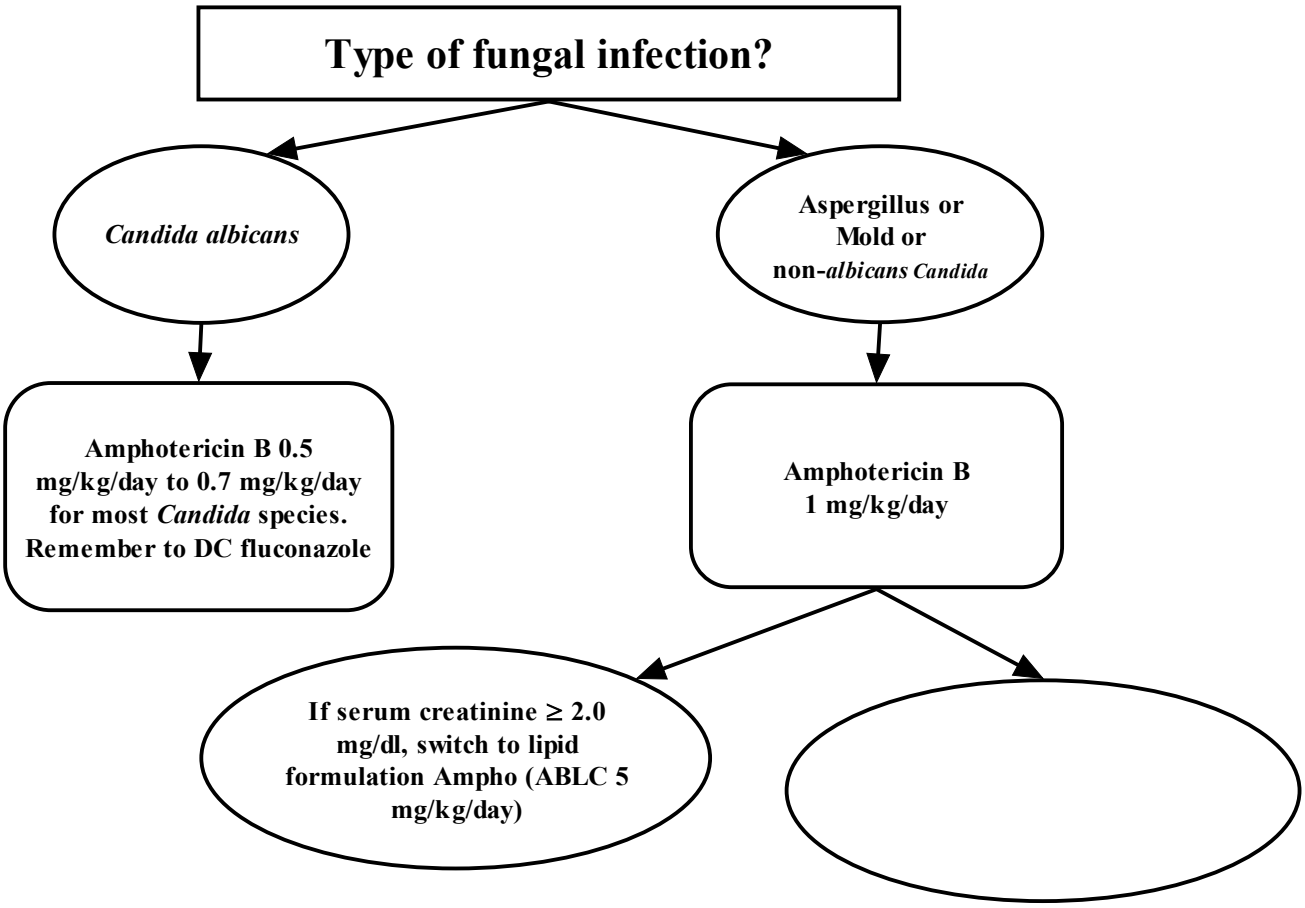


Reference: ***Antimicrob Agents Chemother*** **1995; 39(3): 650 – 55.**

Antifungal Therapy



Proven or Probable Fungal Infections



Severe nephrotoxicity is rare in autologous BMT patients and non-transplant patients and the use of a lipid Amphotericin B should be infrequent. In contrast, in patients receiving cyclosporine or tacrolimus (FK506), the probability of severe nephrotoxicity is substantial and the creatinine should be monitored carefully.

Criteria for Proven, Probable, or Suspected Fungal Infections: see next pages

DEFINITIONS OF IFI IN PATIENTS WITH CANCER OR UNDERGOING HSCT

Category, type of infection	Description
Proven invasive fungal infections	
Deep tissue infections	
Molds[a]	Histopathologic or cytopathologic examination showing hyphae from needle aspiration or biopsy specimen with evidence of associated tissue damage (either microscopically or unequivocally by imaging); or positive culture result for a sample obtained by sterile procedure from normally sterile and clinically or radiologically abnormal site consistent with infection, excluding urine and mucous membranes
Yeasts[a]	Histopathologic or cytopathologic examination showing yeast cells *(Candida* species may also show pseudohyphae or true hyphae) from specimens of needle aspiration or biopsy excluding mucous membranes; or positive culture result on sample obtained by sterile procedure from normally sterile and clinically or radiologically abnormal site consistent with infection, excluding urine, sinuses, and mucous membranes; or microscopy(India ink, mucicarmine stain) or antigen positivity[b] for *Cryptococcus* species in CSF
Fungemia	
Molds[a]	Blood culture that yields fungi, excluding *Aspergillus* species and *Penicillium* species other than *Penicillium marneffei,* accompanied by temporally related clinical signs and symptoms compatible with relevant organism
Yeasts[a]	Blood culture that yields *Candida* species and other yeasts in patients with temporally related clinical signs and symptoms compatible with relevant organism
Endemic fungal infections[c]	
Systemic or confined to lungs	Must be proven by culture from site affected, in host with symptoms attributed to fungal infection; if culture results are negative or unattainable, histopathologic or direct microscopic demonstration of appropriate morphological forms is considered adequate for di-morphic fungi *(Blastomyces, Coccidioides* and *Paracoccidioides* species) having truly distinctive appearance; *Histoplasma capsulatum* variant *capsulatum* may resemble *Candida glabrata*
Disseminated	May be established by positive blood culture result or positive result for urine or serum antigen by means of RIA
Probable invasive fungal infections	At least 1 host factor criterion (see page 87); and 1 microbiological criterion; and 1 major (or 2 minor) clinical criteria from abnormal site consistent with infection
Possible[d] invasive fungal infections	At least 1 host factor criterion; and 1 microbiological or 1 major (or 2 minor) clinical criteria from abnormal site consistent with infection

[a] Append identification at genus or species level from culture, if available ; [b] False-positive cryptococcal antigen reactions due to infection with *Trichosporon beigelii* [1], infection with *Stomatococcus mucilaginosis* [2], circulating rheumatoid factor [3], and concomitant malignancy [4] may occur and should be eliminated if positive antigen test is only positive result in this category. [c] Histoplasmosis, blastomycosis, coccidioidomycosis, and paracoccidioidomycosis. [d] This category is not recommended for use in clinical trials of antifungal agents but might be

considered for studies of empirical treatment, epidemiological studies, and studies of health economics.

Host factor, microbiological, and clinical criteria for invasive fungal infections in patients with cancer and recipients of hematopoietic stem cell transplants.

Type of criteria	Criteria
Host factors	Neutropenia (<500 neutrophils/mm^3 for > 10 days)
	Persistent fever for > 96 h refractory to appropriate broad-spectrum antibacterial treatment in high-risk patients
	Body temperature either > 38°C or < 36°C and any of the following predisposing conditions: prolonged neutropenia (>10 days) in previous 60 days, recent or current use of significant immunosuppressive agents in previous 30 days, proven or probable invasive fungal infection during previous episode of neutropenia, or coexistence of symptomatic AIDS
	Signs and symptoms indicating graft-versus-host disease, particularly severe (grade $\geq$2) or chronic extensive disease
	Prolonged (> 3 weeks) use of corticosteroids in previous 60 days
Microbiological	Positive result of culture for mold (including *Aspergillus, Fusarium,* or *Scedosporium* species or Zygomycetes) or *Cryptococcus neoformans* or an endemic fungal pathogen[a] from sputum or bronchoalveolar lavage fluid samples
	Positive result of culture or findings of cytologic/direct microscopic evaluation for mold from sinus aspirate specimen
	Positive findings of cytologic/direct microscopic evaluation for mold or *Cryptococcus* species from sputum or bronchoalveolar lavage fluid samples
	Positive result for *Aspergillus* antigen in specimens of bronchoalveolar lavage fluid, CSF, or $\geq$ 2 blood samples
	Positive result for cryptococcal antigen in blood sample[b]
	Positive findings of cytologic or direct microscopic examination for fungal elements in sterile body fluid samples (e.g., *Cryptococcus* species in CSF)
	Positive result for *Histoplasma capsulatum* antigen in blood, urine, or CSF specimens
	Two positive results of culture of urine samples for yeast in absence of urinary catheter
	Candida casts in urine in absence of urinary catheter
	Positive result of blood culture for *Candida* species
Clinical	Must be related to site of microbiological criteria and temporally related to current episode
Lower respiratory tract infection	
Major	Any of the following new infiltrates on CT imaging: halo sign, air-crescent sign, or cavity within area of consolidation[c]
Minor	Symptoms of lower respiratory tract infection (cough, chest pain, hemoptysis, dyspnea); physical finding of pleural rub; any new infiltrate not fulfilling major criterion; pleural effusion
Sinonasal infection	
Major	Suggestive radiological evidence of invasive infection in sinuses (i.e., erosion of sinus walls or extension of infection to neighboring structures, extensive skull base destruction)
Minor	Upper respiratory symptoms (e.g., nasal discharge, stuffiness); nose ulceration or eschar of nasal mucosa or epistaxis; periorbital swelling; maxillary tenderness; black necrotic lesions or perforation of hard palate
CNS infection	

Major	Radiological evidence suggesting CNS infection (e.g., mastoiditis or other parameningeal foci, extradural empyema, intraparenchymal brain or spinal cord mass lesion)
Minor	Focal neurological symptoms and signs (including focal seizures, hemiparesis, and cranial nerve palsies); mental changes; meningeal irritation findings; abnormalities in CSF biochemistry and cell count (provided that CSF is negative for other pathogens by culture or microscopy and negative for malignant cells)

Disseminated fungal infection

Papular or nodular skin lesions without any other explanation; intraocular findings suggestive of hematogenous fungal chorioretinitis or endophthalmitis

Chronic disseminated candidiasis

Small, peripheral, targetlike abscesses (bull's-eye lesions) in liver and/or spleen demonstrated by CT, MRI, or ultrasound, as well as elevated serum alkaline phosphatase level; supporting microbiological criteria are not required for probable category

Candidemia Clinical criteria are not required for probable candidemia; there is no definition for possible candidemia

[a] *H. capsulatum* variant *capsulatum, Blastomyces dermatitidis, Coccidioides immitis,* or *Paracoccidioides brasiliensis.*
[b] See table 1 footnote *b* for causes of false-positive reactions that must be considered and eliminated from consideration.
[c] In absence of infection by organisms that may lead to similar radiological findings including cavitation, such as *Mycobacterium, Legionella,* and *Nocardia* species.

CONVENTIONAL AMPHOTERICIN B ADMINISTRATION GUIDELINES SHANDS HEALTHCARE BONE MARROW TRANSPLANT UNIT

1. Test doses are not required

2. Premedication required for conventional Amphotericin B administration:

   (1) Acetaminophen 650mg PO 30 minutes prior to Amphotericin B administration

   (2) Diphenhydramine (Benadryl®) 25mg IV/PO 30 minutes prior to amphotericin B administration

   (3) Hydrocortisone 50mg IV 30 *minutes prior to the first 3 doses only*.

   (4) Meperidine 25mg IV prn for chills (may repeat once only). NOTE: in those patients with pre-existing renal impairment, repeated doses of meperidine should be avoided due to the risk of accumulation of nor-meperidine, which can precipitate seizure activity. In these cases prescribe morphine 2 – 5mg IV prn).

   (5) Normal saline 500mL over 1 – 2 hours prior to Amphotericin B should be administered to ALL patients pending fluid status review. Post-hydration is NOT necessary.

Following 3 days of hydrocortisone therapy, the patient should be given subsequent doses without hydrocortisone cover. Should the patient continue to experience chills and rigors, then hydrocortisone may be reintroduced but the appropriate heme-onc fellow or attending physician must be notified.

3. Dose recommendations:

   0.5 – 0.7mg/kg/day for *Candida* spp; and

   1mg/kg/day (maximum 1.5mg/kg/day) for Aspergillus spp. and mold infections

4. Administration guidelines:

Amphotericin B is traditionally administered over 4 – 6 hours. The infusion rate can be reduced to 2 hours in the following circumstances:

(a) Stable renal function, $\leq$ 25% change in CrCL during the last 5 days of amphotericin B therapy
(b) Calculated CrCL > 50mL/min and SCr < 2mg/dL

(c) No history of cardiac disease

TREATMENT OF VIRAL INFECTIONS

HERPES ZOSTER

Severe (> 1 dermatome, trigeminal nerve or disseminated):

- Acyclovir 500mg/m^2/dose (or 10 mg/kg/dose) IV q8h for 7 days; may continue for an additional 7 days if new vesicles continue to appear beyond day 5 (given as one hour infusion; ensure patient is well hydrated).

Not severe or as follow up to IV dosing regimen (patients must be watched carefully):

- Valacyclovir (Valtrex®) 1000mg PO TID x 7 days
- Famciclovir (Famvir®) 500mg PO TID x 7 days – ***NON-FORMULARY***

HERPES SIMPLEX (Mucocutaneous)

Treatment:

Severe (Grade 3+ mucositis, cutaneous dissemination):

- Acyclovir 250mg/m^2/dose (or 5 mg/kg/dose) IV q8h for 7 days; may continue for an additional 7 days if new vesicles continue to appear beyond day 5.

Not severe or as follow up to IV dosing regimen:

- Valacyclovir 500mg po TID (14 – 21 days total treatment course)
- Acyclovir 400mg PO 5 times daily (14-21 days-total treatment course)

Prophylaxis:

- Valacyclovir 500mg PO QD until ANC > 250 OR
- Acyclovir 250 mg dose IV q12h (if patient unable to take PO). Oral acyclovir dose is 400mg PO TID.

CYTOMEGALOVIRUS (CMV):

CMV antigenemia testing weekly post engraftment (or day +17) through Day +100

CMV Disease (interstitial pneumonia, etc)

Ganciclovir 5 mg/kg IV q12h x 14 days, then
Maintenance Ganciclovir 5 mg/kg IV QD x 30 days
Add IVIG 500 mg/kg IV QOD x 14-21 days (Use Cytogam® if IVIG unavailable)
Cytogam 400 mg/kg IV on days 1, 2, and 7; then 200 mg/kg on day 14
May continue CMV treatment for continued symptoms or acute infection

CMV Viremia only:

Ganciclovir 5 mg/kg IV q12h x 14 days then
Maintenance Ganciclovir 5 mg/kg IV QD Monday-Friday x 7 days then return to weekly CMV antigenemia testing
If pt able to tolerate oral medications, consider starting therapy with Valcyte 900mg PO BID for 2 weeks, followed by 900mg PO QD x 7 days.
For suspected CMV resistance, consider Foscarnet 60 mg/kg/dose IV q8h or 90 mg/kg/dose IV q12 (must adjust for renal dysfunction – see recommendations in this section)

For persistent antigenemia see guidelines on following pages.

INDICATION	REGIMEN (ADULTS)	START	DURATION
HERPES SIMPLEX VIRUS			
Prophylaxis			
Able to tolerate oral medications	Valacyclovir 500mg po qd	Day zero	Until neutrophil recovery; ANC > 250
Unable to tolerate oral medications	Acyclovir 250mg IV q12h	When patient unable to continue with oral medications	Until mucosa improves then change to oral medications
Treatment			
Severe	Acyclovir 250mg/m^2 (or 5mg/kg) IV q8h	At diagnosis	x 7 – 14 days (see note # 1)
Not severe or as follow-up to IV therapy	Acyclovir 400mg PO 5x/day for 14 – 21 days	Following IV therapy or at diagnosis according to severity	Total course length of 14 days
CYTOMEGALOVIRUS			
Pre-emptive therapy*			
Induction	Ganciclovir 5mg/kg q12h OR Valcyte® 900mg PO BID	Weekly antigenemia returns positive x 1 (see note # 2)	x 14 days x 14 days
Maintenance	Ganciclovir 5mg/kg IV QD x 1 week OR Valcyte® 900mg PO QD	After induction After induction	x 7 days then return to weekly CMV antigenemia testing x 7 days as above
Treatment e.g. colitis, pneumonia			
Induction	Ganciclovir 5mg/kg q12h IVIG see note #3	At diagnosis	x 14 days
Maintenance	Ganciclovir 5mg/kg IV qd IVIG – See note # 3	After induction	x 30 days (M – F only)
VARICELLA-ZOSTER VIRUS			
Treatment	Acyclovir 500mg/m^2 (OR10mg/kg) IV q8h	At diagnosis	x 10 – 14 days (see note # 4)
Prophylaxis following exposure to infected individual	Varicella-zoster immunoglobulin 5 vials (1.25mL each or 625 unit's total) intramuscularly. For pediatric dosing see note # 5	Administer within 96 hours (preferably within 48 hours) after close contact with a person who has chickenpox or shingles	X 1 dose

VARICELLA-ZOSETER VIRUS			
Prophylaxis against reactivation	Acyclovir 800mg PO BID Valacyclovir 500mg PO QD	At engraftment	For 12 months post initiation
ADENOVIRUS			
Treatment	Cidofovir (See note # 5 for dose)	At diagnosis	Until clinical resolution and clearance from original site

NOTES:

1. Treat initially for 7 days, but may continue with another 7 days of IV therapy if new vesicles continue to appear beyond day 5

2. Ganciclovir should be started in allogeneic patients when there is any degree of CMV antigenemia. For autografts, start when antigenemia is $\geq$ 5 cells/slide. For CD34 selected autografts start GCV with any degree of antigenemia. Depending upon the underlying patient issues this will be a clinical decision e.g. presence of active GVHD, falling WBC count and the degree of positivity on the slides all guide practice. If concerned repeat the CMV antigenemia on Thursday.

3. IVIG 500mg/kg QOD x 14 – 21 days should also be administered. If IVIG is unavailable use Cytogam® at 400mg/kg IV on days 1, 2 and 7; then 200mg/kg on day 14.

4. For severe VZV infections (> 1 dermatome, trigeminal nerve or disseminated) start with IV dosing for 7 days. This may be continued for an additional 7 days if new vesicles continue to appear beyond day 5. For non-severe cases (1 dermatome) or as follow-up to IV dosing regimen Valacyclovir 1000mg po TID x 7 days or famciclovir (NON-FORMULARY).

5. Pediatric dosing of VZV immunoglobulin ***(OBTAIN FROM BLOOD BANK OR CIVITAN)***:
   125 units (1.25mL) per 10kg body weight (22 lbs.) administered intramuscularly. Maximum dose is 625 units (5 vials). Doses should be administered as follows:

Body weight (kg)	**Dose**	**Number of vials**
0 – 10	125 units	1
10.2 – 20	250 units	2
20.1 – 30	375 units	3
30.1 – 40	500 units	4
> 40kg	625 units	5

6. Cidofovir dosing for adenovirus: there are various reports concerning cidofovir dosing for adenovirus, primarily in the pediatric literature. The doses studied range from: 1mg/kg 3 times per week [Hoffman JA, et al. *BBMT* 2001; 7:388-94] to 3 – 5mg/kg/week x 2 – 4 weeks and then every other week [Hayashi M, et al. *Blood* 2000 abstract 810]

CMV ANTIGENEMIA GUIDELINES

- CMV antigenemia testing weekly post-engraftment through day +100 for allogeneic (sibling, MUD, cord, mismatched) transplant patients.
- Consider available open clinical trials.

A. Before day +100:

1. Treat *any* antigenemia with ganciclovir 5mg/kg IV q12h x 2 weeks, then 5 mg/kg IV QD x 1 wk. Alternatively, valganciclovir 900mg po BID x 2 weeks followed by 900mg po QD x 1 wk can be used [if altered renal function, adjust dose]
2. Stop treatment after three weeks only if Ag negative.
3. Consider continuing maintenance GCV 5mg/kg/day or valganciclovir 900mg/d through D +100 if patient is at high risk for CMV recurrence or if patient has had several episodes of CMV antigenemia.
4. If antigenemia persists after four weeks of treatment, or if # of cells/slide is increasing after three weeks of treatment, consider switching to Foscarnet.
5. If antigenemia recurs during maintenance phase (QD dosing), return to induction dose (BID dosing).

B. After day +100:

1. CMV antigenemia testing weekly for high-risk patients (i.e., active GVHD, immunosuppressive treatment, recurrent CMV during first 100 days, low CD4 counts, MUD recipients, T-cell depleted grafts, etc)
2. Treat antigenemia $\geq$ 5 cells/slide with GCV 5mg/kg IV q12h x 2 weeks, then 5mg/kg/day x 1 wk; or, valganciclovir 900mg po BID x 2 weeks, then 900mg po QD x 1 week.
3. If antigenemia is < 5 cells/slide, repeat CMV within one week; if still positive, treat as above in #2.
4. Stop treatment after three weeks only if Ag negative.
5. If antigenemia persists after four weeks of treatment, or if # of cells/slide is increasing after three weeks of treatment, consider switching to Foscarnet.
6. If antigenemia recurs during maintenance phase (QD dosing), return to induction dose (BID dosing).

C. Considerations while on treatment:

1. Check ANC at least 2x/week. If ANC only falling, support with G-CSF or GM-CSF.
2. Consider holding GCV or valganciclovir x 2 days for treatment-associated pancytopenia, or consider changing to foscarnet.
3. Adjust GCV dose in patients with renal insufficiency: CrCl 50-79 ml/min, 2.5mg/kg q12h; 25-49 ml/min, 2.5mg/kg q24h; <25 ml/min, 1.25 mg/kg q24h.
4. Adjust valganciclovir dose in patients with renal insufficiency: CrCl 40-59ml/min, 450mg po BID; 25-39 ml/min, 450mg po QD; 10-24 ml/min, 450mg po QOD; <10, consider changing to appropriate doses of ganciclovir.
5. Monitor electrolytes closely, especially when using Foscarnet.

GUIDELINES FOR THE ADMINISTRATION OF CIDOFOVIR

Cidofovir is a nucleotide analog. Cidofovir suppresses cytomegalovirus replication by selective inhibition of viral DNA synthesis. Cidofovir inhibits herpes virus polymerase alpha, beta, and gamma. Incorporation of cidofovir into the growing viral DNA chain results in reductions in the rate of viral DNA synthesis.

Renal impairment is a major toxicity of cidofovir. To prevent nephrotoxicity, adequate prehydration and administration of probenecid must occur. The following must be followed whenever administering cidofovir:

Probenecid:

- Administer 2g orally, 3 hours prior to the cidofovir dose
- Administer 1g orally 2 hours AND 8 hours following the completion of a 1-hour infusion of cidofovir

Hydration:

- Administer 1000mL 0.9% sodium chloride with each infusion of cidofovir.
- Administer the saline over 1 – 2 hours preceding the cidofovir infusion
- If a patient is able to tolerate additional fluid, a second liter of NS should be administered. If the second liter is to be administered, initiate it at the start of the cidofovir infusion or immediately afterwards, infused over 1 – 3 hours.

DOSE MODIFICATION GUIDELINES FOR CIDOFOVIR
SHANDS UNIVERSITY HOSPITAL BMT PROGRAM

CMV Usual Dosage:

CMV induction:

5mg/kg every week x 2 doses [for patients with a SCr of $\leq$ 1.5mg/dL, a calculated CrCl > 55mL/min, and a urine protein < 100mg/dL – equivalent to < 2+ proteinuria)

CMV maintenance:

5mg/kg every other week

Dose modifications:

CrCL (mL/minute)	Dose
41 – 55 mL/min	2mg/kg
30 – 40 mL/min	1.5mg/kg
20 – 29 mL/min	1mg/kg
< 19 mL/min	0.5mg/kg

NOTES:

For patients started at full-dose cidofovir, if the SCr increases by 0.3 – 0.4mg/dL, reduce the cidofovir dose from 5mg/kg/dose to 3mg/kg/dose.

Discontinue therapy for SCr $\geq$ 0.5mg/dL or the development of $\geq$ 3+ proteinuria

DOSE MODIFICATION GUIDELINES FOR FOSCARNET
SHANDS UNIVERSITY HOSPITAL BMT PROGRAM

Creatinine Clearance (mL/min per kg)	Induction Dosage for CMV (in mg/kg) Equivalent to 60mg/kg Every 8 hours	Induction Dosage for CMV (in mg/kg) Equivalent to 90mg/kg Every 12 hours
> 1.4	60 every 8 hours	90 every 12 hours
> 1 – 1.4	45 every 8 hours	70 every 12 hours
> 0.8 – 1.0	50 every 12 hours	50 every 12 hours
> 0.6 – 0.8	40 every 12 hours	80 every 24 hours
> 0.5 – 0.6	60 every 24 hours	60 every 24 hours
≥0.4 – 0.5	50 every 24 hours	50 every 24 hours
< 0.4	Not recommended	Not recommended

Creatinine Clearance (CrCl) per kilogram is to be calculated using the following formula:

MALES: CrCl (per kg) = $\frac{(140 - \text{age})}{72 \times \text{SCr}}$

FEMALES: CrCl (per kg) = AS above x 0.85

Where age is in years and serum creatinine (SCr) is in mg/dL

Recommendations for maintenance dosage based on the patient's creatinine clearance is as follows:

Creatinine Clearance (mL/min per kg)	Maintenance dosage for CMV (in mg/kg) equivalent to 90mg/kg once daily	Maintenance dosage for CMV (in mg/kg) equivalent to 120mg/kg once daily
> 1.4	90 every 24 hours	120 every 24 hours
> 1 – 1.4	70 every 24 hours	90 every 24 hours
> 0.8 – 1.0	50 every 24 hours	65 every 24 hours
> 0.6 – 0.8	80 every 48 hours	105 every 48 hours
>0.5 – 0.6	60 every 48 hours	80 every 48 hours
≥ 0.4 – 0.5	50 every 48 hours	65 every 48 hours
< 0.4	Not recommended	Not recommended

Hydration guidelines:

Pre- and post-hydration with 500mL normal saline (0.9% sodium chloride) helps to minimize the risk of nephrotoxicity.

This should be considered in ALL patients who can tolerate the fluid.

HEPATITIS GUIDELINES

Hepatitis A: No recommendations at this time.

Hepatitis B: See next page for specific guidelines

In general, HBsAg positivity should be monitored by determination of the HBV DNA quantitative PCR. Also, check Hbe Ag and anti-Hbe antibody. If liver enzymes are elevated, consider liver biopsy to look for cirrhosis and chronic inflammation. Patients with HBV DNA should receive prophylaxis with Lamivudine (Epivir®) at a dose of 150mg PO QD. Alternatively, famciclovir (*NON-FORMULARY*) could be used. Treatment should continue for a minimum of 3 months in the autologous BMT setting and for 6 months in the allogeneic BMT setting. Antiviral treatment should be continued beyond 6 months if immunosuppressive therapy is continued. After stopping antiviral therapy, one should monitor HBV DNA levels monthly and LFT's for 3-6 months to be vigilant for a flare-up.

Donor: If the patient is HBsAg positive and the donor is anti-HBsAg negative, consider hepatitis immunization of the donor.

Hepatitis C:

In general, if the patient is hepatitis C antibody positive, one should assess the LFT's and hepatitis C by PCR (quantitative). If the LFT's are abnormal, a liver biopsy should be considered if feasible to look for cirrhosis or active inflammation. In the presence of cirrhosis or inflammation, the patient should be informed of increased risk of hepatic toxicity after BMT and should re-assess whether it is practical to proceed forward with BMT. One could consider antiviral therapy with interferon and ribavirin if the underlying disease permits this option.

If the donor is hepatitis C RNA positive, transmission of infection is likely and one should consider an alternative donor if possible. If not, one needs to inform the recipient of the risk of transmission and hepatotoxicity and together decide whether the risk warrants proceeding forward. If the underlying disease permits a wait of 3-6 months, then consideration of antiviral treatment of the donor is warranted, although the effects of interferon on the stem cell product is unknown and may be deleterious and this should be conveyed to the recipient as well.

All hepatitis C+ patients and donors: Check hepatitis A serology. If negative, give the hepatitis A vaccine.

Reference:

Strasser SI, McDonald GB. Hepatitis viruses and hematopoietic cell transplantation: A guide to patient and donor management. *Blood* 1999; 93(4): 1127 – 36.

INTERPRETATION OF SERUM HEPATITIS MARKERS IN PATIENTS AND DONORS BEFORE HSCT

Patient Result	Donor Result	Interpretation	Recommendation
Hepatitis B Virus			
Anti-HBs positive	Negative	Patient has had prior exposure to HBV or has been vaccinated	Proceed with transplantation
Negative	Anti-HBs positive	Donor has had prior exposure to HBV or has been vaccinated	Proceed with transplantation
Anti-HBc positive (HbsAg + anti-HBs negative)	Negative	Patient has had prior exposure to HBV and is at risk for viral reactivation after transplant	Test for HBV DNA by PCR from 2 weeks post-transplant; consider antiviral therapy if serum positive for HBV DNA.
Negative	Anti-HBc positive (HBsAg and anti-HBs negative)	Donor has had prior exposure to HBV	Test donor for HBV DNA by PCR; if the result is negative, there is a negligible risk of viral transmission. If positive, consider antiviral therapy.
HBsAg positive	Negative	Current HBV infection in patient	Assessment for liver disease in patient, as patients with cirrhosis have a high risk for fatal VOD. If recipient is HBV DNA positive, institute antiviral therapy before transplant. If negative, monitor HBV DNA posttransplant and institute antiviral therapy if becomes positive.
HBsAg positive	Anti-HBs $\pm$ anti-HBc positive	Current HBV infection in the patient. Donor has immunity to HBV.	Assessment for liver disease in patient, as patients with cirrhosis have a high risk for fatal VOD. If recipient is HBV DNA positive, institute antiviral therapy before transplant. If negative, monitor HBV DNA posttransplant and institute antiviral therapy if becomes positive.
HBsAg positive	HBsAg positive	Current HBV infection in the patient and the donor	Assessment for liver disease in recipient, as patients with cirrhosis have a high risk for fatal VOD. Assessment for liver disease in donor, as there is an anesthesia risk during marrow harvest if the donor has cirrhosis. If recipient is HBV DNA positive, institute antiviral therapy before transplant. If negative, monitor HBV DNA posttransplant and institute antiviral therapy if becomes positive.
Negative	HBsAg positive	Current HBV infection in the donor	Assessment for liver disease in donor, as there is an anesthesia risk during marrow harvest if the donor has cirrhosis. Consider an alternate donor. Consider antiviral treatment of donor before stem cell harvest. Monitor recipient HBV DNA levels post-transplant and consider antiviral therapy if patient develops viremia.

Hepatitis C Virus			
Anti-HCV positive but HCV RNA negative	Negative	Patient has had passive acquisition of HCV antibody or has recovered from prior HCV infection or has a falsely negative HCV RNA	Repeat HCV RNA by a more sensitive method; check HCV RNA posttransplant.
HCV RNA positive	Negative	Current HCV infection in patient	Assessment for active liver disease or cirrhosis in patient before Transplant. Observe patient for development of chronic hepatitis after transplantation. Consider antiviral therapy in long-term follow-up.
Negative	HCV RNA positive	Current donor infection; HCV transmission is likely	Consider alternate donor; if this donor is the best available match, consider treatment of donor before marrow or stem cell harvest.

Abbreviations: anti-HBs, antibody to hepatitis B surface antigen; anti-HBc, antibody to hepatitis B core antigen; HBsAg, hepatitis B surface antigen; anti-HCV, antibody to hepatitis C virus; VOD, venocclusive disease; PCR, polymerase chain reaction.

Reference: Strasser SI, McDonald GB. Hepatitis viruses and hematopoietic cell transplantation: A guide to patient and donor management. *Blood* 1999; 93(4): 1127 – 36.

RESTRICTED ANTIINFECTIVES AT SHANDS – CRITERIA FOR USE

I. Caspofungin (Cancidas)

Caspofungin is an echinocandin antifungal agent that is indicated for the treatment of Aspergillus infections in patients who fail or are intolerant to other therapies (i.e. amphotericin B). Caspofungin also has excellent activity against *Candida* spp. Due to its limited indications, high cost, and potential for misuse, it listed in the Formulary as a restricted agent.

Criteria for Use

Approval of Infectious Diseases or Dr. Wingard (through BMT pharmacists) for BMTU patients required for all uses.

1. Treatment of oropahryngeal/esophageal candidiasis refractory or intolerant to other antifungal therapy (azoles and amphotericin B products)
2. Treatment of Candida fungemia in patients refractory after 7 days of therapy with other antifungal therapy (azoles or amphotericin B products)
3. Alternative to lipid amphotericin B products in the treatment of candidiasis or aspergillosis in patients who would meet criteria to receive lipid amphotericin B products
4. Treatment of probable or definite aspergillosis in patients who are refractory (i.e. stable disease or disease progression based on CT scan findings) to 14 days of therapy with amphotericin B products or patients who have progression of disease after 7 days of amphotericin B therapy (i.e. 25% worsening of CT scan findings)

*Note: Caspofungin should not be used for treatment of mucormycosis or *Cryptococcus neoformans*

II. Intravenous Itraconazole (Sporanox®)

Intravenous itraconazole was approved by the FDA for the treatment of blastomycosis (pulmonary and extrapulmonary), histoplasmosis (including cavitary pulmonary disease and disseminated nonmeningeal histoplasmosis), and aspergillosis (pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy). Due to its limited indications, high cost and potential for misuse, it is listed in the Formulary as a restricted agent.

Criteria for Use

Approval of Infectious Diseases or Dr. Wingard (through BMT pharmacists) for BMTU patients required for all uses.

1. Treatment of probable or definite aspergillosis in patients who are refractory (i.e. stable disease or disease progression based on CT scan findings) to 14 days of therapy with amphotericin B products, patients who have progression of disease after 7 days of amphotericin B therapy (i.e. 25% worsening of CT scan findings), or patients who are intolerant to amphotericin B.

2. Alternative to lipid amphotericin B products in the treatment of aspergillosis or other susceptible fungal infections in patients who would meet the criteria to receive lipid amphotericin B products (Note: Due to accumulation of the hydroxypropyl-beta-cyclodextrin vehicle in the formulation, iv itraconazole is contraindicated in patients with an estimated CrCl of < 30 mL/min)

3. Alternative to amphotericin B or lipid amphotericin B for empiric antifungal therapy in Bone Marrow Transplant patients and Acute Leukemia patients with persistent fever and neutropenia. (i.e. > 96 hours)

III. Lipid Amphotericin B:

Lipid amphotericin is an alternative to conventional amphotericin B deoxycholate in the treatment of serious infections fungal infections. Lipid amphotericin B has no proven efficacy advantages over conventional amphotericin B but may be less nephrotoxic. Due to the expense of lipid amphotericin B, criteria for use were developed by the Anti-infective Subcommittee of the Pharmacy and Therapeutics Committee. These criteria are intended to ensure patient's who need lipid amphotericin B receive it, while using the conventional formulation in patients who are able to tolerate it. There are two formulary lipid amphotericin B products:

- amphotericin B lipid complex (Abelcet®)-preferred formulary agent
- liposomal amphotericin B (AmBisome®)

A. Abelcet® only can be approved for use by the clinical pharmacists using the criteria below for therapy ≤ 7 days. Therapy for > 7 days requires approval of Infectious Diseases (excluding BMT patients where Dr. Wingard can approve all use through BMT clinical pharmacists).

B. LIPID AMPHOTERICIN B CRITERIA FOR USE

1. Conventional amphotericin B is considered first line for empiric therapy in febrile neutropenic patients and therapy for presumed and documented fungal infections including Aspergillosis.

2. Lipid amphotericin B should be reserved for:

   a) Empiric antifungal therapy in febrile neutropenic patients,
   b) Presumptive antifungal therapy (i.e. presumptive treatment of Aspergillosis based on CT scan or other findings), or
   c) Treatment of invasive fungal infections documented by positive fungal culture or histopathology

   in patients who meet one of the following criteria listed under A, B, C or D:

   A. Patients with severe pre-existing renal dysfunction (not end-stage renal disease) defined as:

      1. Serum Creatinine ≥ 2.5 mg/dL
      2. Serum Creatinine ≥ 2.0 mg/dL and on other nephrotoxic drugs defined as cyclosporine, aminoglycosides, tacrolimus (FK506), foscarnet (not vancomycin)
      3. Estimated creatinine clearance (CrCL) <40 mL/min
      4. Estimated CrCL < 50 mL/min and on other nephrotoxic drugs

   B. Patients who develop renal dysfunction on conventional amphotericin B defined as:

      1. Serum Creatinine ≥ 2.5 mg/dL
      2. Serum Creatinine ≥ 2.0 mg/dL and on other nephrotoxic drugs
      3. Estimated CrCL < 40 mL/min
      4. Estimated CrCL < 50 mL/min and on other nephrotoxic drugs
      5. Decline in estimated CrCL ≥50% since conventional amphotericin B therapy was started

   C. Patient has had prior renal failure during previous hospitalization while receiving conventional amphotericin B.

   D. Failure of conventional amphotericin B therapy. Failure is defined as a new fungal lesion that

forms while receiving therapy, an existing fungal lesion that increases in size while receiving therapy, or persistent positive fungal cultures while receiving therapy. **The patient must be on conventional amphotericin B therapy for at least 7 days before a determination of failure can be made.**

NOTE:

1. Lipid amphotericin B is not indicated as a substitution for infusion-related reactions due to conventional amphotericin B.
2. Amphotericin B lipid complex (ABLC, Abelcet®) is the preferred lipid amphotericin B agent at Shands at UF. Use of liposomal amphotericin B (AmBisome®) requires the approval of Infectious Diseases or Dr. Wingard for all uses. Liposomal amphotericin B (AmBisome®) should be reserved for patients who:
    i. Continue to develop worsening renal function on Abelcet®
    ii. Have disease progression while receiving Abelcet®

IV. Synercid®:

Synercid® is a combination of two streptogramin antibiotics (quinupristin and dalfopristin) used in the treatment of serious infections due to resistant gram-positive pathogens. Due to its limited indications, adverse effect profile, and cost, the use of Synercid® is restricted to the following criteria at Shands at UF.

Criteria for Use

1. Approval of Infectious Diseases is required for all uses.
2. Treatment of serious infections due to vancomycin resistant *Enterococcus faecium* (not active versus *Enterococcus faecalis*)
3. Treatment of gram-positive infections

V. Linezolid (Zyvox®)

Linezolid is a novel antibiotic in the oxazolidinone class used in the treatment of serious infections due to resistant gram-positive organisms. Due to its limited indications, cost, and adverse effect profile, the use of linezolid is restricted at Shands at UF.

Criteria for Use

1. Approval of Infectious Diseases is required for all uses
2. Treatment of serious infections due to vancomycin resistant *Enterococcus faecium* or *Enterococcus faecalis*.
3. Treatment of gram-positive infections in patients who fail or are intolerant to other therapies (i.e. vancomycin)

AMERICAN HEART ASSOCIATION PROPHYLAXIS GUIDELINES FOR PREVENTION OF BACTERIAL ENDOCARDITIS

CARDIAC CONDITIONS REQUIRING ANTIBIOTIC PROPHYLAXIS:

Prophylaxis recommended

- previous endocarditis
- prosthetic valves
- most congenital heart disease
- all acquired valvular heart disease
- hypertrophic cardiomyopathy
- mitral valve prolapse with valvular regurgitation
- surgically constructed systemic-pulmonary shunts, or conduits

Prophylaxis NOT recommended

- isolated secundum atrial septal defect
- previous coronary artery bypass graft surgery
- pacemakers and implanted defibrillators
- mitral valve prolapse **without** valvular regurgitation
- previous Kawasaki disease **without** valvular dysfunction
- previous rheumatic fever **without** valvular dysfunction
- complete surgical or device closure of atrial septal defect, ventricular septal defect or patent ductus arteriosus (more than 6 months after repair)
- physiological, functional or innocent murmurs

PROCEDURES REQUIRING ANTIBIOTIC PROPHYLAXIS AGAINST ENDOCARDITIS:

<u>Dental procedures:</u>

Prophylaxis recommended

Any procedure that causes bleeding from the gingiva, mucosa or bone including:

- dental extractions
- surgical drainage of dental abscess
- maxillary or mandibular osteotomies
- surgical repair or fixation of a fractured jaw
- re-implantation of avulsed teeth
- periodontal procedures including
- probing, scaling, root planing and surgery
- endodontic surgery and instrumentation beyond root apex
- placement of orthodontic bands (but not brackets)
- intra-ligamentary local anaesthetic injections

Prophylaxis NOT Recommended

- natural shedding of primary deciduous teeth
- dental examination, other than periodontal probing
- local anaesthetic injections (apart from intraligamentary)
- intra-canal endodontic treatment
- restorative dental treatment (operative or prosthetic)
- rubber-dam placement
- placement/removal of prosthetic or orthodontic appliances
- taking of impressions

- fluoride treatment
- taking of intra-oral radiographs
- orthodontic appliance adjustment
- brushing, flossing

Respiratory tract procedures:

Prophylaxis recommended

- tonsillectomy/adenoidectomy
- rigid bronchoscopy
- surgery involving bronchial mucosa

Not recommended

- flexible bronchoscopy +/- biopsy
- endotracheal intubation
- tympanostomy tube insertion

Genitourinary Tract Procedures:

Prophylaxis recommended

- prostatic surgery, transrectal prostatic biopsy; urethral dilatation, cystoscopy
- vaginal delivery in presence of infection or prolonged labor
- circumcision (ritual, especially in Aborigines)
- surgical procedures in the presence of infection

Prophylaxis NOT recommended

- vaginal hysterectomy
- vaginal delivery
- cesarean section
- surgical procedures in the absence of infection

Gastrointestinal tract procedures:

Prophylaxis recommended

- sclerotherapy for esophageal varices
- endoscopic retrograde cholangiography
- biliary tract surgery
- surgical operations involving the intestinal mucosa **except for** endoscopy, biopsy and percutaneous endoscopic gastrostomy

Not recommended

- transesophageal echocardiography
- endoscopy +/- biopsy
- percutaneous endoscopic gastrostomy

Other Procedures:

Prophylaxis recommended

- Incision and drainage of local abscesses

Prophylaxis NOT recommended

- Procedures through surgically prepared skin
- Cardiac catheterization including balloon angioplasty
- Implantation of pacemakers, defibrillators and coronary stents

RECOMMENDED PROPHYLACTIC REGIMENS FOR DENTAL, ORAL, OR UPPER RESPIRATORY PROCEDURES

Situation	Drug	Adult Dose	Pediatric Dose
Standard general prophylaxis	Amoxycillin	2g orally 1 hour prior to procedure	50mg/kg orally 1 hour prior to procedure
Unable to take oral medications	Ampicillin	2g IM or IV within 30 minutes prior to procedure	50mg/kg IM or IV within 30 minutes prior to procedure
Allergic to penicillin	Clindamycin OR	600mg orally 1 hour prior to procedure	20mg/kg orally 1 hour prior to procedure
	Cephalexin[#] or Cefadroxil[#] OR	2g orally 1 hour prior to procedure	50mg/kg orally 1 hour prior to procedure
	Azithromycin or clarithromycin	500mg orally 1 hour prior to procedure	15mg/kg orally 1 hour prior to procedure
Allergic to penicillin and unable to take oral medications	Clindamycin *OR* Cefazolin[#]	600mg IV, within 30 minutes prior to the procedure	20mg/kg IV within 30 minutes prior to the procedure
		1g IM or IV, within 30 minutes prior to the procedure	25mg/kg IM or IV within 30 minutes prior to the procedure

[#] Cephalosporins should not be used in patients with immediate-type hypersensitivity reactions (urticaria, angioedema, or anaphylaxis) to penicillin's

PROPHYLACTIC REGIMENS FOR GENITOURINARY/GASTROINTESTINAL (EXCLUDING ESOPHAGEAL) PROCEDURES

Situation	Agent	Regimen
High-risk patients	Ampicillin + gentamicin	Adults: ampicillin 2g IM or IV + gentamicin 1.5mg/kg (not to exceed 120mg) within 30 minutes of starting the procedure; 6 hours later, ampicillin 1g IM/IV or amoxicillin 1g orally
		Children: ampicillin 50mg/kg IM/IV (not to exceed 2g) + gentamicin 1.5mg/kg within 30 minutes of starting the procedure; 6 hours later, ampicillin 25mg/kg IM/IV or amoxicillin 25mg/kg orally
High-risk patients allergic to ampicillin/amoxicillin	Vancomycin + gentamicin	Adults: Vancomycin 1g over 1-2 hours + gentamicin 1.5mg/kg IV/IM (not to exceed 120mg); complete injection/infusion within 30 minutes of starting the procedure
		Children: Vancomycin 20mg/kg IV over 1-2 hours + gentamicin 1.5mg/kg IV/IM; complete injection/infusion within 30 minutes of starting the procedure
Moderate-risk patient	Amoxicillin or ampicillin	Adults: amoxicillin 2g orally 1 hour before procedure, or ampicillin 2g IM/IV within 30 minutes of starting the procedure
		Children: amoxicillin 50mg/kg orally 1 hour before procedure, or ampicillin 50mg/kg IM/IV within 30 minutes of starting the procedure
Moderate-risk patients allergic to ampicillin/amoxicillin	Vancomycin	Adults: Vancomycin 1g IV over 1-2 hours; complete infusion within 30 minutes of starting procedure
		Children: Vancomycin 20mg/kg IV over 1-2 hours; complete infusion within 30 minutes of starting procedure.

GRAFT VERSUS HOST DISEASE (GVHD)

GVHD PROPHYLAXIS – ADULTS

Allogeneic (Matched Related, Matched Unrelated, Related Mismatched, Cords):

If not otherwise specified by protocol, tacrolimus (IV/PO as Prograf®) will be used for GVHD prophylaxis along with mini-dose Methotrexate. Tacrolimus will be given as a continuous intravenous infusion beginning on day -3 (IBW) at a dose adjusted to achieve whole blood concentration of 10 to 20 ng/ml (See table below). Patients who develop CNS toxicity or HUS-TTP on tacrolimus may be changed to cyclosporine A at the discretion of the attending.

Mini-Dose Methotrexate (MTX):

Methotrexate 5 mg/m^2 IV on day's +1, +3, +6, +11
For adult patients with renal dysfunction, hepatic dysfunction, mucosal toxicity and third spacing (edema, ascites, effusions) refer to the Methotrexate modifications algorithm (page 108) for guidance on when to withhold the methotrexate dose. Consider MTX levels or continuing the calcium leucovorin if the SCr is > 2mg/dL.

Leucovorin:
Leucovorin 5 mg PO/IV q6h x 4 doses will be given beginning 24 hours following Methotrexate doses on Day +3, +6, and +11 in all patients receiving methotrexate. Do not give leucovorin after the Day +1 methotrexate.

CYCLOSPORINE + TACROLIMUS - ADULTS

Drug	Initial Dose	Target Range	Dosage Forms
Cyclosporine (CSA)	1.5 mg/kg IV q12h (administered over 2 hours) (1:3 conversion to PO CSA) 4.5 mg/kg PO q12h	150-450 ng/ml	Injection: Sandimmune® 50mg Oral capsules: 25 mg, 100mg caps (Neoral®; Gengraf®) Oral liquid: 100 mg/ml liquid (Sandimmune®, Neoral®)
Tacrolimus (FK-506)	0.03 mg/kg IV as continuous infusion (0.04 mg/kg in Pediatric patients) (1:4 conversion to PO FK506) 0.12 mg/kg/day PO adults 0.16mg/kg/day PO peds	10-20 ng/ml	Injectable mixed as 0.02 mg/ml in D5W or NS Oral: Prograf® 0.5mg, 1 mg, 5 mg capsules only; a liquid formulation (0.5mg/mL) can be compounded. Topical ointment: for localized skin GVHD use a topical tacrolimus preparation: Protopic® 0.03% and 0.1%, 30g and 60g tubes available

METHOTREXATE MODIFICATIONS

RENAL DYSFUNCTION

SEVERITY	MILD	MODERATE	SEVERE	LIFE THREATENING
SWOG GRADE	1	2	3	4
SERUM CREATININE	1.5 X BL	> 2.0 – 2.5 X BL	>2.5 – 3.0 X BL	> 3.0 X BL or Dialysis
%METHOTREXATE DOSE REDUCTION (day 1, 3, 6, 11)	50 – 100%	HOLD	HOLD	HOLD

HEPATIC DYSFUNCTION

SEVERITY	MILD	MODERATE	SEVERE	LIFE THREATENING
SWOG GRADE	1	2	3	4
TOTAL BILIRUBIN	2 – 9 mg/dL	10 – 19 mg/dL	20 – 39 mg/dL	$\geq$ 40 mg/dL
SGOT or SGPT	> 200-399 U/L	$\geq$ 400 IU/L	$\geq$ 700 IU/L	$\geq$ 700 IU/L
% METHOTREXATE DOSE REDUCTION (day 1, 3, 6, 11)	50 – 100%	100%	100%	100%

MUCOSAL TOXICITY

SEVERITY	MILD	MODERATE	SEVERE	LIFE THREATENING
SWOG GRADE	1	2	3	4
STOMATITIS	Painless ulcers, erythema or mild soreness	Painful erythema, edema or ulcers but can eat	Painful erythema, edema, or ulcers and cannot eat	Requires parenteral or enteral support
PHARYNGITIS/ ESOPHAGITIS	Painless ulcers, mild soreness or mild dysphagia	Painful erythema, edema or ulcers or moderate dysphagia but can eat without narcotics	Cannot eat solids or requires narcotics to eat	Requires parenteral or enteral support or complete obstruction or perforation
OTHER MUCOSITIS	Erythema, or mild pain not requiring treatment	Patchy and produces serosanguinous discharge or requires non-narcotic for pain	Confluent fibrinous mucositis or requires narcotic for pain or ulceration	Necrosis
% METHOTREXATE DOSE REDUCTION (day 1, 3, 6, 11)	0%	0%	50 – 100%	50 – 100%

THIRD SPACING, EDEMA, ASCITES

SIGNIFICANT Third spacing or Edema or Ascites	DAY 1 Post-Transplant	DAY 3 Post-Transplant	DAY 6 Post Transplant	Day 11 Post-Transplant
% METHOTREXATE DOSE REDUCTION	50 – 100%	50 – 100%	50 – 100%	100%

CYCLOSPORINE DOSE ADJUSTMENT/TAPERING GUIDELINES

Name:_____

DOSE (100%) =_____mg IV q12h = _____mg PO BID
(1.5mg/kg IV q12h) (4.5mg/kg PO BID Neoral®)

REMINDERS: Conversion factor for IV: PO is approximately 1:3. Give IV dose over at least 2 hours. Round IV doses to the nearest 5mg; PO doses to nearest 25mg

BASELINE (Day of CyA start) CREATININE = _____mg/dL
(if day of CyA start creatinine < 0.6 use admission creatinine as baseline)

1. DOSE ADJUSTMENT BASED ON CREATININE

Grade	1	2	3
Serum creatinine	1 – 1.5 X BL	1.6 – 1.9 X BL	> 1.9 x BL
% of CyA dose reduction	0 - 25%	50 – 75%	Hold and resume at 50% of current dose if renal dysfunction is stable
If creatinine			
Decrease daily IV dose to			
Decrease PO dose to			

II. DOSE ADJUSTMENTS BASED ON LEVELS

(If 2 of 3 consecutive levels are below/above these range, discuss dose changes according to this schema with the attending physician. If no signs of toxicity and levels are high, recommend no dose modifications).

MONOCLONAL CyA ASSAY	Low (2 of 3)	Normal	High (2 of 3)	High (2 of 3)
CyA (ng/mL)	< 150	150 – 450	451 – 600	601 – 750
% change in dose	Increase 10 - 25%	No change in dose	Consider holding 1-2 doses, restart when level < 300 with a 25 – 50% reduction	Hold dose until levels < 300, with 50 – 75%% dose reduction

III. DOSE REDUCTIONS BASED ON HEPATIC DYSFUNCTION

Total Bilirubin	2 – 9 mg/dL	10 – 19mg/dL
AST/ALT	> 200 – 399 U/L	$\geq$ 400 IU/L
% change in dose	0 – 25%	25 – 75%

IV. TAPERING SCHEDULE

Following tapering schedule outlined below if no evidence of chronic GVHD. If chronic GVHD therapy required, follow taper per chronic GVHD algorithm or attending physician request.

FOR ALLOGENEIC (RELATED and MUD) TRANSPLANT FOR HEMATOLOGICAL MALIGNANCY PATIENTS:

a. At week 9 post BMT, decrease dose to 80% of week 8 dose.
b. At week 12 post BMT, decrease dose to 60% of week 8 dose.
c. At week 16 post BMT, decrease dose to 40% of week 8 dose.
d. At week 20 post BMT, decrease dose to 20% of week 8 dose.
e. At week 26 post BMT, discontinue FK506 (if no evidence of GVHD).

APLASTIC ANEMIA PATIENTS:

Do NOT taper immunosuppression. Continue immunosuppression for 1 year without a taper.

TACROLIMUS DOSE ADJUSTMENT/TAPERING GUIDELINES

Name:_____

DOSE (100%) =_____mg IV q12h = _____mg PO BID
(0.03mg/kg.day) (0.12mg/kg/day divided q12h)

REMINDERS: Conversion factor for IV: PO is approximately 1:4. If on oral fluconazole, use IV: PO of 1:2 – 3. Give IV doses as a continuous 24-hour infusion. Round PO doses to the nearest 1.0mg; If total daily PO dose is an odd number (i.e. 5mg/day), the dose may be split unevenly (3mg qam, 2mg qpm).

BASELINE (Day –1)) CREATININE = _____mg/dL
(if day –1 creatinine < 0.6 use admission creatinine as baseline)

1. DOSE ADJUSTMENT BASED ON CREATININE (Reference: BMT 1999; 24:1054)

Grade	1	2	3
Serum creatinine	1 – 1.5 X BL	1.6 – 1.9 X BL	> 1.9 x BL
% of FK506 dose reduction	0 - 25%	50 – 75%	Hold and resume at 50% of current dose if renal dysfunction is stable
If creatinine			
Decrease daily IV dose to			
Decrease PO dose to			

2. DOSE ADJUSTMENTS BASED ON LEVELS (Reference: BMT 1999;24:1053 – 1056)

(If 2 of 3 consecutive levels are below/above these ranges, discuss dose changes according to this schema with the attending physician. If no signs of toxicity and levels are high, recommend no dose modifications).

	Very Low	Low	Normal	Normal	High	Very High
FK506 conc (ng/mL)	< 5	5 - 9	10 - 15	16 - 20	21 - 25	> 30
% change in dose	Increase 25 - 50%	Increase by 0 - 25%	No change	Decrease by 0 – 25%	Hold 6 hours and resume at 50% dose	Hold and resume at 25% dose when level is < 20

3. DOSE REDUCTIONS BASED ON HEPATIC DYSFUNCTION

Total Bilirubin	2 – 9 mg/dL	10 – 19mg/dL
AST/ALT	> 200 – 399 U/L	$\geq$ 400 IU/L
% change in dose	0 – 25%	25 – 75%

4. TAPERING SCHEDULE

Following tapering schedule outlined below if no evidence of chronic GVHD. If chronic GVHD therapy required, follow taper per chronic GVHD algorithm or attending physician request.

FOR ALLOGENEIC (RELATED and MUD) TRANSPLANT FOR HEMATOLOGICAL MALIGNANCY PATIENTS:

f. At week 9 post BMT, decrease dose to 80% of week 8 dose.
g. At week 12 post BMT, decrease dose to 60% of week 8 dose.
h. At week 16 post BMT, decrease dose to 40% of week 8 dose.
i. At week 20 post BMT, decrease dose to 20% of week 8 dose.
j. At week 26 post BMT, discontinue FK506 (if no evidence of GVHD).

APLASTIC ANEMIA PATIENTS:
Do NOT taper immunosuppression. Continue immunosuppression for 1 year without a taper.

ACUTE GVHD STAGING AND GRADING

Clinical Stage of Acute GVHD according to Organ System

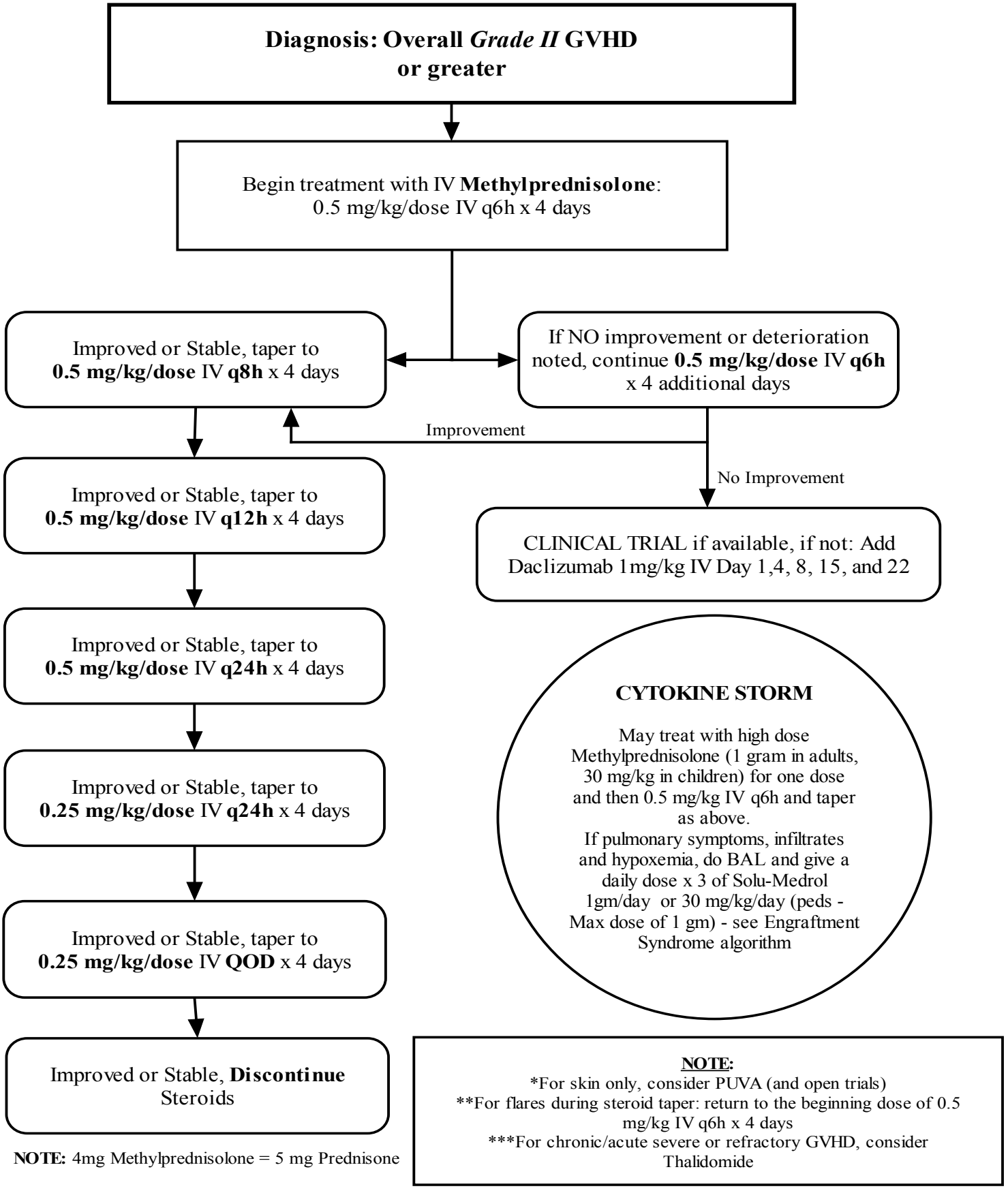
STAGE	SKIN	LIVER	INTESTINE
+	Maculopapular rash < 25% of body surface	Bilirubin 2-3 mg/dL	> 500 ml diarrhea per day or (nausea, anorexia or vomiting with biopsy confirmation of upper GI GVHD)
++	Maculopapular rash 25-50% of body surface	Bilirubin 3-6 mg/dL	> 1000 ml diarrhea per day
+++	Maculopapular rash > 50% body surface area or Generalized erythroderma	Bilirubin 6-15 mg/dL	> 1500 ml diarrhea per day
++++	Generalized erythroderma with bullous formation and desquamation	Bilirubin > 15 mg/dL	> 1500 ml diarrhea per day plus severe abdominal pain with or without ileus

OVERALL GRADE OF ACUTE GVHD BY ORGAN STAGE[§]

GRADE	SKIN	GI	LIVER
I	1-2	0	0
II	0 0 1-3 1-3 3	1 0-1 1 0-1 0	0-1 1 0-1 1 0
III	0-3 0-3 0-3	0-2 2-3 0-3	2-3 0-3 4[#]
IV	0-3 4	4 0-4	0-4 0-4

[§] Grade II-IV GVHD with only single organ involvement should be biopsy confirmed.
[#] If Karnofsky performance status is < 30%, then Grade IV.

GVHD Treatment Algorithm



NOTE: 4mg Methylprednisolone = 5 mg Prednisone

NOTE:
*For skin only, consider PUVA (and open trials)
**For flares during steroid taper: return to the beginning dose of 0.5 mg/kg IV q6h x 4 days
***For chronic/acute severe or refractory GVHD, consider Thalidomide

MECHANISM OF ACTION OF IMMUNOSUPPRESSIVE AGENTS

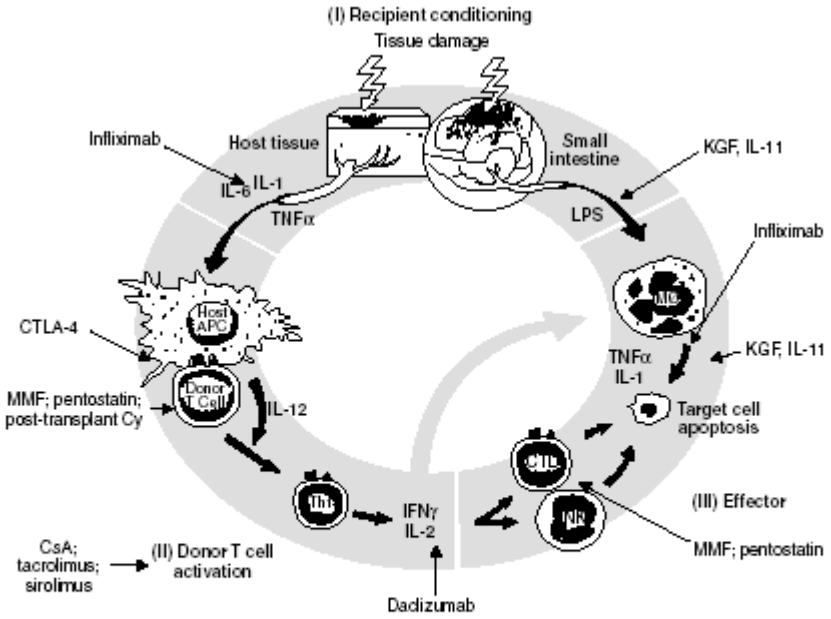


Fig. 1. Acute graft versus host disease (GVHD) pathophysiology and pharmacotherapeutic intervention. The three sequential phases of GVHD (I, II, III) are detailed. Agents discussed are shown in relation to the phases of GVHD they disrupt (Adapted from Hill and Ferrara,[113] © American Society of Hematology, with permission). APC = antigen-presenting cells; CsA = cyclosporin; CTL = cytotoxic T cells; CTLA-4 = CTLA-4 monoclonal antibody; Cy = cyclophosphamide; IL = interleukin; IFN = interferon; KGF = keratinocyte growth factor; LPS = lipopolysaccharide; MΦ = monocyte; MMF = mycophenolate mofetil; NK = natural killer cell; Th1 = T helper-1 cell; TNF = tumour necrosis factor.

Reference: Jacobsohn DA, et al. *Drugs* 2002; 62(6): 879 – 89.

REFRACTORY GVHD – TREATMENT OPTIONS

Acute GVHD:

Drug	Dose	Frequency	Site of Action	Comments
ATGAM (horse)	15mg/kg IV 40mg/kg	QD – BID x 7-10 days QD x 4 days		Infusion related reactions common. Premedication required.
Beclomethasone ***WIRB20010912***	2mg	PO QID	Local	Grade II GVHD with GI symptoms + prednisone vs. placebo + prednisone
Daclizumab (Zenepax®)	1mg/kg IV	Day 1, 4, 8, 15, and 22	IL-2 directed monoclonal antibody	Vital signs before, and then 15, 30, and 90 minutes after the start of the infusion
Infliximab (Remicaid®) *** Restricted***	10mg/kg IV	Weekly x 4 doses	Neutralizes the biological activity of TNF	Permission for use must be given by P + T Committee Chairman
Mycophenolate Mofetil (MMF)	15mg/kg PO/IV	BID	Inhibits IMPDH leading to inhibition of purine synthesis	Marrow suppressive, may require G-CSF support; diarrhea common, assess cause i.e., medication vs. GVHD

Chronic GVHD:

Drug	Dose	Frequency	Comments	Reference
Clofazimine	300mg PO 100mg PO	QD x 90 days After 90 days onwards		Lee SJ, et al. *Blood* 1997;89:2298 – 302
Etanercept (Enbrel®) *** Non-Formulary***	25mg SQ 25mg SQ	2 x per week x 2 – 4 weeks, *then* weekly x 4 weeks		Chiang KT, et al. ASH 401a [abstract 1728]
Mycophenolate Mofetil (MMF) plus Tacrolimus	MMF: 1g PO BID, increasing to 1,5g BID if no initial response. When patient achieves a CR, taper MMF to 1g PO BID on alternate days for 2 weeks, and then 0.5g BID for 2 weeks, then discontinue. FK506: 1mg PO BID (maintain a trough of 5-10mg/L). When a CR taper by 50% of previous dose every 2 weeks. When 1mg PO QD dosing is achieved continue for 2 weeks then discontinue			Mookerjee C, et al. *BMT* 1999;24:517 - 20
Pentostatin ***Clinical Trial Available***	4mg/m^2 IV	Every other week x 24 weeks	Dose reduction for renal impairment: If CrCl < 50mL/minute/1.73m^2 reduce by 50%. If < 30mL/min – do not give	Vogelsang – personal communication
Thalidomide	100mg, increasing as tolerated to 200mg	QID QID		Parker PM, et al. *Blood* 1995;86:3604 – 9

ATGAM® (ATG, ANTITHYMOCYTE GLOBULIN, HORSE) GUIDELINES FOR ADMINISTRATION

Indication: Treatment of acute Graft Versus Host Disease (aGVHD)
Component of certain conditioning regimens prior to BMT to T-cell deplete to attempt to prevent the occurrence of aGVHD.

Mechanism of Action:
ATGAM is a lymphocyte-selective immunosuppressant. Its antilymphocytic effect is believed to reflect an alteration of the function of the T lymphocytes, which are responsible in part for cell-mediated immunity and are involved in humoral immunity.

Usual Dose: We recommend 20 mg/kg/day (round to nearest 50mg) for minimum of 5 days; continue for an additional 5 days if response not complete. Stop after 5 days if no improvement.

Premeds: Acetaminophen 650mg, Diphenhydramine 50mg, and Methylprednisolone (Solu-Medrol®) (2mg/kg). Pediatric patients administer APAP 10mg/kg, diphenhydramine 1mg/kg and methylprednisolone at the same dose as adults.

Skin Testing:
Apply an intradermal skin test starting with 0.1 ml of a 1:1000 v/v dilution (5 mcg horse IgG) of ATGAM in 0.9% NS on one arm, with a contralateral injection of an equal volume of 0.9% NS as a negative-control reagent. Observe the patient and the skin-test site at least every 15 to 20 minutes over the first hour after the intradermal injection.

A local reaction of 10 mm or greater with wheal, erythema or both, with or without pseudopod formation and itching or a marked local swelling, constitute a positive test. The predictive value of this test has not been proven clinically. Allergic reactions such as anaphylaxis have occurred in patient's whose skin test is negative.

In the presence of a positive skin test to ATG, consider alternative forms of immunotherapy. The risk to benefit ratio must be carefully weighed. A systemic reaction such as generalized rash, tachycardia, dyspnea, hypotension, or anaphylaxis precludes any additional administration of ATGAM.

Administration:
ATGAM will be mixed in 0.9% NS at a concentration no greater than 4 mg/ml. It should be administered through a central line over a minimum of 4 hours through an in-line filter with a pore size of 0.2 to 1.0 micron. Not compatible with D5W.

Patient Monitoring:
Monitor vital signs every 30 minutes x 4, then every 60 minutes thereafter until infusion complete.

Adverse Effects:
Fever, chills, thrombocytopenia, leukopenia, rashes, systemic infection, serum sickness-like symptoms, dyspnea or apnea, arthralgia, chest, back or flank pain, diarrhea, nausea or vomiting, hypertension, pair or swelling at infusion site, eosinophilia, headache, myalgia,

hypotension, anaphylaxis, tachycardia, edema, malaise, seizures.

GUIDELINES FOR THYMOGLOBULIN® (RABBIT ATG) ADMINISTRATION

Indication:

Treatment of acute Graft Versus Host Disease (aGVHD)
Component of certain conditioning regimens prior to BMT to T-cell deplete to attempt to prevent the occurrence of aGVHD.

Pharmacology:

Induces immunosuppression in vivo by T-cell clearance from the circulation and modulation of T-Cell activation, homing, and cytotoxic activities. Thymoglobulin® includes antibodies against T-cell markers such as CD2, CD3, CD4, CD8, CD11a, CD18, CD25, CD44, CD45, HLA-DR, HLA Class I heavy chains, and β_2 microglobulin. In patients, T-cell depletion is usually observed within a day from initiating Thymoglobulin® therapy. Thymoglobulin® has not been shown to be effective for treating antibody (humoral) mediated rejections.

Usual Dose:

Vancouver Regimen: 2.5 mg/kg/day IV QOD for 4 doses (8 days)
Conversion from horse ATG to rabbit ATG is 10:1

Premeds:

Acetaminophen, Diphenhydramine, and Methylprednisolone (SoluMedrol® 2mg per kg)

Skin Testing:

Not indicated

Administration:

Thymoglobulin® should be mixed in saline or dextrose at a concentration not to exceed 0.5 mg/ml (total volume usually between 50 to 500 ml). It should be administered through a 0.22-micron filter into a high-flow vein over a minimum of 6 hours for the first dose and over at least 4 hours for subsequent doses.

Monitoring:

Monitor vital signs every 30 minutes x 4, then every 60 minutes thereafter until infusion complete.

Adverse Effects:

Adverse effects are very similar to those seen for ATGAM, although the incidence of infusion related adverse effects are reportedly less with Thymoglobulin®. Thymoglobulin® may cause more leukopenia.

CHRONIC GRAFT VERSUS HOST DISEASE – STAGING

Limited GVHD:

- Localized skin involvement with or without:
  - Hepatic dysfunction (without histologic confirmation)
  - Platelet count > 100K

Extensive GVHD

- Generalized skin involvement OR
- Localized skin involvement and/or hepatic dysfunction plus any of the below:
  - Liver histology of chronic aggressive hepatitis, bridging necrosis, cirrhosis
  - Involvement of the eye: Schirmer's test < 5mm wetting
  - Involvement of minor salivary glands or oral mucosa: Dx by Bx
  - Involvement of any other target organ

Table 1. Clinical manifestations of chronic graft-versus-host disease

Organ	Clinical manifestation	Evaluation	Intervention
Skin	Erythematous papular rash (lichenoid) or thickened, tight, fragile skin (sclerodermatous)	Clinical and biopsy to confirm the diagnosis of GVHD	Moisturize (petroleum jelly), treat local infections, protect from further trauma
Nails	Vertical ridging, fragile	Clinical	Nail polish may help to decrease further damage
Sweat glands	Destruction leading to risk for hyperthermia		Avoid excessive heat
Hair	Scalp and body hair thin and fragile; can be partially or completely lost	Clinical	
Eyes	Dryness, photophobia, and burning Progression to corneal abrasion	Regular ophthalmological evaluation including Schirmer test	Preservative-free tears during the day and preservative-free ointment at night
Mouth	Dry, sensitivity to mint, spicy food, tomato Whitish lace-like plaques in the cheeks and tongue identical to lichen planus Erythema and painful ulcerations, mucosal scleroderma with decreased sensitivity to temperature possible	Regular dental evaluation (with appropriate endocarditis prophylaxis) Viral and fungal cultures at diagnosis and at any worsening	Avoid foods that are not tolerated Regular dental care, preceded by appropriate endocarditis prophylaxis
Respiratory tract	Bronchiolitis obliterans can manifest as dyspnea, wheezing, cough with normal CT imaging findings and marked obstruction at pulmonary function tests Chronic sinopulmonary symptoms, infections, or both also common	Pulmonary function tests including FEV_1, FVC, DLCO, helium lung volumes Computed tomography imaging in symptomatic patients (rule out infections if findings are abnormal) Lung biopsy if clinically indicated	Investigational therapy
Gastrointestinal	Abnormal motility and strictures Weight loss	Swallowing studies, endoscopy if clinically indicated Nutritional evaluation	Systemic treatment of GVHD Endoscopic/surgical treatment of strictures Nutritional intervention
Liver	Cholestasis (increased bilirubin, alkaline phosphatase) Isolated liver involvement needs histologic confirmation	Liver function tests Liver biopsy if clinically indicated	No specific therapy is proven superior FK506 may concentrate in the liver
Musculoskeletal	Fasciitis Myositis is rare Osteoporosis may occur secondary to hormonal deficits, use of steroids, decreased activity	Periodical physical therapy evaluation to document range of motion Bone density evaluation, especially for patients using steroids	Aggressive physical therapy program
Immune system	Profound immunodeficiency Functional asplenia High-risk for pneumococcal sepsis, *P carinii* pneumonia, and invasive fungal infections Variable IgG levels	Assume all patients are severely immunocompromised and asplenic	*P carinii* pneumonia prophylaxis (until 6 months after no GVHD) and pneumococcus prophylaxis (lifetime) Delay vaccinations to 6 months after GVHD has resolved
Hematopoietic system	Cytopenias Occasional eosinophilia	Counts Bone marrow aspirate and biopsy, antineutrophil and antiplatelet antibodies when indicated	Systemic treatment of GVHD
Others	Virtually all manifestations of autoimmune disease have been described in association with chronic GVHD	As clinically indicated	

GVHD indicates graft-versus-host disease.

MANAGEMENT OF CHRONIC GRAFT VERSUS HOST DISEASE SEATTLE PROTOCOL

Treatment Week of Therapy	Prednisone (mg/kg/day PO)		Tacrolimus (mg/kg/day PO)	
	Day A	Day B	Day A	Day B
1	1.0	1.0	0.12	0.12
2	1.0	1.0	0	0.12
3	1.0	0.5	0	0.12
4	1.0	0.25	0	0.12
5	1.0	0.12	0	0.12
6	1.0	0.06	0	0.12
7	1.0	0	0	0.12
8	1.0	0	0	0.12 re-evaluation #1. (see appendix C)
↓	1.0	0	0	0.12
20	1.0	0	0	0.12 Re-evaluation #2 (see appendix C)
21	0.75	0	0	0.12
22	0.50	0	0	0.12
↓	0.50	0	0	0.12
40	0.50	0	0	0.12 Re-evaluation #3.

NOTES:

1. Prednsione is given as a single AM dose
2. Oral tacrolimus is to be given in divided doses (BID)
3. Tacrolimus blood levels are to be drawn whenever clinically indicated. If prescribing fluconazole concomitantly the dose of tacrolimus may need to be adjusted downwards.
4. Antibiotic prophylaxis:
   - TMP-SMX (Septra®) to be given daily on Saturday, Sunday and Mondays as 1 double strength tablet (800/160mg) daily.
   - Penicillin is given daily as one 500mg capsule po TID unless body weight is < 30kg in which case the dose is 50mg/kg/day, split into 3 doses
   - For patients who are allergic to PCN, erythromycin 250mg PO BID can be substituted.
   - Prophylaxis is to be continued until the patient has been off treatment for 6 months without a flare of GVHD.
5. For patients receiving cyclosporine, substitute cyclosporine 10mg/kg/day (in 2 divided doses).

NOTE: Do not check levels of CyA or tacrolimus, only adjust the dose if there is clinical signs of toxicity.

CORTICOSTEROID COMPARISON CHART

Glucocorticoid	Pregnancy Category	Approximate equivalent dose	Route of administration	Relative anti-inflammatory potency	Relative mineralocorticoid potency	Protein Binding (%)	Half-Life	
							Plasma (min)	Biologic (hr)
Short-Acting								
Cortisone	D	25	PO, IM	0.8	2	90	30	8 – 12
Hydrocortisone	C	20	IM, IV, PO	1	2	90	80 – 118	8 – 12
Intermediate-Acting								
Methylprednisolone	-	4	PO, IM, IV	5	0	_	78 – 188	18 – 36
Prednisolone	B	5	PO	4	1	90 – 95	115 – 212	18 – 36
Prednisone	B	5	PO	4	1	70	60	18 – 36
Triamcinolone	C	4	PO, IM, inntra-articular, intradermal, intrasynovial, soft tissue injection	5	0	_	200+	18 – 36
Long-Acting								
Betamethasone	C	0.6-0.75	PO, IM, IV, intra-articular, intradermal, intrasynovial, soft-tissue injection	20 – 30	0	64	64	35 – 54
Dexamethasone	C	0.75	PO, IM, IV, intra-articular, intradermal, intrasynovial, soft-tissue injection	25 – 30	0	_	_	36 – 54
Mineralocorticoid								
Fludrocortisone	C	-	PO	10	125	42	42	18 - 36

Reference: Lexi-Comp Drug Information Handbook 1999 – 2000.

NOTE: for the treatment of GVHD, patients should be dosed on TOTAL body weight, not ideal body weight.

ENGRAFTMENT SYNDROME

Definition:

Engraftment syndrome is a post bone marrow transplant clinical syndrome that can occur when the WBC starts to recover. It is characterized by a maculopapular skin rash and fever (up to 40°C) in the absence of documented infection. Other manifestations may include refractoriness to platelet transfusions, diarrhea, diffuse alveolar hemorrhage, and autoimmune thrombocytopenia or hemolytic anemia.

Treatment:

- If NO pulmonary symptoms, and O_2 saturation greater than 95% on room air:

  Give 1 mg/kg prednisone (dose based on total body weight, when TBW: IBW ratio exceeds 1.3 use an adjusted weight i.e. IBW + 0.4 (TBW-IBW)) PO BID x 3 days

  Then 0.5 mg/kg BID x 2 days

  Then 0.5 mg/kg QD x 2 days,

  Then stop

- If patient has pulmonary symptoms*, start with:

  Give 1000mg SoluMedrol® (Methylprednisolone) IV QD x 3 days
  (Pediatric Dose: 30 mg/kg/day based on TBW. If TBW:IBW ratio is > 1.3 then use an adjusted body weight, see above for formula)

  Then 500mg IV QD x 3 days

  Then 250mg IV QD x 3 days

  Then 125 mg IV QD x 3 days

  Then switch to PO Prednisone 60 mg PO QD x 3 days

  Then 30mg PO QD x 3 days

  Then stop

  *Call a pulmonary consult for bronchoscopy to rule out infection

- Continue patients on 100mg PO QD Fluconazole prophylaxis until off steroids (if ANC recovered then fluconazole 100mg daily, if ANC not recovered continue on prophylaxis dose as dictated by type of transplant).

PROCEDURES

ADMINISTRATION OF BONE MARROW OR STEM CELL PRODUCT

***Note:**
1. Special Considerations for ABO Incompatible and Cryopreserved Marrow
2. The previous practice of infusing bone marrow 4-6 hours after radiation is no longer necessary. Infuse bone marrow to patients post radiation without delay**.**

Equipment List:
A. Blood pressure cuff and stethoscope
B. Thermometer
C. IV set without filter for non-cryopreserved marrow
D. Blood component recipient set for cryopreserved marrow
E. Non-Sterile gloves
F. 3 way stopcock
G. Normal saline flush
H. Cardiac monitor
I. Pulse oximeter
J. Bone marrow transplant form
K. Emergency Drug Box:
Solu-Medrol 500mg, Epinephrine 1:1000, Benadryl® 50mg

Prepare Patient:
1. Prior to transfusion, assess patients and family's understanding of the transplant procedure. Explain the process, possible side effects, and symptomatic treatment available.

2. Obtain baseline vital signs just prior to marrow infusion.

3. Place patient on cardiac monitor.

Key Point:
If the patient is receiving autologous marrow, explain the side effects of DMSO, "garlic" taste in mouth, nausea and vomiting, anaphylactic reaction; pungent odor.

Method:
1. Bring transplant drug box to the patient's bedside.

2. The lab technician delivers the bone marrow to the patient's room. The lab technician will label the bone marrow volume in the bag.

3. Before the bone marrow infusion is started, notify the MD/PA/HO to establish a communication mechanism during and post transplant. Verify written orders prior to infusion.

4. Monitor patient for signs of fluid volume overload. For cryopreserved marrow, each fifty milliliters (ml) should be given over 15 minutes if tolerated. Diuretics can be used to prevent fluid overload.

ADMINISTRATION OF BONE MARROW OR STEM CELL PRODUCT (CONTINUED)

5. Attach bone marrow to appropriate tubing IV set. Marrow has already been filtered in the O.R. For non-cryopreserved marrow filter is not necessary and may damage cells. Cryopreserved marrow is infused with filtered IV tubing.

6. Flush IV line with normal saline.

7. Attach to a three-way stopcock and an IV line directly. Do not run through a needle except a clicklock system.

8. Begin infusion slowly and assess for immediate side effects. Increase rate after 10 to 15 minutes. Remain with the patient.

9. During infusion, take vital signs every 5 minutes times 4, every 15 minutes times 2, then hourly until the end of the infusion. Take VS more frequently if indicated.

Key Points:

- Routine blood check is not necessary because the marrow is delivered immediately and directly from donor to recipient. The nurse performing the transplant should know donor and recipient ABO types prior to transplant.

- It is not necessary for MD/PA/HO to be present on the unit or in hospital during infusion.
- MARROW IS NOT TO BE IRRADIATED!

- Filtering of cryopreserved marrow helps to decrease patient's reaction to DMSO.

- The physician determines the rate of administration, but it generally infuses over 2 to 4 hours. Infusion should start as soon as possible after marrow arrives on the unit.

Management of Complications:

1. **Anaphylaxis:**
   Institute emergency medical treatment and prepare Epinephrine for administration.

2. **Fever:** Slow the infusion and administer Acetaminophen as ordered.

3. **Rigors** (severe shaking chills):
   Administer Meperidine as ordered. Rigors pose a threat to the thrombocytopenic patient and can result in intracranial bleeding. Assess neurological status every 15 minutes until rigors have subsided.

4. **Allergic Plasma Reaction** (urticaria, hives, wheezing, hypotension):
   Stop the transfusion and keep the line open with normal saline. Treat the patient as ordered. Continue the transfusion only upon the physicians' order.

5. **Dyspnea and Cyanosis:**
   Stop the transfusion and keep the line open with normal saline. Obtain a chest x-ray and ABG as ordered. Prepare oxygen for administration and treat patient as ordered.

ADMINISTRATION OF BONE MARROW OR STEM CELL PRODUCT (CONTINUED)

6. **Hypotension:**
   Moderate - Continue infusion and monitor patient closely. The rate may be slowed.

   Severe - Stop the transfusion and institute emergency treatment as ordered.

7. **Hemolytic Reaction:**
   This is characterized by back or abdominal pain, fever, chills, vomiting, hemoglobinuria, or hypotension. Slow or stop the infusion, treat the fever and hypotension as ordered. Have mannitol ready. Monitor urine output and hydrate patient as ordered.

Key Points:

- Be aware that continued fever especially associated with signs of flushing, vomiting, diarrhea, or shock may be indicative of bacterial contamination of the marrow. If this is suspected, notify the physician, stop the infusion, and start transfusion reaction procedure.

- The cause of respiratory reaction is due to sequestered agglutinated white cells within the pulmonary vasculature. It may also be due to fat or bone fragments embolus, or reaction to DMSO.

SPECIAL CONSIDERATIONS FOR ABO INCOMPATIBLE AND CRYOPRESERVED MARROW

The following pre-medication and IV fluid medications should be ordered for all patients who receive a graft from an ABO incompatible donor or a cryopreserved marrow. The diuretic and fluid measures are intended to be cautions against the potential for incompatibility reaction or nephrotoxicity from cell debris that may accompany the thawed stem cell product.

1. At 11 pm on day prior to transplant, begin hydration (if not already on maintenance fluids): NS at 2 ml/kg/hr **(see pediatric section, page 205 for hydration volumes for kids)**

2. Have available at bedside on day of transplant:
    a. Diphenhydramine (Benadryl®) 50 mg IV [Pediatric dose 1mg/kg]
    b. Epinephrine 1:1000 (1 amp: 1 mg) IV (Notify MD if patient wt<50kg)
    c. Hydrocortisone (Solu-Cortef®) 500 mg IV
    d. Normal saline 500 ml (prime bag) and 3-way stop-cock (autologous)
    e. Atropine 1 mg IV (1 ml vial)

3. Set up oxygen and suction in room, emergency cart outside door.

4. Place patient on cardiac monitor.

5. 15 minutes prior to transplant infusion, premedicate with:

Medication	Adult Dose	Pediatric Dose
Mannitol 25%	50 ml (12.5 gm) infused rapidly over 3-5 min	0.2 gm/kg up to 12.5 gm infused over 3-5 minutes
Diphenhydramine	50 mg IV push	1 mg/kg IV push
Hydrocortisone	250 mg IV push	100 mg/m^2 IV push

6. After infusion completion, continue hydration with NS at 2 ml/kg/hr x 12 hours [refer to pediatric section for hydration requirements for pediatric patients].

7. When urine output is < 1.5 ml/kg/hr x 4 hours, then give furosemide (Lasix®) 20-40 mg IV push. For children < 12 years, give 0.5-1 mg/kg/dose.

GUIDELINES FOR PLATELET TRANSFUSION

Indications for Platelet Transfusion

1. Usage guidelines

    1. Stem cell transplant patients being actively treated (within 2 – 3 weeks of chemotherapy, prior to neutrophil recovery) with platelet count less than 20,000/µl and without active bleeding.
    2. Acute leukemia patients undergoing non-transplant therapy (and both BMT and leukemia patients who are NOT under active treatment, beyond neutrophil recovery) with platelet counts of less than 10,000/µl and without active bleeding.
    3. Patients with active bleeding and platelet count less than 50,000/µl.
    4. Patients who have been scheduled for an operative procedure within 12 hours of transfusion and the platelet count is less than 50,000/µl.

2. Documentation of the Outcome

    A platelet count shortly before and 30-90 minutes after platelet transfusion should be documented in the chart.

3. Dose

    Give 1 unit per 10 kg of ideal body weight for adults (with a minimum of 6 and a maximum of 10 units per transfusion). For children <2.0 years, give a dose of 10cc/kg. For children $\geq$ 2.0 years give 1 unit per 10-kg body weight.

Calculation of Corrected Count Increment (CCI)

$$CCI = \frac{\text{(post-transfusion platelet count - pre-transfusion platelet count) x BSA } (m^2)}{\text{Number of platelets transfused } (\times 10^{11})}$$

6×10^{10} platelets in a unit of platelet concentrates
3×10^{11} platelets in a unit of pheresis platelets

i. Post-transfusion platelet count should be determined between 30 minutes and 90 minutes after completion of platelet transfusion

ii. Pre-transfusion platelet count ideally should be determined within one hour before transfusion, if a patient is suspected to have developed platelet transfusion refractoriness.

Indications for the use of gamma-irradiated, CMV-negative, leukocyte-depleted, washed or HLA-matched blood components in BMT patients

Background

Graft versus host disease (GVHD) is a serious transfusion complication that can occur after receiving cellular blood components such as red blood cells and platelet concentrates in severely immune-compromised patients. Frozen acellular blood components (e.g., fresh frozen plasma and cryoprecipitate) do not cause GVHD in patients. Irradiation of blood components with 25 Gy gamma ray is sufficient to prevent transfusion associated GVHD. Gamma irradiation does not have any other

beneficial effects.

Transmission of cytomegalovirus (CMV) through blood transfusion is not a major concern for patients without severely suppressed immunity. Most individuals will be infected by CMV in their lifetime. CMV is transmitted through leukocytes in donor blood. The estimated risk of transfusion-associated CMV infection is 0.2 to 1% for each unit of cellular blood products. Both CMV seronegative and leukocyte-depleted blood components can be used to prevent CMV transmission.

Leukocyte-depleted blood components are prepared by filtering blood through high efficiency leukocyte-removal filters. After filtration, more than 99.9% of leukocytes in a unit of red blood cells or a pool of random donor platelet concentrates are removed. Leukocyte-depletion is ineffective to prevent HLA alloimmunization in patients who have been sensitized previously and to avoid transfusion-associated GVHD.

Washing is used to remove plasma and/or leukocytes from blood products. This procedure also removes unwanted metabolites in plasma (e.g., ammonia, lactic acid, K+). Washed blood products are also used to prevent allergic reactions to donor plasma proteins. Since majority of patients (>80%) do not develop urticaria or febrile reaction following subsequent transfusions, the use of washed blood components should be considered only when patients have developed more than one episode of transfusion-associated urticaria or febrile reactions. Washing platelets can result in significant quantitative loss of platelets (20%-80%) and functional impairment. Washed platelets should be ordered only for patients with severe recurrent allergic reactions to donor plasma.

HLA-matched or crossmatch compatible single donor pheresis platelets are prepared from specially selected donors by platelet pheresis procedure. These products are useful for patients who require platelet transfusion support and become refractory to random donor platelets due to the development of antibodies to HLA or platelet-specific alloantigens.

Due to significant additional cost for specially processed or selected blood components, these products should be used only when medically indicated.

Guidelines

Gamma Irradiation (NEJM 1990; 323:315-321)

All patients admitted to BMT unit for allogeneic/autologous bone marrow transplantation and patients with lymphohematopoietic malignancies will receive gamma irradiated platelets and red cells.

CMV-Negative Products (Rev Inf Dis 1983; 5:977; JID 1998;157:523; Rev Inf Dis 1990; 12:5754)

Allogeneic transplantation recipients who are negative for CMV serology and receive CMV negative donor organs or tissues.

Any CMV negative (or unknown CMV serology) patient who is a candidate for allogeneic BMT in the future.

Leukocyte-depleted platelets and red cells (Blood 1994; 85:603)

Replacement for CMV negative products

Patients with recurrent non-hemolytic febrile transfusion reaction to cellular blood products (at least twice). If febrile reactions persist after filtration, then consider washing. NOTE: Washing red blood cells reduces and does not deplete leukocytes.

Washed Cellular blood products

Patients with documented recurrent urticaria (at least twice), and/or anaphylactic reactions to cellular blood components. (Washing does not remove leukocytes from platelets.)

Clinical conditions that require avoidance of ammonia, K^+ and/or lactic acid in the stored blood units.

HLA-matched or crossmatch-compatible pheresis platelets

HLA-matched pheresis platelets

Patients who respond poorly to two consecutive transfusions of random donor platelets (corrected count increment <7500/µl) and are tested positive for anti-HLA antibodies.

Patients who respond poorly to two consecutive transfusions of random donor platelets (corrected count increment <7500/µl) and do not respond to one additional transfusion with fresh, ABO compatible donor platelets should be tested for anti-HLA antibodies and anti-platelet antibodies. The best HLA-matched pheresis platelets can be ordered to test for the possible presence of immune refractoriness due to anti-HLA antibodies. (NOTE: Best matched pheresis platelets are not always available.)

Crossmatch-compatible pheresis platelets

Patients who respond poorly to two consecutive transfusions of random donor platelets (corrected count increment <7500/µl), and do not respond well to transfusion of fresh, ABO compatible donor platelets and HLA-matched pheresis platelets.

Patients who require platelet transfusion, respond poorly to two consecutive transfusions of random donor platelets (corrected count increment <7500/µl), and tested positive for antibodies to platelet specific alloantigens.

[NOTE: Call Linda or Belinda in Blood Bank for any questions.]

Platelet Transfusion Triggers

Non-bleeding prophylaxis

Transfuse if platelet count < 20,000 and patient is under active BMT treatment (this refers to less than 2 – 3 weeks post chemotherapy, prior to neutrophil engraftment). For acute leukemia induction/consolidation, patients during and after active treatment, and BMT patients NOT under active treatment (beyond neutrophil recovery), use 10,000 as the trigger.

Give one transfusion and check CCI (to define refractoriness)

If platelet count is less than 5,000, repeat transfusion

If count is 6-10,000, give a transfusion 12 hours later (with pre- and post-platelet counts) unless not under active treatment

Give no more than 2 transfusions per day

Treatment of hemorrhage

Transfuse if platelet count <50,000; for cerebral hemorrhage, transfuse until platelets exceed 100,000.

Classify bleeding as minor or major (see attached)

Give a transfusion and check CCI

If post-count is less than 50,000 and bleed is minor, repeat count every 12 hours and give transfusion if less than 50,000 (no more than 2 transfusions per day).

If post-count is less than 50,000 (or 100, 000 for CNS hemarrhage) and bleed is major, repeat transfusion; 12 hour later repeat (2) and (4). Continue to recheck every 12 hours, until bleeding is controlled.

The patient should receive no more than 4 transfusions per day.

Prophylaxis for Major Procedures

Transfuse until platelet count exceeds 50,000

Keep at that level for a minimum of 24 hours after procedure, then resume previous transfusion trigger.

Prophylaxis for Central Catheter Placement

- If platelet count is <50,000, give one transfusion just prior to placement. Placement may be performed irrespective of post-transfusion count.

GRADING OF BLEEDING EPISODES

Slight - Petechiae, small hematoma, slight mucosal bleeding (including melena or hematemesis to the degree expected secondary to mucositis), slight vaginal bleeding without significant decrease in hematocrit, microscopic hematuria not requiring red cell transfusion.

Minor – Gross hematuria or mucosal bleeding (upper or lower GI, or vaginal) associated with a significant decrease in hematocrit. Any bleeding which requires increased red cell transfusion, but not meeting the criteria of a major bleed.

Major – Severe gross hematuria, fulminant mucosal bleeding (includes GI, vaginal) with rapid decrease in hematocrit, retinal bleeding with visual impairment, pulmonary hemorrhage, CNS hemorrhage.

This section of the Supportive Care Guidelines was collaboratively authored by Dr Wingard, Dr Zumberg, Dr Kao and Dr Lottenberg.

SKIN BIOPSY

1. Obtain the following supplies from the clinic procedure room or the supply room on the BMTU:
    - 3.5mm dermal biopsy punch
    - 3 betadine or chloraprep swabs
    - 3cc syringe
    - 25 gauge needle
    - 2-5cc of 1% or 2% lidocaine (consider mixing with 0.5cc sodium bicarbonate for children to reduce discomfort with lidocaine)
    - sterile needle driver or hemostat
    - sterile scissors
    - 2-0 or 3-0 suture
    - sterile gauze
    - sterile gloves
    - zinc formalin in specimen container
    - silk tape if pressure dressing required, or adhesive bandage
    - 4 sterile blue towels

2. Set up the above supplies on a sterile field, and maintain sterile procedure.
3. Clean and drape the area to be biopsied with betadine or chloraprep and sterile blue towels. (NOTE: Ideally, the skin biopsy site should include a hair follicle.) Use lidocaine to anesthetize a dime-sized area.
4. Use two fingers to make skin taut. Place the 3.5mm punch on the skin and rotate with moderate downward pressure until the entire blade is within the skin. Remove the biopsy blade.
5. Gently pull the punch from the skin using the needle driver or hemostat, revealing the base, which remains anchored to the subcutaneous tissue. Cut through the base of the biopsy using the scissors, and place the specimen in formalin.
6. Tamponade briefly with gauze and place suture. An adhesive bandage over the suture will be adequate for most patients. However, if patient has low platelets or is anticoagulated, a pressure dressing may be required.
7. Label the specimen container with the patient's name, medical record number, the specimen type and site (e.g., "skin biopsy – left anterior thigh"), and the words "Rush Path" in red ink.
8. Fill out a surgical pathology request form, again indicating specimen type and site, and again requesting **"Rush Path"** in **red ink.** (This is necessary to obtain a pathology report within 24 hours.)
9. The specimen must be hand delivered to the surgical pathology suite on the 2nd floor.
10. Write a procedure note in the patient's chart.

BONE MARROW BIOPSY

1. Obtain informed consent from the patient (*before* administering any premedication).
2. Obtain a custom bone marrow biopsy tray and IBF fixative from the procedure room in clinic or the supply room on the BMTU. If the patient is overweight, a larger needle than the one provided in the tray may be required. NOTE: This tray contains one green-top tube and two purple-top tubes, which are required for cytogenetics, flow cytometry, and PCR testing. Additional tubes may be needed if you are sending STR for same-sex donor chimerism (one yellow-top ACD tube) or if you are obtaining additional samples for research protocols (tube types vary depending on the study).
3. Position patient either on his or her side or in the prone position. Locate the area over either posterior iliac crest by palpation, and then clean and drape this area using sterile technique. (Betadine swabs are provided in the trays.)
4. Use lidocaine to anesthetize the skin above the crest, and then a quarter-sized area on the bone itself. Allow approximately five minutes to achieve full anesthesia.
5. Insert the aspiration needle through the anesthetized skin and anchor it approximately 1cm into the iliac crest. Remove the stylette and quickly attach the 20cc syringe to the aspiration needle. Use a brisk pull on the syringe to obtain the aspirate. (Flow cytometry requires ~1cc, cytogenetics requires 1-2cc, and STR requires ~2cc. NOTE: If you are requesting STR with lymphocyte sorting, 6cc of aspirate is required.)
6. Place the necessary aliquots of aspirate into the appropriate tubes and gently agitate.
7. Insert the biopsy needle into the same puncture site on the skin, *but locate a new area of anesthetized bone* for obtaining the biopsy specimen. Again anchor the needle through the cortical bone and remove the stylette. Using steady pressure and a rotating motion, drive the biopsy needle at least 2cm into the bone (a 2cm specimen is ideal for morphologic analysis). You may then use the provided green-topped rod to estimate the amount of specimen in the needle. Rotate the biopsy needle several times and insert the yellow capture device until you feel it close around the specimen; you may rotate the needle again after inserting this device.
8. Remove the entire needle (with the capture device in place) from the patient. Make touch preps of the biopsy using the provided slides, and then fix the biopsy specimen in IBF.
9. A second biopsy specimen may be taken for flow and/or cytogenetics if the aspirate sample appears aspicular; this specimen should be placed in a sterile container with saline.
10. After hemostasis is achieved, place a pressure dressing over the site and instruct the patient to lie supine (to maintain pressure on the site) for approximately 20 minutes.
11. Label all specimen containers with the patient's name and medical record number. Specimens for flow, morphology, cytogenetics, and PCR go to the Heme Path lab and STR tubes go to the HLA lab, both on the third floor.
12. Write a procedure note in the patient's chart.

LUMBAR PUNCTURE

1. Obtain informed consent. Use premedication sparingly for this procedure, as patient cooperation is necessary for proper positioning.
2. Lumbar puncture trays can be located in the clinic procedure room or in the BMTU supply room.
3. Ideally, this procedure should be done with the patient lying on his or her side, curled in the fetal position, as this is the only position in which intracranial pressure can be accurately measured. However, if the patient is unable to lie on the side or if you have difficulty obtaining a specimen, the patient may be positioned upright, with the upper body curled over a bedside table.
4. Clean and drape the area over the L4-L5 space using sterile technique. (Antiseptic solution is not provided in the LP tray; you may use betadine or chloraprep)
5. Use 1-3cc of lidocaine to achieve local anesthesia.
6. Insert a 20 or 22 gauge needle into the space between the L4 and L5 spinous processes. The needle should be inserted bevel up, and at a slightly cephalad angle.
7. Once accurate placement of the needle is achieved (confirmed by flow of clear fluid from the needle when the stylette is removed), intracranial pressure can be measured (if indicated) using the manometer and stopcock in the LP tray.
8. CSF is obtained by allowing the fluid to drain from the needle into the specimen tubes. 10cc of fluid is sufficient for cell count, chemistries, micro studies, and cytospin; less is required if all of these studies are not necessary. NOTE: When giving intrathecal chemotherapy, remove the same volume of CSF as the chemo being given (e.g., if the chemo is a 5cc volume, remove at least 5cc of fluid before administering).
9. **Administration of IT chemotherapy:** After obtaining CSF samples, screw the chemotherapy syringe onto the LP needle while it is still in the cerebrospinal space. Slowly aspirate once the syringe is attached to confirm that the needle has not been jostled out of position. Infuse the chemotherapy slowly over five minutes. Remove the empty syringe from the needle and place the stylette back into the needle. Slowly remove the needle from the patient and hold pressure over the site until hemostasis is achieved.
10. A sterile adhesive bandage should be placed over the site, and the patient instructed to lie supine for approximately one hour to minimize headaches and fluid leaks.
11. All specimen tubes should be labeled with the patient's name and medical record number, and sent with the appropriate forms and labels to the corresponding labs. A completed half-sheet Service Requisition Form should be sent to Heme Path with the specimen to request cytospin or flow cytometry.
12. **All supplies that had contact with chemotherapy (e.g., syringe, needle, gauze, drapes, gloves, etc) should be placed in the yellow chemotherapy biohazard containers.**
13. Write a procedure note in the patient's chart.

BONE MARROW HARVEST PROCEDURE

EQUIPMENT:

A. Prepackaged bone marrow harvest tray.
B. Two Lee -Lock harvest needles. 11G 3 1/2-inch to 5-inch depending on patient's size amount of adipose tissue. For pediatric patients a 13G 3 1/2-inch Lee -Lock may be used.
C. Plastic syringes: 6 syringes 30-35ml.
D. Metal beaker 500ml
E. Goggles and sterile gloves
F. Gauze pads, 4 X 4
G. Adhesive bandage
H. Dura-Prep or Betadine solution to cleanse the skin
I. Sterile drapes
J. Heparinized solution provided by the Medical Technologist from the Stem Cell Lab
K. Antibacterial ointment

CONTENT STATEMENT:

ISSUE	INTERVENTIONS	NOTE
INDICATIONS	• Family member who is HLA matched and has a hematologic disease for which the treatment is myeloablative therapy followed by a stem cell rescue • An unrelated patient who is HLA matched • A patient who has a hematologic disease or cancer which myeloablative therapy is used followed by stem cell rescue	
CONTRAINDICATIONS	• Infection of the soft tissues overlying the harvest site. • Fever • Bleeding diathesis or profound thrombocytopenia. • Major organ failure. • Cancer (this will be evaluated on an individual basis.)	
PRE-OP EVALUATION	• Complete History and Physical within 30 days or procedure. This must include immunization history, number of pregnancies, and any prior blood transfusions. • Labs to include: CBC, renal, metabolic, and liver batteries, virology's to include EBV, HSV, and Hep. BAg, Hep C, Anti HIV, HIV ag, HTVL, anti HBc and HCV, CMV, ABO/Rh, type and screen. • CXR, and EKG. • Evaluation by anesthesia. • Consents must be signed prior to harvest.	

PATIENT PREPARATION	• Explain the procedure and risks to the patient and ask for informed consent for the harvest. • Informed consent must also be obtained by Anesthesiologist for GETA or spinal anesthesia.	
PATIENT POSITIONING	• Position for the patient is a prone. Prone on gel foam bolsters after induction of anesthesia. Ensure that all bony prominence are positioned on cushions. • Optimize bed height.	• You must make sure the patient's genitalia and breast are free from pressure points. Ensure that all bony prominence are positioned on cushions.
ANATOMIC REVIEW	The hematopoietic marrow occupies the axial skeleton and the proximal portions of the bones of the extremities in adults. The preferred site for bone marrow aspiration and biopsies are the posterior superior iliac spines (PSIS), which are palpable as knobby prominence at the medial margins of the iliac crests posteriori. At these sites, the bones are thick and the risk of damage to the underlying structures is low	
PROCEDURE	1. Consent and History and Physical must be in OR chart, call blood bank to have autologous back up unit available if needed. 2. The following should be documented prior to the procedure: For the recipient: Disease, IBW, blood type, CMV Status. For the donor: IBW, ABW, HCT, HOB, WBC, blood type, and CMV status. 3. Scrub hands and apply goggles and sterile gloves. Observe sterile technique at all times. 4. Cleanse the harvest site widely with Dura-prep or Betadine solution 5. Drape the area with sterile sheets and towels. 6. Lock the obturator in place in the shaft of the Lee-Lock harvest needle. Hold the needle with the wings in the palm of the hand with shaft stabilized between the index and middle fingers and the thumb. Pass the needle perpendicular through the skin, through the periosteum, Perpendicular to the bone directly over the PSIS. Use a rotator, clockwise-counterclockwise motion to advance the needle. A noticeable "give" will be felt when the needle penetrates the outer table of bone and enters the marrow cavity. The needle should now be fixed in the bone. Remove the obturator. 7. Load syringe with ~0.5ml of Heparinized solution. Fix the needle in one hand, vigorously aspirate with the syringe to create a negative suction. The thick marrow will slowly accumulate in the syringe. Aspirate less than 10ml for each pull. Rotate the	

	Lee-Lock needle after each aspiration. Pass the syringe off to the scrub R.N. or medical technologist. Repeat procedure for approximately 10 pulls. Replace obturator into Lee-Lock and reposition needle slightly into another area of the iliac crest. You do not need to re-puncture the skin in most cases. 8. Check for presence of spicules. Remove the needle when sampling is complete. 9. If no material is aspirated on the first attempt, replace the obturator, cautiously advance the needle 1-2 mm, and repeat procedure. If this is unsuccessful, withdraw the needle to the periosteum and redirect it slightly. If this aspirate is again dry, try aspirating with a 30-35 ml syringe to create more suction , Replacing the needle and syringe is sometimes helpful they may contain clots 10. . Both sides of the iliac crests are harvested at the same time. 11. The medical technologist will call for a cell count ½ way through the procedure. The M.D. will determine how much volume is needed based on the recipients IBW. 12. The medical technologist is responsible for processing the marrow during and after the procedure. 13. Control hemostasis with pressure for 5 minutes. Apply typical antibiotic and an adhesive bandage, If the patient has a bleeding diathesis, apply a pressure dressing. 14. Monitor the patient's blood pressure closely during procedure. 15. Inform the anesthesiologist when the harvest is complete approximately 15 min. before completion. 16. The anesthesiologist will recover the patient and extubate him. The P.A. must stay with the patient until he is in the PACU.	
POSSIBLE COMPLICATIONS	• If a needle breaks off in the bone, attempt to clamp the end and call a surgeon for assistance. This may require minor surgery. Avoid hemorrhaging by applying pressure over the site after the harvest • Rare complications include bone marrow emboli, osteomyelitis, and anemia have been reported	

AFTER CARE INSTRUCTIONS	• Obtain a post-op CBC (Optional per Attending MD). • Patient may be discharged to home after recovery from anesthesia. Patients must stay in area for 24 hours after procedure. • BMT Coordinator will meet patient in post op recovery for review of follow-up instructions and document appropriately • The patient will be instructed to return to the BMT Outpatient Clinic the following day for a wound check and post harvest assessment by the Outpatient clinic attending or PA. • Patient may resume diet as tolerated. • Patient may resume normal activity as tolerated. • Give patient a prescription for ferrous sulfate 325mg. 1PO TID X 30 days. • For pain the patient may take Tylenol 500mg. 2 PO q 6 hours prn pain OR you may give a prescription for a mild narcotic analgesic. • The patient may remove the pressure dressing in 24 hours and apply Band-Aids. • The patient should be instructed to call for temp>101.5 and observe for signs of infection or bleeding.	

Reference: Standard Operating Procedures, BMT program 2002

BLOOD PRODUCTS

GUIDELINES FOR USE OF BLOOD PRODUCTS FOR BMT PATIENTS

Guidelines for Packed Red Blood Cell (PRBC) transfusions:

Transfusion Trigger:

Unless other specified by protocol or individual patient requirement, the transfusion trigger for pRBC's will be set at 20%.

Suggested Criteria for Higher Transfusion Trigger:

- Pulmonary edema
- Cardiac history
- Pneumonia
- Capillary Leak
- Unstable Angina
- Respiratory distress
- Hypotension

CMV Negative Blood Products:

CMV negative blood products will be given to all allogeneic (unrelated and related donor) patients who are CMV negative and whose donor is CMV negative.

Autologous patients have a very small chance of developing significant CMV disease and therefore **WILL NOT** be routinely given CMV negative blood products.

Blood Product Substitution:

If a patient requires CMV negative blood products, a leuko-depleted platelet product is an acceptable substitution for a CMV negative blood product when the latter is not available. Randomized studies have demonstrated that leuko-depletion prevents CMV infection.

It is acceptable to substitute a blood group O platelet in place of a blood group type specific platelet product when the latter is not available. The Blood Bank will ascertain the ABO isoagglutinin antibody titer for relevant blood type of the recipient. Studies have shown that the risk for adverse event is low when the platelet production antibody level is less than 1:64. In the event the product's antibody titer exceeds 1:64, the product will be processed for plasma volume reduction to minimize risk of hemolysis.

FRESH FROZEN PLASMA (FFP) - ADMINISTRATION GUIDELINES

Solvent-Detergent Treated Fresh Frozen Plasma (SD-Plasma):

Fresh frozen plasma pre-treated with solvent-detergent (SD) to inactivate lipid-enveloped viruses recently became available for patient use. SD treatment reduces the risk of transmitting HIV, HTLV, hepatitis B, and hepatitis C. However, SD treatment does not inactivate non-lipid enveloped viruses (e.g. parvovirus, hepatitis A, etc.) and prions.

SD-Plasma Usage Guidelines:

The use of SD-plasma may be considered for patients who require long term transfusion support of FFP. These patients include those with congenital deficiency of specific blood clotting factors for whom no other virally inactivated clotting factor concentrate is available, and those with severe TTP who require chronic transfusions of FFP.

SD-FFP is not recommended for replacement of regular FFP in other clinical settings. Like FFP, SD-plasma has limited clinical utility and should not be used as a volume expander or as a source of protein supplementation.

Request for SD-Plasma:

SD-plasma is not in stock at Shands Hospital. The product can be ordered as needed from the distributor through the Blood Bank at Shands. If a request for SD-plasma is placed to the Blood Bank before 4:30pm, SD plasma will be available before noon the next day.

Cost: One unit FFP $39
One unit SD-plasma $125

**Information supplied by K. J. Kao (Blood Bank memo 3/24/99).

USE OF RHOGAM

1. The use of Rh immunoglobulin (Rhogam) for Rh negative patients who receive Rh positive stem cell grafts is not recommended, because the recipients will become Rh positive. This statement applies to standard allogeneic HSCT, not non-myeloablative transplants.
2. Use of Rh immunoglobulin should only be considered for those patients who have received Rh negative stem cell grafts and may become alloimmunized to Rh antigen from transfusions of Rh positive blood components.
3. Use of Rh immunoglobulin may be considered for Rh negative patients who have childbearing potential.
4. One vial of Rh immunoglobulin (Rhogam) is required for every 15 ml of Rh positive packed red cells in a cellular product. (Granulocyte apheresis products contain approximately 50-150 ml packed red cells). If Rhogam to be used for prevention of Rh alloimmunization from granulocyte transfusions, the patients will require injections of multiple doses of Rhogam for multiple days and may suffer from hemolysis of donor red cells.
5. Ordering Rhogam for prevention of Rh alloimmunization should be determined by weighing benefit against risks. Multiple injections of Rh immunoglobulin are painful and costly. Only 10% of Rh negative and immunosuppressed patients or patients with hematological malignancies becomes Rh sensitized. Prudent clinical judgement and common sense must be used in considering the use of Rhogam in bone marrow transplant patients. Decisions can be made in consultation with Transfusion Service Director.

Prepared by: Michelle Sugrue in collaboration with KJ Kao 2/21/02

ELECTROLYTES

REFERENCE RANGES (LABORATORY)

Parameter	PLASMA Sample Reference Range	SERUM Sample Reference Range
Sodium (Na^+)	137 – 145	137 – 145
Potassium (K^+)	3.3 – 4.6	3.6 – 5.0
Chloride	98 – 107	98 – 107
Carbon Dioxide (CO_2)	22 – 30	22 – 30
Urea Nitrogen (BUN)	7 – 17	7 – 17
Creatinine	0.7 – 1.2	0.7 – 1.2
Glucose	65 – 109	65 – 109
Calcium (Ca^{2+})	8.4 – 10.2	8.4 – 10.2
Magnesium (Mg^{2+})	1.8 – 2.8	1.8 – 2.8
Phosphorus (PO_4^{3-})	2.5 – 4.5	2.5 – 4.5
Uric Acid	2.5 – 7.5	2.5 – 7.5
Protein (Total)	6.3 – 8.2	6.3 – 8.2
Albumin	3.5 – 5	3.5 – 5
Bilirubin (Total)	0.2 – 1.3	0.2 – 1.3
Bilirubin (Direct)	0 – 0.4	0 – 0.4
Alkaline Phosphatase	43 – 122	43 – 122
AST	15 – 46	15 – 46
ALT	11 – 66	11 – 66
LDH	313 – 618	313 – 618

ELECTROLYTE FACTS + FIGURES

Calcium:

100mg $CaCl_2$ = 1.4 mEq Calcium and 1.4 mEq Chloride
100mg Calcium gluconate = 0.45 mEq Calcium

Magnesium:

1mg magnesium sulfate = 0.008 mEq Magnesium

Product	Elemental Mg^{++} per dose (mg)	mEq Mg^{++} per dose	Bioavailability per dose
Magnesium Chloride (Slow-Mag®)	64	5.26	1.04
Magnesium Gluconate	27	2.2	0.42
Magnesium Oxide (MagOx®)	241.3	19.8	0.39
Magnesium L-lactate dihydrate (MagTab® SR)	84	7	2.87

Phosphate:
Potassium phosphate = phosphate 3mM and potassium 4.4 mEq per mL
Sodium phosphate = phosphate 3mM and sodium 4 mEq per mL
1mM = 31 mg phosphorous
Neutra-Phos® powder = 7.1 mEq potassium and 8 mmol phosphate

ADULTS MANAGEMENT OF ELECTROLYTES – PLASMA REFERENCE RANGES

	Potassium		Calcium		Magnesium		Phosphate	
Abnormality	Hypokalemia	Hyperkalemia	Hypocalcemia	Hypercalcemia	Hypomagnesemia	Hyper-magnesemia	Hypo-phosphatemia	Hyper-phosphatemia
Plasma Level	< 3.3 mEq/L	> 4.6 mEq/L	< 8.4 mg/dL	> 10.2 mg/dL	< 1.8 mEq/L	> 2.8 mEq/L	< 2.5 mg/dL	> 4.6 mg/dL
Symptoms	Fatigue; weakness in legs; cramps	Vague muscular weakness; flaccid muscle paralysis in legs; parasthesias of face, tongue, feet, and hands	Numbness & tingling of fingers, circumoral region, and toes; muscle cramps, spasms, tremors, twitching; convulsions; depression; emotional instability; anxiety; psychosis	Muscle weakness; confusion; emotional instability; anxiety; psychosis; lethargy; coma	Muscle weakness; muscle twitching & cramps; paresthesias; depression; agitation; confusion; psychosis; anorexia; nausea; vomiting	Drowsiness; muscle weakness; coma	Parasthesias; muscle weakness (hand grasp, speech difficulty); muscle pain & tenderness; confusion; apprehension; delirium; coma; seizures	Tetany; tingling of fingertips, circumoral region, and toes; numbness; muscle spasms
Action	If K^+ 3.0 - 3.2, then give KCl 40 mEq PO with next dose of oral meds if pt able to tolerate. If unable to tolerate, give 40mEq KCL IV. Recheck serum K within 1 hour of completing IV bolus. If K^+ 2.7 – 2.9, give KCl 40 mEq IV and repeat K^+ within 1 hour of completing bolus. If K^+ < 2.7, give 80mEq KCl. Recheck serum K within 1 hour of completing bolus. Redose K^+ according to above ranges	If K^+ > 5.5, then obtain EKG and call H.O.	Calculate corrected serum calcium (use the following formula): $Ca_{corrected}$ = total serum calcium + [0.8 x (4.0-measured albumin)] If $Ca_{corrected}$ < 8 give Calcium Gluconate 4 g IV.	If total serum calcium > 11, then call H.O.	If Mg^{++} 1.5 - 1.7 and no symptoms, then give MagTab SR PO with next dose of oral meds, if pt able to tolerate. If unable to tolerate give $MgSO_4$ 4g x 1 over 2 hours. If Mg^{++} 1.1 - 1.4 give Mag Sulfate 4 gm IV over 2 hours. Repeat Mg level within 1 hour of completing boluses. If Mg still 1.1 – 1.4 give another 4g $MgSO_4$. If Mg^{++} < 1.1, give 8g $MgSO_4$ over 4 hours. Repeat Mg level within 1 hour of completing boluses. Administer further $MgSO_4$ according to above parameters	If Mg^{++} > 3.0 then call H.O.	If serum phosphorous < 2.5mg/dL, then give IV Na Phosphate at dose of 15mmol over 4-6 hours. Phosphate is administered in the form of NaPhos or KPhos. If Na high (> 140), then give as Potassium Phosphate, otherwise administer as $NaPO_4$.	If serum phosphorous > 6.0 then call H.O.

IV Admini-stration	40 mEq in 100 ml D5W or NS and run over 2 hrs. (Max rate: 20 mEq/hr without cardiac monitor or 40 mEq/hr with monitor		4g in 100 ml NS or D5W over 2 hours.		4 gm in 1000 ml NS or D5W over 2 hours. 8g in 100mL NS or D5W over 4 hours.		Dilute every 3 mM phosphate in 25 ml for central lines and 60 ml for peripheral lines. Give no faster than 0.05 mM/kg/hr	

ADULT ELECTROLYTE BOLUS GUIDE GUIDELINES BASED ON SERUM SAMPLE RESULTS

	Potassium		Calcium		Magnesium		Phosphate	
Abnormality	Hypokalemia	Hyperkalemia	Hypocalcemia	Hypercalcemia	Hypomagnesemia	Hyper-magnesemia	Hypo-phosphatemia	Hyper-phosphatemia
Serum Level	< 3.6 mEq/L	> 5.0 mEq/L	< 8.4 mg/dL	> 10.2 mg/dL	< 1.8 mEq/L	> 2.8 mEq/L	< 2.5 mg/dL	> 4.5 mg/dL
Symptoms	Fatigue; weakness in legs; cramps	Vague muscular weakness; flaccid muscle paralysis in legs; paresthesias of face, tongue, feet, and hands	Numbness & tingling of fingers, circumoral region, and toes; muscle cramps, spasms, tremors, twitching; convulsions; depression; emotional instability; anxiety; psychosis	Muscle weakness; confusion; emotional instability; anxiety; psychosis; lethargy; coma	Muscle weakness; muscle twitching & cramps; paresthesias; depression; agitation; confusion; psychosis; anorexia; nausea; vomiting	Drowsiness; muscle weakness; coma	Paresthesias; muscle weakness (hand grasp, speech difficulty); muscle pain & tenderness; confusion; apprehension; delirium; coma; seizures	Tetany; tingling of fingertips, circumoral region, and toes; numbness; muscle spasms

Action	If K^+ 3.3 - 3.5 and no symptoms, then give KCl 40 mEq PO with next dose of oral meds. If unable to tolerate PO, give 40 mEq IV over 2 hrs. If K^+ 3.3 – 3.5 and symptoms present, or K^+ 3.0 – 3.2, then give KCl 40 mEq IV over 2 hrs and repeat K^+ within 1 hr of end of infusion. If repeat level still < 3.3, then call H.O. If K^+ < 3.0 mEq/L or dysrhythmia, give KCl 80 mEq IV over 4 hrs. Repeat K^+ within 1 hr of completion of infusion. If repeat level still < 3.0 then call H.O.	If K^+ > 5.5, then obtain EKG and call H.O.	If total serum Ca < 8.4, then calculate corrected serum calcium: $Ca_{corrected}$ = total serum calcium + [0.8 x (4.0-measured albumin)] If $Ca_{corrected} \leq 8.0$, give Calcium Gluconate 4 gm IV over 2 hrs	If total serum calcium > 11, then call H.O.	If Mg^{++} 1.5 – 1.7 and no symptoms, then give MagTab SR 2 tablets PO with next dose of oral meds. If unable to tolerate oral, give $MgSO_4$ 4gm IV over 2 hrs. Repeat Mg within 1 hr of end of IV replacement. If Mg^{++} > 1.4mg/dL and pt symptomatic without life-threatening conditions, give $MgSO_4$ 4gm IV over 2 hrs. Repeat Mg within 1 hr of completion. If Mg^{++} 1.1 – 1.4, give $MgSO_4$ 4 gm IV over 2 hrs. Repeat Mg within 1 hr of completion. If Mg^{++} < 1.1, give $MgSO_4$ 8gm IV over 4 hrs. Repeat Mg within 1 hr of completion.	If Mg^{++} > 3.0 then call H.O.	If serum phosphorous < 2.5 mg/dL give IV PO_4 at dose of 15 mmol over at least 4 hrs. Phosphate is administered in the form of NaPhos or KPhos. Give as sodium phosphate unless serum Na is > 140. If Na is > 140, call HO with low phosphorous level. If serum K is low (normal 3.6 – 5), give as KPhos.	If serum phosphorous > 6.0, then call H.O.
IV Admini-stration	40 mEq in 100 ml, run over 2 hrs. (Max rate: 20 mEq/hr without cardiac monitor or 40 mEq/hr with monitor)		4 gm in 100ml NS or D5W over 2 hrs		4gm in 50ml NS or D5W over 1-2 hours		Dilute every 3 mM phosphate in 25 ml for central lines and 60 ml for peripheral lines. Give over 4-6 hrs.	

MISCELLANEOUS

DISCHARGE CRITERIA

1. Attending physicians on the Bone Marrow Transplant Service will determine when a patient is ready to be discharged.

2. The multidisciplinary team will discuss the patient in rounds and consider the following criteria in making decisions for discharge:

   A. ANC greater than 250 for 1 day.
   B. If ANC < 250 and febrile or infected, the infection must be responding to treatment.
   C. No IV antibiotics or, if necessary, arrangements must be made with a home care agency.
   D. Criteria for amount of calories and fluid that must be taken enterally (PO or tube-fed) is a minimum of 75% of caloric and fluid needs

3. Successful completion of discharge teaching, with mastery of central venous catheter care.

4. Prior to discharge, arrangements will be made for follow-up care in the Bone Marrow Transplant Clinic and clinic follow-up for will be completed.

5. Discharge supplies ordered by Unit Clerk prior to discharge

6. Discharge teaching is to be completed prior to discharge

7. Discharge medications are to be **reviewed by the Clinical Pharmacy Specialist <u>before</u>** being sent to the Outpatient Pharmacy

   Septra® DS 1 tablet Saturday/Sunday/Monday in all autologous and allogeneic BMT patients.

BMTU PATIENT ACTIVITY GUIDELINES

1. Patients may ambulate in designated BMTU hallway wearing a mask or with approval of staff; autologous patients who are non-neutropenic may ambulate outside unit with mask. Neutropenic autologous patients may NOT ambulate outside the BMT unit. Patients being treated for leukemia should be treated as per the autologous transplant patients. If a patient wishes to sit after hours in the hallway by the College of Medicine, the attending physician must give permission.

2. Patients and families will be asked to return to their rooms during walking rounds each morning.

3. Patients may use the commodes in their bathrooms using hats to maintain In's and Out's.

4. Patients may take showers using precautions to protect their CVL.

Visitation Guidelines

1. Only two visitors are permitted in the LAF room at one time.

2. All visitors must wash their hands prior to entering the patient's room.

3. Persons with colds, fevers, and signs of infections will not be permitted to visit.

4. Children should be at least 13 years of age to visit in a patient's room on the BMTU. Patients may schedule visits in the designated room with children 12 and under. All children will receive a health screen per RN, prior to patient visitation. Under special circumstances visitation restrictions will be lifted.

5. Visiting children must remain in family room and must be supervised.

6. Persons who have had the live oral polio vaccine may not visit until 4 weeks post administration of vaccine.

7. Persons who have the chicken pox vaccine may not visit until 4 weeks post administration of vaccine.

8. Patients and families will not be permitted in the nursing station at anytime.

9. Patient and visitors may not sit in hallways.

10. Visitors may not use patient's bathroom.

11. Visitors are not permitted to eat in patient's room, but they may drink.

12. Visitors may be asked to leave during any special procedures, x-rays, or during an emergency.

NUTRITION IN THE BMT PATIENT

Low Bacteria Diet - General Rules:

1. Food should be well cooked.
2. Food should be stored in clean containers.
3. Canned or well-processed foods.
4. Patients may drink tap water and have ice from hospital ice machine.
5. All meal trays are to be delivered as per the usual hospital protocol.

Low Bacteria Diet Guidelines

Foods to Avoid when ANC < 500	*Foods to Avoid when ANC > 500*
1. Fresh fruits 2. Raw or uncooked vegetables 3. Meats that are not well cooked 4. Shell fish (lobster, shrimp, crabs, oysters, and clams) 5. No raw eggs 6. Homemade or soft ice cream 7. Creamed filled deserts 8. Raw nuts or unprocessed peanut butter 9. Raisins or other dried fruits 10. Spices or herbs added after cooking, including **pepper** 11. No well water (unless boiled 15 min)	1. No raw eggs 2. No sushi or raw shell fish 3. No well water (unless boiled 15 min.)

Criteria for Initiation of Total Parenteral Nutrition (TPN):

When the patient eats < 50% of his/her estimated calorie and fluid needs for more than 7 days (See table below)

Estimated Minimum Caloric & Fluid Needs

Patient	Age	Kcal/kg	Fluid
Infants	0-6 months 6-12 months	108 98	140 125
Children	1-3 years 4-6 years 7-10 years 11-14 years 15-18 years	102 90 70 55 45	110 90 70 60 50
Adults	Harris-Benedict x 1.5 for minimum kcal/day [males: 66.7 + [13.7 x weight (kg)] + [5 x height (cm)] - 6.8 x age (years)] [female: 65.1 + [9.6 x weight (kg)] + [1.8 x height (cm)] - 4.7 x age Two liters per day for minimum fluid needs		

DRUGS WITH POTENTIAL FOR PHOTOSENSITIVITY (DC with PUVA therapy)

Amiodarone
Amantidine
Captopril
Carprofen
Chlordiazepoxide
Chloroquine
Chlorothiazide and related thiazide diuretics
Chlorpromazine and related phenothiazines
Cinoxacin
Ciprofloxacin
Cyproheptadine
Cytostatics
Dacarbazine
Dapsone
Desipramine
Diflunisal
Dimenhydrinate
Enoxacin
Ethionamide
Fansidar®
Furosemide
Gatifloxacin
Griseofulvin
Haloperidol
Imipramine
Isotretinoin
Ketoconazole
Ketoprofen
Methyldopa
Nalidixic acid
Naproxen
Nifedipine
Norfloxacin
Nortriptyline
NSAIDS
Ofloxacin
Oral contraceptives
Pefloxacin
Phenelzine
Piroxicam
Promethazine
Protriptyline
Psoralens
Pyritinol
Quinine
Quinidine
Retinoic acids
Sulfonamides
Sulindac
Terfenadine
Tetracyclines
Trazodone
Triamterene
Triflusal
Trimethoprim
Voriconazole

 This list is intended to highlight drugs which can cause photosensitivity reactions. This list is not intended to be all-inclusive. Consult Dermatology or Pharm.D. to check the photosensitivity potential of any drug not found on this list prior to starting PUVA.

COMMONLY USED PREMEDICATION REGIMENS

TAXANES

Paclitaxel[1,2]	Dexamethasone 20mg PO at 12 and 6 hours prior to paclitaxel *OR* 20mg IV as a single dose 30 minutes prior to paclitaxel Diphenhydramine 25-50mg IV or PO 30 minutes prior to paclitaxel, and H_2-Receptor Antagonist (Cimetidine 300mg IV or PO, Famotidine 20mg IV or PO, Ranitidine 50mg IV or 150mg PO) 30 minutes prior to paclitaxel For weekly paclitaxel regimens, the starting dose of dexamethasone can be reduced to 10mg and tapered as tolerated over time to 4mg
Docetaxel[3,4]	Dexamethasone 8mg po BID x 3 days, starting the day prior to treatment For weekly docetaxel regimens, dexamethasone 8mg PO BID x 3 doses (24mg/week), starting the evening prior to treatment is often used

MONOCLONAL ANTIBODIES

Gemtuzumab Ozogamicin[5]	Diphenhydramine 50mg PO 1 hour prior to treatment Acetaminophen 650-1000mg PO 1-hour prior to treatment, repeat q4h PRN
Rituximab [6,7]	Diphenhydramine 50mg PO 30 minutes prior to treatment Acetaminophen 650mg PO 30 minutes prior to treatment
Alemtuzumab[8]	Diphenhydramine 50mg PO 30 minutes prior to treatment Acetaminophen 650mg PO 30 minutes prior to treatment

MISCELLANEOUS

Aldesleukin (interleukin-2) High dose, bolus (600,000units/kg/dose)[9]	Acetaminophen 650mg PO prior to each dose q8H NSAID (Indomethacin 25mg PO prior to each dose q8H or Naproxen 500mg PO BID during therapy H_2Receptor Antagonist (Cimetidine 300mg PO/IV at HS or Famotidine 20mg PO/IV at HS or Ranitidine 150mg PO or 50mg IV at HS)
Aldesleukin (interleukin-2) Low dose, outpatient SQ or continuous infusion[10]	Acetaminophen 650mg PO prior to each dose or q4h PRN
Bleomycin[11]	Acetaminophen 650mg PO 30 minutes prior to treatment, repeat q4h PRN
Interferon-alfa[12]	Acetaminophen 650mg PO 30 minutes prior to treatment, repeat q4h PRN

See page 89 for amphotericin B premedication; page 115 for ATGAM, and page 116 for thymoglobulin premedication regimens.

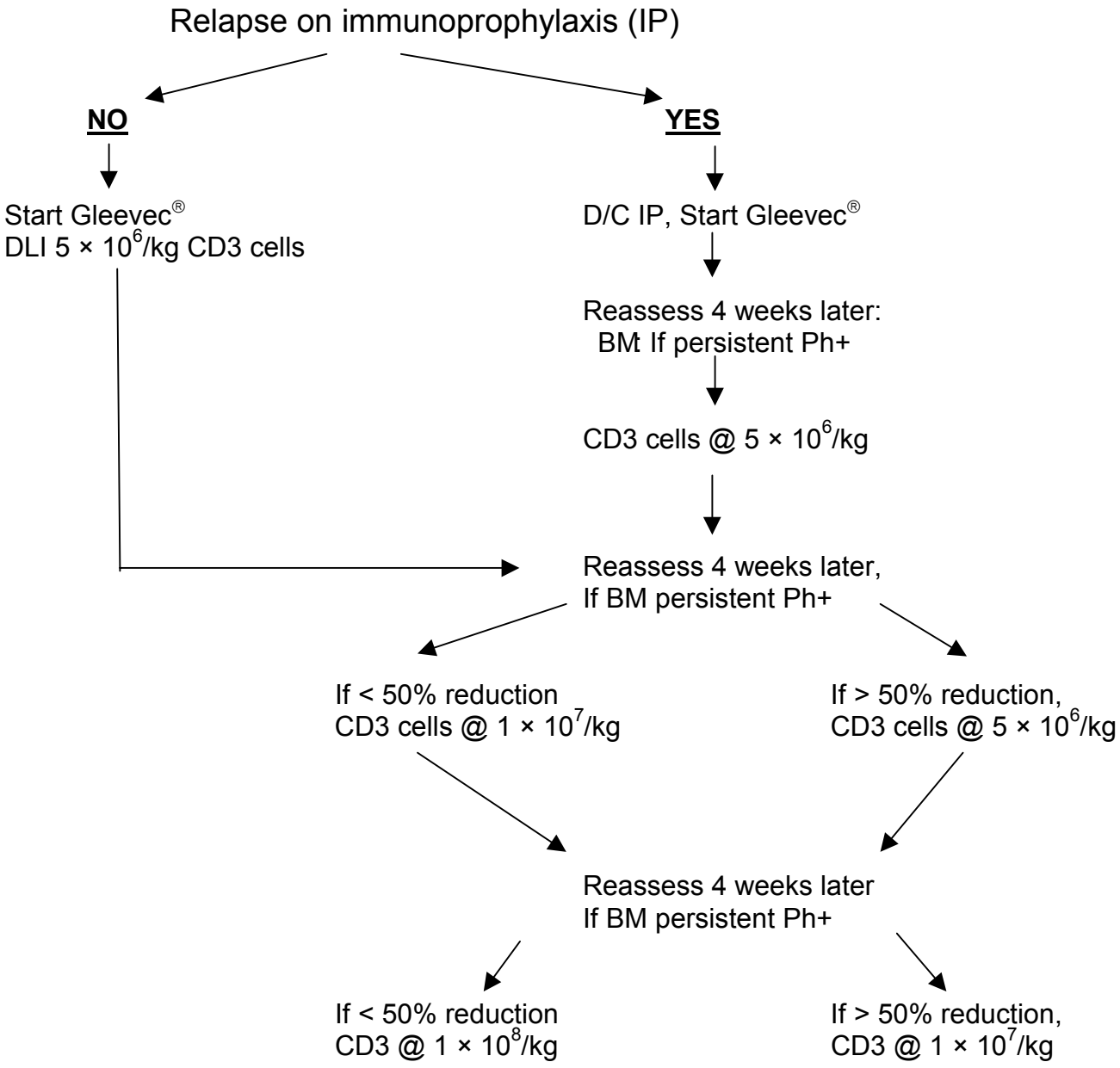
POST-TRANSPLANT CONSIDERATIONS

ADOPTIVE IMMUNOTHERAPY

1. CML

Evaluate the status of the disease (bone marrow or peripheral blood) at day 100 and at 6 months:

A. Cytogenetic (if any Ph+ by FISH or cytogenetics at any time following transplant) or molecular relapse (PCR^+ detected after 6 months following transplant if patient was negative at 6 months. Consider repeating x 2 before treating) and if no GVHD.



B. CML: Hematologic relapse. As above, except start at 1×10^7 CD3/kg.

C. CML: Blast crisis. Consider acute leukemia DLI guidelines.

2. ACUTE LEUKEMIA

At relapse and if GVHD less than Stage II

↓

Stop immunosuppression

↓

Induction with FLA (no G-CSF) if SCr < 1.5 or use Cytarabine + Daunorubicin (7+3) or HiDAC

↓

Adoptive Immunotherapy (2 - 4 days after completion of chemo)
1×10^{8} $CD3^{+}$/kg

↓

Wait one month:
If in remission and no GVHD, repeat DLI up to 2 additional DLI @ 6 to 8 week intervals.

or

If residual leukemia and GVHD < Stage II 5×10^{8} $CD3^{+}$/kg.

or

If cyto or molecular marker known and persists < 50% of baseline, increase DLI by half a log.

↓

Residual leukemia → consider 2^{nd} transplant

VACCINATIONS POST BONE MARROW TRANSPLANTATION

Vaccine Guidelines		
Time After BMT	**Vaccination**	**Comments**
≥6 months	Influenza	See comments below. Lifelong, seasonal administration, beginning pre-BMT and resuming ≥ 6 months post- HSCT (BII).
12 months	DTaP (Diphtheria-Tetanus-Acellular Pertussis) < 7 yrs Td (Diphtheria-Tetanus) ≥ 7 yrs Polio (Inactivated) Hib (Haemophilus b) Hepatitis B (series) Pneumovax®	No Sabin PolioVirus (OPV) post BMT for patients or family members. Hepatitis B dosing in immunocompromised patients is 40µg/dose
14 months	DTaP (Diphtheria-Tetanus-Acellular Pertussis) < 7 yrs Td (Diphtheria-Tetanus) ≥ 7 yrs Hib conjugate Polio (Inactivated) Hepatitis B (dose #2)	If Hep C+, check Hep A antibody. If Hep A antibody negative, give Hepatitis A vaccine.
24 months	DTaP (Diphtheria-Tetanus-Acellular Pertussis) < 7 yrs Td (Diphtheria-Tetanus) ≥ 7 yrs Polio (Inactivated) Hib conjugate Hepatitis B (dose #3) Pneumovax Immunize with MMR.	No patient should have the MMR until 2 years post BMT. They must not be receiving active immunosuppressive medications and not have active GVHD. Family members may receive MMR.

Alternative Immunization Sites:

Alachua County Health Department	
Alachua Clinic	462-2542
Family Progress Center Clinic	955-7010
Main Unit	955-2364

Influenza Vaccine: Administration of the influenza vaccine is recommended for immunocompromised patients because infection with the influenza virus may cause serious complications in these patients. After bone marrow transplantation, patients may have a low antibody response to the influenza vaccine and repeated administration has not been shown to increase antibody response. However, because symptoms may be prolonged and the risk of complications is increased, immunization is recommended; many of the patients will develop protective antibodies. (This is an inactivated vaccine).
Varicella Vaccine: contraindicated in recipients < 24 months post-BMT. Use of varicella vaccine in BMT recipients is restricted to research protocols for recipients ≥ 24 months post-BMT that are presumed immunocompetent.

USE OF BISPHOSPHONATES POST TRANSPLANT - ADULTS

Indication	Drug	Dose/Regimen	Cost
Multiple Myeloma patients with osteolytic bone lesions	Pamidronate (Aredia®) Zoledronic acid (Zometa®)	90mg IV once a month 4mg IV over 15 minutes Q month	$487.20 (per dose) $646.70 (per dose)
Breast cancer with skeletal metastasis	Pamidronate Zoledronic acid	90mg IV once a month 4mg IV once a month	$487.20 (per dose) $646.70 (per dose)
Corticosteroid induced osteoporosis*	Alendronate Pamidronate	70mg PO Q week 30mg every 3 months	$59.64 (per month)
Females with ovarian failure not eligible for hormonal therapy	Alendronate (Fosamax®)	70mg PO Q week	$59.64 (per month) = cash price

Prices from Pharmacy Stores on 4/24/02

* References for pamidronate: NOTE pamidronate 30mg every 3 months has been shown to be effective in preventing steroid induced osteoporosis, however is not reimbursed by the majority of insurance providers for this indication. If the patient's insurer will not provide coverage prescribe alendronate 70mg PO Qweek.

Hodsman A et al. Prevention and management of Osteoporosis: Consensus statements from the Scientific Advisory Board of the Osteoporosis Society of Canada. *Canadian Med. Assoc. J* 1996; 155(7): 945 – 48
Boutsen Y et al. *Bone* 1996; 1(6): 609
Gallacher SJ et al. Intravenous Pamidronate in the treatment of osteoporosis associated with corticosteroid dependent lung disease: an open pilot study. *Thorax* 1992; 47(11): 932 – 36.

Administration Guidelines:

Pamidronate (Aredia®):

Osteolytic bone lesions of multiple myeloma- Dilute the recommended dose of 90 mg in 500 mL of Sterile 0.45% or 0.9% of NaCl, or 5% Dextrose Injection and give over 4 hours on a monthly basis

Hypercalcemia of malignancy- Administer the single dose as an IV infusion over 2 to 24 hours for the 60 and 90mg doses.

Zoledronic Acid (Zometa®):

Osteolytic bone lesions of multiple myeloma and metastatic bone lesions from solid tumors: 4mg infused over 15 minutes every 3 – 4 weeks. Serum creatinine should be measured prior to each dose and treatment should be withheld for renal deterioration. Renal deterioration is defined as follows:

Patients with normal baseline, an increase of 0.5mg/dL;
Patients with abnormal baseline creatinine, an increase of 1mg/dL.

Only resume treatment with Zometa® once the creatinine has returned to within 10% of baseline.

GUIDELINES FOR ERYTHROPOIETIN (EPO) USE POST BMT

Criteria for Use: Hgb ≤ 11 g/dL, RBC transfusion-dependent

Mechanism of Action:

Induces erythropoiesis by stimulating the division and differentiation of committed erythroid progenitor cells; induces release of reticulocytes from bone marrow into the blood stream, where they mature to erythrocytes

Product Availability:

- Epogen®, Procrit® (epoietin alfa): 2,000, 3,000, 4,000, 10,000, 20,000, and 40,000 units/ml vials
- Aranesp® (darbopoietin alfa)*: 25, 40, 60, 100, and 200 mcg/ml vials

Warnings: Use with caution in patients with porphyria, hypertension, or seizure history

Baseline Assessment:

- Baseline erythropoietin level
- Serum ferritin > 100 ng/dL
- Transferrin saturation of 20-30%
- Iron therapy (325 mg PO 2-3 times daily) unless increased iron stores already exist
- Folic acid, vitamin B_{12}, reticulocyte count

Dosing:

- 40,000 units SC Q week
- Darbopoietin alfa: 100 mcg SC Q week or 200 mcg SC Q other week*
- Darbopoietin alfa starting doses based on weekly EPO doses:

EPO dose (units/week)	**Darbopoietin dose** (mcg/week)
<2,500	6.25
2,500-4,999	12.5
5,000-10,999	25
11,000-17,999	40
18,000-33,999	60
34,000-89,999	100
≥ 90,000	200
Note: Conversions are from data in renal patients. Conversions in oncology patients may differ.	

- **Reduce dose if**: Hgb > 13 g/dL or Hct > 36%
  - Resume at 75% of previous dose when Hgb ≤ 12 gm/dL or Hct ≤ 30%
  - Evaluate need for continued dosing

- **Increase dose if:** increase in Hgb < 1 gm/dL or Hct < 5 points after 4 weeks of therapy
  - Increase epoietin alfa dose to 60,000 units SC Q week
  - Reevaluate nutritional cofactors (iron status, B_{12}, folic acid)
  - If 4 weeks of therapy at higher dose has not produced an increase in Hgb by ≥ 1 gm/dL, in

Hct by ≥ 5 points, or reduced transfusion requirements, consider discontinuation of EPO therapy

- Doses > 60,000 units/week are not associated with an improved outcome

Pertinent Pharmacokinetic Features: Onset of effect in several days, peak effect in 2-3 weeks

Monitoring Parameters: Hgb/Hct, blood pressure, serum ferritin

Adverse Effects: Hypertension, fatigue, headache, fever, edema, chest pain, nausea, vomiting, diarrhea, clotted IV access, arthralgias, asthenia, MI, CVA/TIA, rash, hypersensitivity reactions (Significant AEs are uncommon in nondialysis patients.)

Reimbursement Assistance: Amgen, 1-800-272-9376

* Note: as of 5/1/2002, darbopoietin has NOT been approved by the FDA for use in oncology patients. The current FDA-approved indication is for anemia associated with chronic renal insufficiency or chronic renal failure.

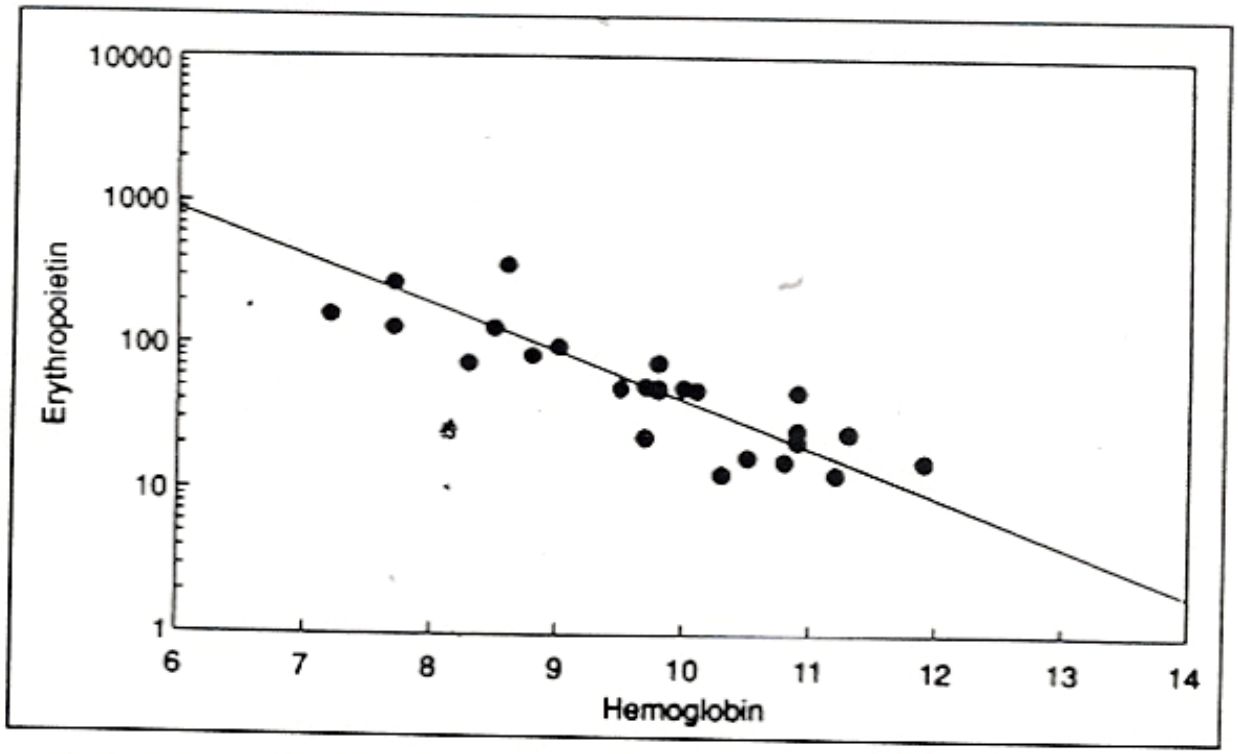


Fig. 9.2. Erythropoietin-hemoglobin relationship in 27 iron deficient patients. This can be used as a nomogram for determining the adequacy of erythropoietin response to anemia in BMT.

BONE MARROW BIOPSIES POST TRANSPLANT—LIST OF TESTS TO ORDER

AML/ALL	Cytogenetics Flow Cytometry Aspirate for morphology Core biopsy Ph+ ALL: send FISH for bcr/abl
AMLM3/APL	Aspirate for morphology Cytogenetics Flow Cytometry Core biopsy FISH + 15/17 PCR for RARA/PML (+15/17)
CML	Aspirate for morphology Flow Cytometry ONLY if accelerated phase or blast crisis Cytogenetics and FISH for bcr/abl Core biopsy
CLL	Core biopsy Aspirate for morphology, flow cytometry Cytogenetics
MDS/SAA	Core biopsy Aspirate for morphology Cytogenetics Flow cytometry if RAEB or RAEB-t is present
NHL	Aspirate for morphology Flow cytometry Cytogenetics Core biopsy (need bilateral if ordered for initial staging)
HD	Aspirate for morphology Core biopsy Cytogenetics
EWINGS	Core biopsy Aspirate for BIS
MM	Aspirate for morphology Core biopsy Cytogenetics Flow cytometry FISH for 13 and 14
NOTES	Follow-up: ALL Allo/Mud/UCB SCT patients: FISH for sex chromosomes for sex mismatches, STR's for chimerism.

**If patient is known to have blasts, consider obtaining informed consent for collecting extra for research. Consents are in procedure room (1-2 purple top tube)*

Cytogenetics/FISH/BIS—Heparin (green tube) Flow/PCR—EDTA (purple tube)
STR's (yellow) Anticoagulant ACID Citrate

POST-TRANSPLANT CHEMOTHERAPY

1. Acute Lymphoblastic Leukemia

Intrathecal therapy (applies to both pediatric and adult populations):

A. CR1 who completed CNS prophylaxis prior to SCT and who had TBI in the preparative regimen should not have post-HSCT IT therapy: risk of leukoencephalopathy outweighs the potential benefits

B. CR1 patients who are taken to HSCT prior to completing adequate CNS prophylaxis per their protocol (e.g., after only 2 cycles of chemotherapy): 5 doses of IT chemotherapy post-HSCT as tolerated

C. CR1 with a history of CNS disease AND all those beyond CR1: 5 doses of IT therapy as tolerated. Patients who have difficulty tolerating it should be taken off therapy.

Choice of Therapy:

Adults: Intrathecal Methotrexate 12.5mg plus hydrocortisone 15mg (total number of injections listed above) *followed by*
Calcium leucovorin rescue 5mg PO x 4 doses, starting 24 hours after IT injection

Pediatrics: See pediatric section for dosing – dose and injections volume is age dependent.

When to administer? The first IT dose should be administered during the pre-BMT evaluation. Four additional doses (total of 5) should be administered, starting after stabilization of graft, administered at 2-weekly intervals (or as tolerated). The goal is to complete by Day 100 if possible.

Philadelphia Chromosome positive ALL:

Patients with Philadelphia chromosome positive ALL are also to receive imatinib (Gleevec®) upon stable engraftment and stabilization of the immunoprophylaxis regimen. Dose 600 – 800mg PO QD.

2. Chronic Myeloid Leukemia

Patients who have a history of, or who are transplanted in accelerated phase or in blast crisis are to start imatinib (Gleevec®) upon stable engraftment and stabilization of the immunoprophylaxis regimen.

Adult Dose: start with 200mg PO QD, and titrate up to 800mg PO QD as tolerated.

Pediatric Dose: see pediatric section

LEUKEMIA SECTION

		Newly diagnosed	1st recurrence/ primary refractory*	≥ 2nd recurrence*
De novo AML (non M3)	Age ≤ 60yo	Induction 7+3 followed by consolidation HiDAC x 3; if day 14 BMBx <5% cellularity wait for count recovery if day 14 BMBx 5-20% cellularity with <50% blasts wait for count recovery if day 14 BMBx > 5-20% cellularity with >50%blasts re-induce with 7 + 3, starting on day +15-16 if day 14 BMBx > 20% cellularity with > 5% blasts re-induce with HiDAC	<u>Stratify tx by duration of CR1 and whether the pt had or not HiDAC*:</u> <u>CR< 1 yr:</u> **#1 ECOG4999 [IRB 033-02]** HiDAC (CIVI)/Ida followed by HiDAC/Ida consolidation x 1-2 <u>CR ≥ 1yr:</u> Induction HiDAC+/-anthracycline followed by HiDAC consolidation x 3	HiDAC+/-Ida Mylotarg DNR/VP-16 Cy/VP-16 CECA 2CDA
	Age >60yo	Induce with 7+3, then tailor consolidation according to algorithm (see next page)		
Secondary AML	Age ≤ 60yo	Discuss supportive care as a reasonable option especially for older pts with poor PS and co-morbid conditions. If patient wishes to pursue treatment*: HiDAC/Ida induction, repeat 1-2 times for consolidation		
	Age >60yo	Discuss supportive care as a reasonable option especially for older pts with poor PS and co-morbid conditions. If pt wishes to pursue treatment*: Mitoxantrone/HiDAC induction [Day 1 and 5 only], repeat 1-2 times for consolidation		
MDS		<u>Standard of care for pts with MDS is supportive care. If pt wishes to pursue treatment*:</u> <u>#1 Screen for eligibility for investigational protocol:</u> • **Decitabine [WIRB 200110225]** • **ATG (RAEB<10%blasts, RA) [IRB 545-00]** • **Epo/GCSF versus supportive care [IRB 546-99]** <u>#2 If not eligible for study:</u> and high IPI consider tx like secondary AML	?	?
ALL – FAB L1 and L2		**#1 E2993 [IRB 232-93]** #2 Larson's #8511 (+ Gleevec® if Ph^+)* <u>NOTE</u>: for patients aged < 22 years, consider COG protocols (see pediatric section/research nurses)	Hyper-CVAD <u>course II only</u> repeat cycles x 3 - 4 total (add Gleevec® if Ph^+)* <u>NOTE</u>: for patients aged < 22 years, consider COG protocols (see pediatric section)	
ALL – FAB L3		#1 CALGB 9251 <u>NOTE</u>: for patients aged < 22 years, consider COG protocols (see pediatric section/research nurses)	Hyper-CVAD <u>course II only</u> repeat cycles c 3 – 4 total(add Gleevec® if Ph^+)* <u>NOTE</u>: for patients aged < 22 years, consider COG protocols (see pediatric section)	

* Evaluate patient for HSCT

AML

Newly diagnosed

De novo AML (non M3) Age ≤ 60yo

#1 7+3 induction [7 days cytarabine 100mg/m^2, 3 days idarubicin 12mg/m^2], followed by HiDAC x 3 [3g/m^2 BID Day 1, 3, 5]
If day 14 bone marrow biopsy is < 5% cellular, wait for count recovery to guide therapy
If day 14 bone marrow biopsy is between 5 and 20% cellular, with < 50% blasts, wait for count recovery
If day 14 bone marrow biopsy > 5 – 20% cellular with > 50% blasts, reinduce with 7+3, starting on day 15/16
If day 14 bone marrow biopsy > 20% cellular with > 5% blasts, reinduce with HiDAC

De novo AML Age >60yo

#1 Induce with 7+3 (discuss poor rests of treatment and high induction mortality), then tailor therapy according to algorithm: treatment of newly diagnosed AML in pts >60 year old

1st recurrence/primary refractory

Stratify treatment by duration of CR1 and whether the patient had or not had HiDAC:

CR < 1 year:
#1 ECOG 4999 [IRB 033-02]
#2 HiDAC (continuous infusion)/Idarubicin, followed by HiDAC/Ida consolidation x 1 – 2

CR ≥ 1 year:
Induction: HiDAC +/- an anthracycline
Consolidation: HiDAC x 3

≥ 2nd recurrence

HiDAC/Idarubicin
Mylotarg
DNR/VP-16
ICE
CECA
2-CDA/mitoxantrone

SECONDARY AML

Age ≤ 60 years

May discuss supportive care as a reasonable option, especially for older patients with poor PS and co-morbid conditions. If the patient wishes to pursue treatment:

#1 HiDAC/Idarubicin induction, repeat 1-2 times for consolidation

Age > 60 years

May discuss supportive care as a reasonable option, especially for older patients with poor PS and co-morbid conditions. If the patient wishes to pursue treatment:
#1 HiDAC/Mitoxantrone [Day 1 and 5 only] induction, repeat 1-2 times for consolidation

MDS

Standard of care for patients with MDS not eligible for transplant, is supportive care. If patient wishes to pursue treatment the following options are available at Shands at the University of Florida:

#1 Screen for eligibility for investigational protocol:

- **Decitabine [WIRB 20010225]**
- **ATG (RAEB<10%blasts, RA) [IRB 545-00]**
- **Epo/GCSF vs. supportive care [IRB 546-99]**

#2 If not eligible for study: and high IPI consider treating like secondary AML

ALL-FAB L1 and L2

Newly diagnosed:

#1 ECOG 2993 [IRB 232-93]
#2 Larson's #8511 (+ Gleevec® if Philadelphia chromosome positive)
NOTE: Consider COG protocols if patient < 21.99 years. See table in pediatric section for open protocols.

Primary refractory/recurrent:

#1 Hyper-CVAD course II only repeat cycles x 3 - 4 total

NOTE: Consider COG protocols if patient < 21.99 years. See table in pediatric section for open protocols.

ALL – FAB L3

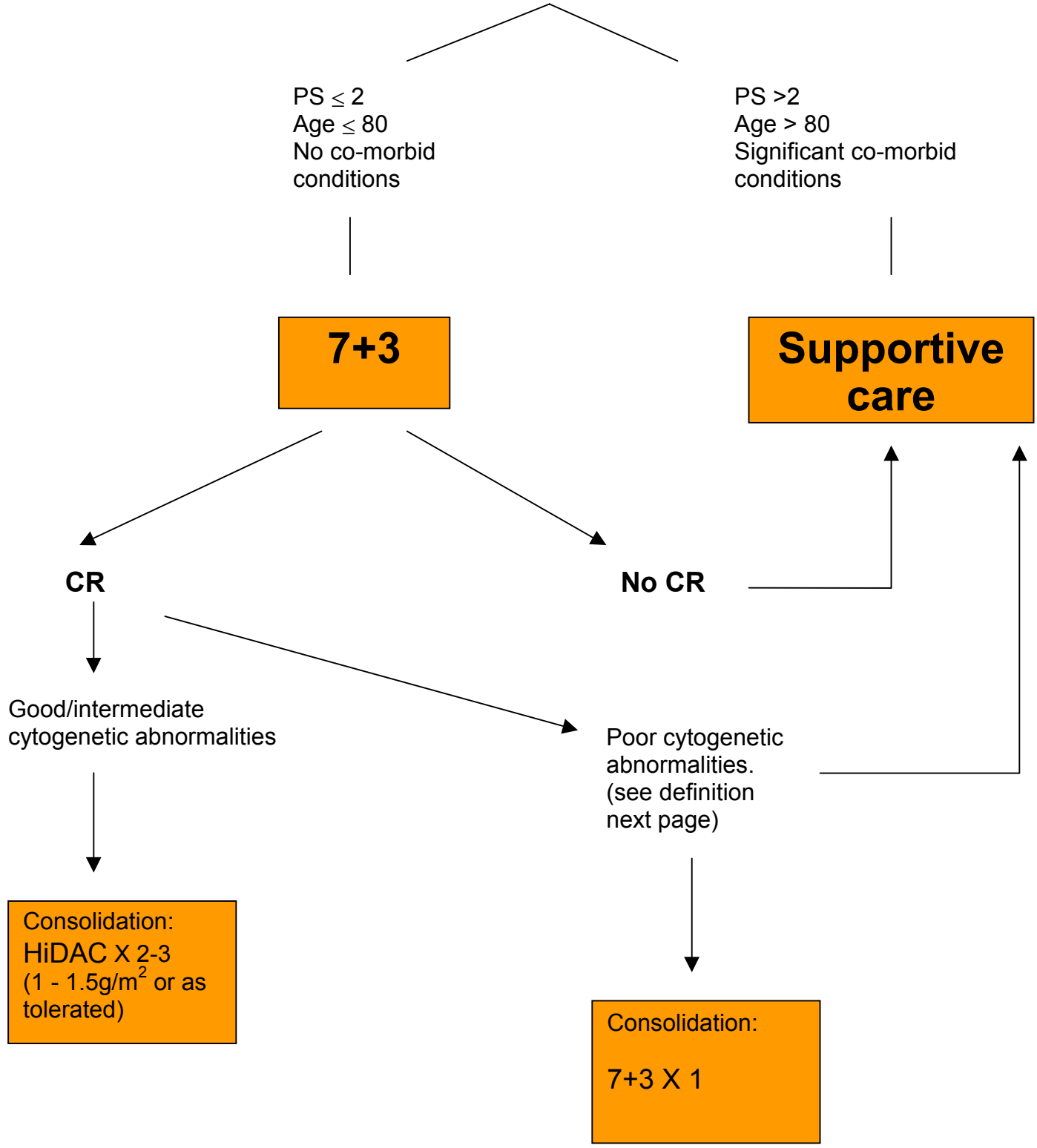
Newly diagnosed

CALGB 9251
NOTE: Consider COG protocols if patient < 21.99 years. See table in pediatric section for open protocols.

Primary refractory/recurrent

#1 Hyper-CVAD course II only repeat cycles x 3 - 4 total
NOTE: Consider COG protocols if patient < 21.99 years. See table in pediatric section for open protocols.

ALGORITHM FOR TREATMENT OF NEWLY DIAGNOSED *DE NOVO* AML AGE >60 YEARS



SHANDS AT THE UNIVERSITY OF FLORIDA BMT/LEUKEMIA PROGRAM
ACUTE MYELOID LEUKEMIA (AML) REGIMENS

7 + 3
Cytarabine 100mg/m^2/day IV CI days 1 – 7
PLUS
Idarubicin 12mg/m^2 IV QD day 1 – 3

IA
Cytarabine 1500 mg/m^2 IV CI QD Days 1 - 4
Idarubicin 12 mg/m^2 IV QD Days 1 - 3

Bishop
Cytarabine 3000mg/m^2 IV Q12H day 1, 3, 5, 7
Daunorubicin 50mg/m^2 IV QD day 1 – 3
Etoposide 75mg/m^2 IV QD Day 1 – 7

CECA
Cyclophosphamide 1000mg/m^2 IV QD Day 1 – 3
Etoposide 200mg/m^2 IV QD Day 1 – 3
Carboplatin 150mg/m^2 CIVI QD Day 1 – 3
Cytarabine 1000mg/m^2 IV QD Day 1 – 3
(Administer sequentially with Cytoxan first, followed by etoposide and then cytarabine)

FLAG
Fludarabine 30mg/m^2 IV QD Day 1 – 5
Cytarabine 2000mg/m^2 IV QD Day 1 – 5

FLANG
Fludarabine 30mg/m^2 IV QD Day 1 – 3
Cytarabine 1000mg/m^2 IV QD Day 1 – 3
Mitoxantrone 10mg/m^2 IV QD Day 1 – 3

HiDAC (< 60 years)
Cytarabine 3000mg/m^2 IV Q12H Day 1, 3, 5

HiDAC (≥ 60 years)
Cytarabine 1000mg/m^2 IV Q12H Day 1, 3, 5

Mitoxantrone/Cytarabine
Cytarabine 2000mg/m^2 IV Q12H for 2 doses on Day 1 and 5 (t = 0 and t = 12)
Mitoxantrone 30mg/m^2 after second dose of Cytarabine on Day 1 and 5
[Reference: Preisler HD, et al. *Leuk Lymphoma* 2001; 41:333 – 6]

VP-16/DNR
Etoposide 100mg/m^2 Day 1 – 5
Daunorubicin 60mg/m^2 Day 1 – 3 (NOTE: daunorubicin substituted for mitoxantrone due to costs)

CYCLOPHOSPHAMIDE-ETOPOSIDE
Etoposide 1800mg/m^2 CIVI over 25 – 26 hours at 70mg/m^2/hour on Day 1
Hydration: D5¼NS + 10mEq KCL at 150mL/hour until 24 hrs post Cytoxan
Cyclophosphamide 50mg/kg IV over 2 hours Day 2 and Day 3
Lasix (refer to protocol)

ECOG 4999 – IRB 033-02

Arm A Cytarabine 1g/m^2/day over 2 hours Day 1 – 4
Gemtuzumab 6mg/m^2 over 2 hours on Day 5
(APAP 650mg + diphenhydramine 25 – 50mg PO pre gemtuzumab)

Arm B Liposomal daunorubicin 135mg/m^2 over 2 hours Day 1 – 3, *followed by*
Cytarabine 1g/m^2/day over 2 hours Day 1 – 4

Arm C Cyclophosphamide 300mg/m^2 over 1 hour Q12H on Day 1 – 3 (total 6 doses)
Mesna 600mg/m^2/day CIVI, starting 1 hour prior to cyclophosphamide and continuing until 12 hours after the completion of the last dose of cyclophosphamide
Cytarabine 1g/m^2/day over 2 hours Day 2 – 6 (administered immediately following the cyclophosphamide on days 2 and 3, and at the same time of day on subsequent days)
Topotecan 1.5mg/m^2/day CIVI Days 2 – 6

HIGH DOSE CLADRIBINE (Reference: *JCO* 1998; 15:1498 – 504)
Cladribine (2-CDA) 15mg/m^2/day Day 1 - 5

ACUTE PROMYELOCYTIC LEUKEMIA (APL/ APML)

AIDA induction Regimen
Idarubicin 12mg/m^2/d on days 2,4,6,8 (total 4 doses)
ATRA 45mg/m^2/d orally (from day 1 until CR)
Dexamethasone 10mgBID for all patients with WBC> 5,000 (RA prophylaxis)

Consolidation:

Course #1 Idarubicin 5mg/m^2/d days 1 - 4
Course #2 Mitoxantrone 10mg/m^2/d days 1 - 5
Course #3 Idarubicin 12 mg/m^2/d on day 1 only
[Reference: *Blood* 1996; 88(4): 1390 – 98; *Blood* 1997; 90(3): 1014 – 21]

Maintenance (begin 3-4 weeks after hematological recovery from consolidation):
6-MP 90mg/m^2/d daily
MTX 15mg/m^2/week po q week
ATRA 45mg/m^2/d for 15 days every 3 months
Continue for 2 years
[Reference: *Blood* 1999; 94(4): 1192 – 1200]

Doses of 6-MP and MTX ↓ by 50% for WBC lower than 3.5, d/c if lower than 2.5

Follow-up:
Frequency PCR on BM aspirate: at diagnosis, upon CR, upon completion of consolidation, q 3mo during the first and second year and q 6 month during the 3rd an 4th year

RELAPSED APL

Arsenic Trioxide Induction Schedule
As_2O_3 As_2O_3 0.15mg/kg daily until BM remission (total induction dose not to exceed 60 doses)

Consolidation Schedule

As_2O_3 0.15mg/kg daily for 25 doses, which may be given on consecutive days or on a schedule of daily M – F for 5 weeks. Start consolidation therapy 3 – 6 weeks after completion of induction therapy.
[Reference: *NEJM* 1998; 339:1341 – 8]

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

ECOG 2993 (IRB 232-92)

Induction Phase I

Daunorubicin 60mg/m^2 IV QD Day 1, 8, 15, 22
Vincristine 1.4mg/m^2 (max 2mg) IV QD Day 1, 8, 15, 22
Prednisone 60mg/m^2 PO QD Day 1 – 28
L-Asparaginase (*E.Coli*) 10,000 units/m^2 IV QD day 17 – 28
Methotrexate 12.5mg IT day 15

Induction Phase II
Cyclophosphamide 650mg/m^2 IV Days 1, 15, 29
Cytarabine 75mg/m^2 IV QD Days 1 – 4, 8 – 11, 15 – 18, 22 – 25
6-mercaptopurine 60mg/m^2 PO days 1 – 28
Methotrexate 12.5mg IT Days 1, 8, 15, 22

Intensification
Methotrexate 3000mg/m^2 IV QD Days 1, 8, 22*
L-Asparaginase (*E.Coli*) 10,000 units/m^2 IV QD Days 2, 9, 23
Leucovorin 10mg/m^2 [* begin 24 hours after MTX infusion]
IV Q6H x 4 doses then 10mg/m^2 PO Q6H x 72 hours

CNS prophylaxis for patients who did not present with occult CNS disease and are not to receive BMT [administer between intensification and consolidation]
Cranial irradiation 24 Gy in 12 fractions over 2 – 3 weeks
Intrathecal cytarabine 50mg – administer weekly for a total of 4 doses, followed by a further 4 doses at least 3 months apart during maintenance therapy

Consolidation cycle I
Cytarabine 75mg/m^2 IV QD Day 1 – 5
Etoposide 100mg/m^2 IV QD Day 1 – 5
Vincristine 1.4mg/m^2 [max 2mg] IV QD Day 1, 8, 15, 22
Dexamethasone 10mg/m^2 PO Day 1 – 28

Consolidation cycle II
Cytarabine 75mg/m^2 IV QD Day 1 – 5
Etoposide 100mg/m^2 IV QD Day 1 – 5

Consolidation Cycle III
Daunorubicin 25mg/m^2 IV QD Day 1, 8, 15, 22
Cyclophosphamide 650mg/m^2 IV day 29
Cytarabine 75mg/m^2 IV QD Days 31 – 34, 38 – 41
6-thioguanine 60mg/m^2 PO Day 29 – 42

Consolidation Cycle IV
Identical to consolidation cycle II

Maintenance chemotherapy

6-mercaptopurine 75mg/m^2 PO QD
Methotrexate 20mg/m^2 PO or IV once a week for 2.5 years
Vincristine 1.4mg/m^2 [max 2mg] IV q3months with prednisone
Prednisone 60mg/m^2 QD x 5 days q3months with vincristine
Intrathecal Cytarabine 50mg: administer 4 doses, each 3 months apart during maintenance
Philadelphia chromosome ALL patients are to receive Interferon therapy 3 x 10^6 units SQ three times a week for 15 months.

NOTE: continue maintenance for 2.5 years from start of intensification.

Hyper CVAD

Course I
Cyclophosphamide 300mg/m^2 IV Q12H on day 1, 2, 3 (6 doses total)
Doxorubicin 50mg/m^2 IV QD day 4
Vincristine 2mg IV QD Day 4 and 11
Dexamethasone 40mg po QD Day 1 – 4, 11 – 14
G-CSF 5mcg/kg SQ QD begin day 4

Course II
Methotrexate 200mg/m^2 IV over 2 hours bolus, followed by Methotrexate 800mg/m^2 IV CI over 24 hours (both on Day 1)
Cytarabine 3000mg/m^2 IV Q12H x 4 doses on Day 2 and 3. Begin at completion of MTX.
Methylprednisolone 50mg IV BID Day 1, 2, and 3

Leucovorin rescue [start 24 hours after the completion of MTX infusion] 15mg po Q6H x 8 doses, increasing to 50mg PO Q6H depending on levels, and continuing until acceptable excretion of MTX as guided by serum concentrations. Check MTX levels immediately following completion of infusion, then 24 hours and 48 hours after the first level.

NOTE: for multiple myeloma another version of Hyper-CVAD is to be prescribed. The reference is Dimopoulos MA, Weber D, Kantarjian H, et al. HyperCVAD for VAD-resistant multiple myeloma. *Am J Hematol* 1996; 52:77 – 81.

LARSON'S ALL REGIMEN [CALGB STUDY 8811, CALGB 9111]

Induction
Cyclophosphamide 1200mg/m^2 IV day 1
Daunorubicin 45mg/m^2 IV QD Day 1, 2, 3
Vincristine 2mg IV QD Day 1, 8, 15, 22
Prednisone 60mg/m^2 PO/IV Days 1 – 21
L-Asparaginase (*E.Coli*) 6000 IU/m^2 SQ/IM Days 5, 8, 11, 15, 18, 22

Dose reduced induction for patient's > 60 years
Cyclophosphamide 800mg/m^2 IV Day 1
Daunorubicin 30mg/m^2 IV QD Day 1, 2, 3
Prednisone 60mg/m^2 PO/IV Days 1 – 7

Course IIA: Early intensification
Methotrexate 15mg IT Day 1
Cyclophosphamide 1000mg/m^2 IV Day 1
6-Mercaptopurine 60mg/m^2 PO QD Day 1 – 14
Cytarabine 75mg/m^2 SQ Day 1 – 4, 8 – 11
Vincristine 2mg IV QD Days 15, 22
L-Asparaginase (*E.Coli*) 6000 IU/m^2 SQ/IM Days 15, 18, 22, 25

Course IIB: Early Intensification Continuation
Methotrexate 15mg IT Day 1
Cyclophosphamide 1000mg/m^2 IV Day 1
6-Mercaptopurine 60mg/m^2 PO QD Day 1 – 14
Cytarabine 75mg/m^2 SQ Day 1 – 4, 8 – 11
Vincristine 2mg IV QD Days 15, 22
L-Asparaginase (*E.Coli*) 6000 IU/m^2 SQ/IM Days 15, 18, 22, 25

Course III
Cranial radiation 2400 cGy Day 1 – 12
Methotrexate 15mg IT QD Days 1, 8, 15, 22, 29
6-Mercaptopurine 60mg/m^2 PO Day 1 – 70
Methotrexate 20mg/m^2 PO QD Days 36, 43, 50, 57, 64

Course IV
Doxorubicin 30mg/m^2 IV QD Day 1, 8, 15
Vincristine 2mg IV QD Days 1, 8, 15
Dexamethasone 10mg/m^2/day PO QD Days 1 – 14
Cyclophosphamide 1000mg/m^2 IV Day 29
6-Thioguanine 60mg/m^2 PO QD Day 29 – 42
Cytarabine 75mg/m^2 SQ QD Days 29 – 32, 36 - 39

Course V: Maintenance
Vincristine 2mg IV QD Day 1 of every 4 weeks
Prednisone 60mg/m^2 PO Day 1 – 5 of every 4 weeks
6-Mercaptopurine 60mg/m^2 PO Days 1 – 28
Methotrexate 20mg/m^2 PO QD Days 1, 8, 15, 22

HOELZER ALL L3 (BFM 86) REGIMEN

Pre-phase
Prednisone 60mg/m^2 po QD Day 1 - 5
Cyclophosphamide 200mg/m^2 IV QD Day 1 – 5

Cycle A
Intrathecal MTX 15mg/Ara-C 40mg/Dexamethasone 4mg Day 1 and 5
Vincristine 2mg IV Day 1
Methotrexate 1500mg/m^2 Day 1 [150mg/m^2 as a loading dose over 30 minutes, and the remaining 1350mg/m^2 over 23.5hours]
Calcium leucovorin rescue [30mg/m^2 IV 36 hours after the start of the MTX infusion. Thereafter oral doses of 30mg/m^2 at 42 hours, 15mg/m^2 at 48 hours, and 5mg/m^2 at 54, 68, and 78 hours. Doses to be increased based on levels – see protocol.
Ifosfamide 800mg/m^2 IV QD Day 1 – 5 inclusive
VP-26 (Teniposide) 100mg/m^2 QD Day 4 and 5 (total of 2 doses)

Cytarabine 150mg/m^2 Q12H Day 4 and 5 (total of 4 doses)
Dexamethasone 10mg/m^2 PO Day 1 - 5

Cycle B
Intrathecal MTX 15mg/Ara-C 40mg/Dexamethasone 4mg
Vincristine 2mg IV Day 1
Methotrexate 1500mg/m^2 Day 1 [150mg/m^2 as a loading dose over 30 minutes, and the remaining 1350mg/m^2 over 23.5hours]
Calcium leucovorin rescue [30mg/m^2 IV 36 hours after the start of the MTX infusion. Thereafter oral doses of 30mg/m^2 at 42 hours, 15mg/m^2 at 48 hours, and 5mg/m^2 at 54, 68, and 78 hours. Doses to be increased based on levels – see protocol.
Cyclophosphamide 200mg/m^2 IV QD Day 1 to 5 inclusive
Doxorubicin 25mg/m^2 Day 4 and 5
Dexamethasone 10mg/m^2 Day 1 to 5 inclusive

A total of 6 alternating 5-day cycles should be administered (i.e. Pre-phase, A cycle, B cycle, A cycle, B cycle, A cycle, B cycle)

CODOX-M – IVAC: regimen consists of alternating cycles of regimen A and B for a total of 4 cycles

CODOX-M [Regimen A]
Cyclophosphamide 800mg/m^2 IV Day 1
Vincristine 1.5mg/m^2 IV Day 1 and 8 [day 1 and 8 in cycle 1; Day 1, 8, and 15 in cycle 3]
Doxorubicin 40mg/m^2 IV Day 1
Cytarabine 70mg (patients > 3 yrs) INTRATHECALLY Day 1 and 3
Cyclophosphamide 200mg/m^2 IV Day 2 – 5
Methotrexate 1200mg/m^2 IV over 1 hour Day 10
Methotrexate 240mg/m^2/hour IV continuous infusion x 23 hours (i.e., 5520mg/m^2 over 23 hours CI) Day 10
Hydration with D5½NS + 150mEq/L NaHCO3 @ 150mL/hour (urine pH must be $\geq$ 7)
Leucovorin 192mg/m^2 IV 36 hours after the start of MTX x 1 dose
Leucovorin 12mg/m^2 IV Q6H, starting 6 hours post first large dose of leucovorin
Growth factor 5mcg/kg SQ from Day 13 until hematologic recovery
Methotrexate 12mg (pts > 3 years age) INTRATHECAL Day 15
Leucovorin 15mg orally 25 hours after IT MTX x 1 dose

IVAC [Regimen B]
Etoposide 60mg/m^2 IV Day 1 – 5
Ifosfamide 1500mg/m^2 IV Day 1 – 5 (administer over 1 hour)
Mesna 360mg/m^2 IV Day 1 – one hour prior to starting Ifosfamide infusion
Mesna 360mg/m^2 every 3 hours Day 1 – 5 (may also put total daily dose of Mesna in an infusion bag and administer as a continuous infusion)
Cytarabine 2000mg/m^2 IV Q12H Day 1 and 2 (total 4 doses; administer over 3 hours each)
Methotrexate 12mg INTRATHECAL Day 5
Leucovorin 15mg orally 24 hours after Methotrexate x 1 dose
Growth Factor Support 5mcg/kg SQ from Day 7 until ANC recovery

Patients with CNS disease at presentation should receive *additional* IT therapy during the 1st 2 cycles as follows: Regimen A: IT cytarabine on day 5 and IT MTX on day 17; Regimen B: IT cytarabine on day 7 and 9

CALGB 9251

Cycle 1
Cyclophosphamide 200 mg/m^2 IV QD Days 1-5
Prednisone 60 mg/m^2 PO QD Days 1-7

Note: Begin Cycle 2 on day 8 of Cycle 1; Cycles are repeated at 3-week intervals.

Cycles 2, 4, and 6
Ifosfamide 800 mg/m^2 IV over 1 hr QD Days 1-5
Mesna 200 mg/m^2 IV at 0, 4, and 8 hrs after each dose Ifosfamide
Methotrexate 150 mg/m^2 IV over 30 minutes, then 1350 mg/m^2 IV over 23.5 hrs (total dose = 1500 mg/m^2 over 24 hrs) on Day 1
Leucovorin 50 mg/m^2 IV x 1 dose, given 36 hrs after the initiation of methotrexate, then 15 mg/m^2 PO/IV Q6H until methotrexate concentration is < 10^{-8}M (0.01µM)
Vincristine 2 mg IV on Day 1
Cytarabine 150 mg/m^2/d CIVI on Days 4 and 5
Etoposide 80 mg/m^2/d IV over 1 hr Days 4 and 5
Dexamethasone 10 mg/m^2 PO QD Days 1-5

Intrathecal chemotherapy# (for cycle 2, 4, and 6):
Methotrexate 15mg IT on Day 1
Cytarabine 40 mg IT on Day 1
Hydrocortisone 50 mg IT on Day 1

Cycles 3, 5, and 7
Cyclophosphamide 200 mg/m^2/d IV Days 1 - 5
Methotrexate 150 mg/m^2 IV over 30 minutes, then 1350 mg/m^2 IV over 23.5 hrs (total dose = 1500 mg/m^2 over 24 hrs) on Day 1
Leucovorin 50 mg/m^2 IV x 1 dose, given 36 hrs after the initiation of methotrexate, then 15 mg/m^2 PO/IV Q6H until methotrexate concentration is < 10^{-8}M (0.01µM)
Vincristine 2 mg IV on Day 1
Doxorubicin 25 mg/m^2/d IV Days 4 and 5
Dexamethasone 10 mg/m^2 PO QD Days 1-5

Intrathecal chemotherapy# (for cycle 3, 5, and 7):
Methotrexate 15mg IT on Day 1
Cytarabine 40 mg IT on Day 1
Hydrocortisone 50 mg IT on Day 1

Cranial Irradiation: 24 Gy administered for 12 fractions after chemotherapy for cycle 3 completed (after day 5, cycle 3) and before cycle 4 (before day 1, cycle 4) given only to patients with marrow or CNS involvement, and given after completion of all chemotherapy.)

Reference: Lee et al, *J Clin Oncol*. 2001; 19(20): 4014-22.

MYELODYSPLASTIC SYNDROME

Thymoglobulin (ATG) [IRB 545-00]

Group 1 Thymoglobulin 3.75mg/kg/day Day 1 – 4 inclusive

Group 2 Supportive Care

APLASTIC ANEMIA

Antithymocyte Globulin	40mg/kg IV QD Day 1 - 4
Methylprednisolone	1mg/kg/day (or 40mg/day whichever is higher) starting Day 1
Prednisone	1mg/kg PO QD Day 5 to Day 10 (or until the symptoms of serum sickness resolve and then rapidly reduced over 2 weeks)
Cyclosporine A*	12mg/kg/day (adults) or 15mg/kg/day (pediatrics) given orally and divided into 2 daily doses. Continue this dose for 14 days, and then adjust the dose to maintain a level between 200 and 400ng/mL (RIA). Cyclosporine A was discontinued without a taper at the 6-month visit.

NOTE: CyA used in this trial was Sandimmune brand, and with Neoral and improved bioavailability the dose will most likely be lower. Consider this when starting therapy.

Reference: Rosenfeld SJ, Kimball J, Vining D, Young NS. Intensive immunosuppression with antithymocyte globulin and cyclosporine as treatment for severe acquired aplastic anemia. *Blood* 1995; 85:3058 – 65.

Supportive care:

1) **Antimicrobial prophylaxis during neutropenia**:

AML:

Fluconazole 100mg PO QD for all pts, start at ANC<500

Valtrex 500mg PO QD (or Acyclovir 400mg PO TID depending on insurance and copay) for all pts start at ANC<500

Gatifloxacin start upon discharge from the hospital (no need for prophylaxis if hospitalized)

ALL:

Sulfamethoxazole/Trimethoprim (Bactrim/Septra): start 1 DS tablet QD Sat/Sun/Mon upon completion of induction. If patient intolerant to Bactrim/Septra, then use Pentamidine 300mg inhalation Q4W.

2) **Myeloid growth factors (G and GM):**

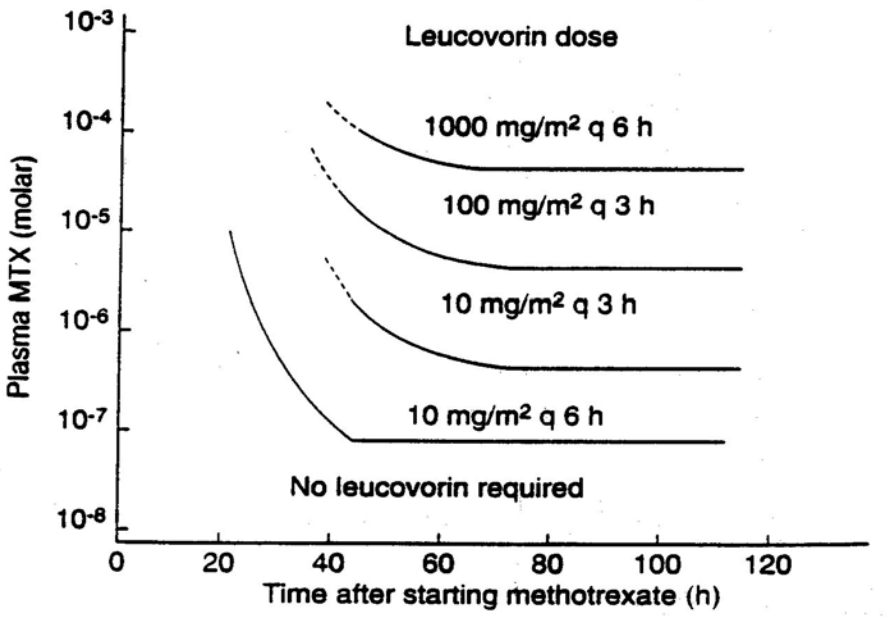
AML:

GM for patients $\geq$ 60yo after induction (once BM clear): dose 250mcg/m^2
No G/GM after consolidation

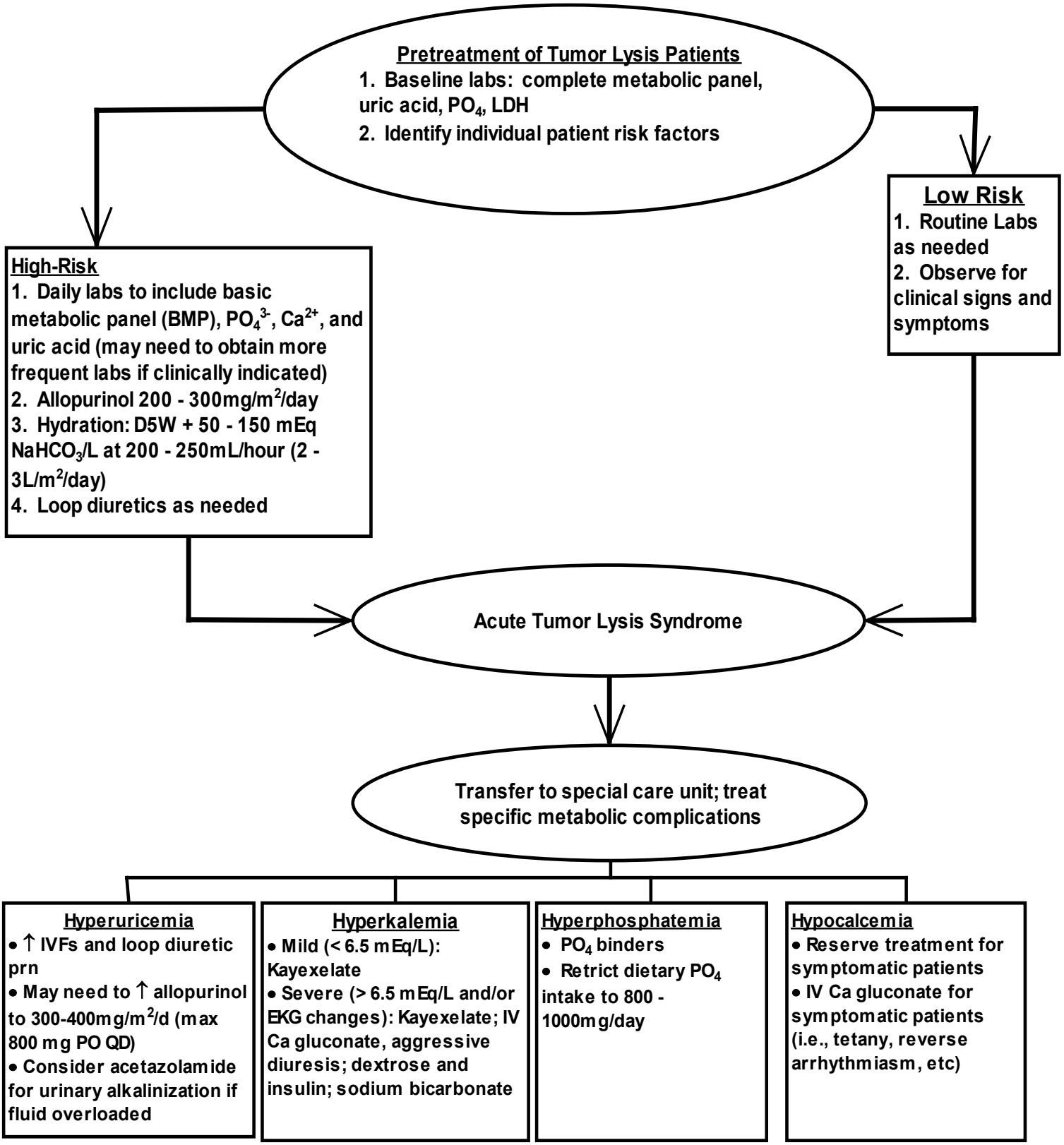
ALL:

G for pts $\geq$ 60yo after induction (once BM clear): dose: 5mcg/kg
No G/GM after consolidation

CALCIUM LEUCOVORIN DOSING BASED ON METHOTREXATE LEVELS NOMOGRAM



TUMOR LYSIS ALGORITHM



PEDIATRIC SECTION

GROWTH FACTORS – GUIDELINES FOR PEDIATRICS		
Transplant Type	**Mobilization**	**Post-Infusion***
Autologous – Bone Marrow	N/A	GCSF - Start day +6 unless specified otherwise by protocol. Discontinue when the ANC is > 500/mm^3 x 3 days and increasing or > 1500 x 1 (whichever is sooner)
Autologous – PBSC	GCSF	GCSF - Start day +6 unless specified otherwise by protocol. Discontinue when the ANC is > 500/mm^3 x 3 days and increasing or > 1500 x 1 (whichever is sooner)
Allogeneic – Bone Marrow	-	No Growth Factor, unless otherwise specified by protocol
Allogeneic – PBSC	GCSF	No Growth Factor, unless otherwise specified by protocol
Matched Unrelated Donor – PBSC and BM	-	No Growth Factor, unless otherwise specified by protocol
Umbilical Cord Blood	-	GCSF – Start Day 0 (4 hours post infusion), unless otherwise specified by protocol. COBLT protocol continue until ANC > 2000 x 3 days, then taper by 50% every other day, and stop when the dose is reduced to 1μg/kg/day.

* If $CD34^+$ counts > 4.5 x 10^6/kg, do not give post-infusion growth factors to minimize risk of engraftment syndrome.

Peripheral Stem Cell Mobilization: (G-CSF only)
Autologous:

1. Mobilization with G-CSF only:
   G-CSF 10 mcg/kg IV QD. First leukapheresis on Day +5
2. Mobilization with Chemotherapy + G-CSF [chemotherapy to be dosed on IBW, unless TBW is < IBW, then use TBW]:
   a. If using salvage disease-specific regimen: Last dose of induction chemotherapy and then G-CSF 10 mcg/kg IBW (if patient is coming to the clinic daily, please prescribe exact doses, if patient having doses at home, round to nearest vial/syringe size) SQ/IV starting Day +4 after chemotherapy. First leukapheresis between day 10 - 14 post chemotherapy.

NOTES:

When the patient's WBC is $\geq$ 1000, the patient will report to the outpatient clinic the following day and daily thereafter for laboratory draws or apheresis procedures. Labs will be sent for WBC and $CD34^+$ flow analysis.

Apheresis will usually begin when the peripheral blood CD34 absolute number is > 5 cells/ul and the WBC is greater than 1000.

Allogeneic:

1. Mobilization with G-CSF
   G-CSF 10 mcg/kg (IBW) SQ/IV QD. First leukapheresis on Day +5

Timing of Stem Cell Collection by Apheresis after GCSF Administration:

Recent studies demonstrate that the yield of $CD34^+$ cells after GCSF administration peaks at 18 hours. Growth factor doses should be administered 12 – 16 hours prior to apheresis.

Scheduling of BID growth factors:

Patients who are scheduled to receive BID growth factors, do not need to return to the clinic exactly 12 hours after the first injection. The second daily dose can be administered early, to facilitate early discharge if this is more convenient for the patient and the inpatient staffing load. However, on the day prior to apheresis the second daily dose of growth factor must be scheduled 12 – 16 hours prior to apheresis to maximize yield.

Shands Hospital at the University of Florida

Anti-Emetic Protocol for Chemotherapy-Induced Nausea and Vomiting in Pediatric Patients

Define Emetogenic Risk of the Regimen.

- Consider patient's prior experience with chemotherapy.
- The total emetogenic risk of the regimen is determined by the contribution of all agents combined.
- Each high or very high-risk agent increases the overall emetogenicity of the regimen by one level.
- Any number of moderate risk agent's increase the overall emetogenicity of the regimen by one level (total).
- Low risk agents do not contribute significantly to the overall emetogenicity of the regimen.
- Consider the duration of emetogenic risk, including anticipatory N/V, acute-onset N/V, and delayed-onset N/V.

Select a Regimen for Prevention of Anticipatory, Acute, and Delayed N/V.

- Choose a regimen appropriate to the degree of emetogenic risk.
- Select less expensive regimens when possible.
- Oral formulations are equally efficacious to intravenous formulations for any given drug.
- Remember PRN orders as a rescue alternative if scheduled regimen fails.

Monitor for Efficacy and Response to Treatment.

- Failure of antiemetic regimen is defined as 3 or more episodes of emesis in any 24-hour period, thus indicating a need for change in scheduled antiemetic regimen.
- Document any episodes of nausea or vomiting for reference for subsequent courses of chemotherapy.
- For patients who fail a prophylactic antiemetic regimen, consider prescribing rescue agents on a scheduled basis for subsequent cycles of chemotherapy.
- Identify and appropriately respond to unacceptable sedation, akathesia or restlessness, dizziness, tremors, dystonias, headache, diarrhea, constipation, etc. that may be drug-induced toxicities of antiemetic therapy.

Risk of Acute N/V (time period within 24 hours of drug exposure)

Very High Risk (60-99%)	High Risk (30-60%)	Moderate Risk (10-30%)	Low Risk (<10%)
Carboplatin Carmustine Cisplatin Cyclophosphamide >750 mg/m^2 Cytarabine >1000 mg/m^2 Dacarbazine Dactinomycin >1.5 gm/m^2 Daunorubicin >60 mg/m^2 Doxorubicin >60 mg/m^2 Ifosfamide >1 gm/m^2 Irinotecan Lomustine Mechlorethamine Melphalan (IV) Methotrexate >1000 mg/m^2 Procarbazine (oral) Streptozocin Thiotepa >250 mg/m^2/dose Total Body Irradiation	Cyclophosphamide <750 mg/m^2 Cytarabine 500-1000 mg/m^2 Dactinomycin <1.5 gm/m^2 Daunorubicin <60 mg/m^2 Doxorubicin 20-60 mg/m^2 Epirubicin Idarubicin Ifosfamide <1 gm/m^2 Methotrexate 250-1000 mg/m^2 Mitoxantrone Craniospinal, Mantle, or Abdominal-Pelvic Irradiation	L -Asparaginase Busulfan Capecitabine Cytarabine 500 mg/m^2 Docetaxel Doxorubicin <20 mg/m^2 Etoposide (IV) Fluorouracil < 1 gm/m^2 Gemcitabine Methotrexate 50-250 mg/m^2 Mitomycin C Paclitaxel Teniposide Thiotepa <250 mg/m^2/dose Topotecan	Bleomycin Chlorambucil (oral) Etoposide (oral) Fludarabine Hydroxyurea Interferon Melphalan (oral) Mercaptopurine Methotrexate <50 mg/m^2 Thioguanine (oral) Vinblastine Vincristine Vinorelbine Cranial, Pelvic, or Extremity Irradiation

Risk of Delayed N/V (time period 24 to 120 hours after drug exposure)

Very High Risk (>90%)
Cisplatin Melphalan (BMT dosing)

Recommended Agents for Prevention of Anticipatory N/V

Preferred agent: **Lorazepam (Ativan)** 0.01 to 0.05 mg/kg/dose (max 2 mg) PO/IV Q6H prn
Alternative agent: None recommended use any rescue agent if needed.

RECOMMENDED AGENTS FOR PREVENTION OF ACUTE-ONSET N/V

Very High Risk Chemotherapy Regimen

Preferred agents: **Dexamethasone (Decadron) 0.3** mg/kg/dose (max 16 mg) PO/IV QD
plus Ondansetron (Zofran) 0.45 mg/kg/dose (max 24 mg) PO/IV QD

High Risk Chemotherapy Regimen

Preferred agents: **Dexamethasone (Decadron) 0.15** mg/kg/dose (max 8 mg) PO QD
Plus Ondansetron (Zofran) 0.3 mg/kg/dose (max 16 mg) PO QD

EXCEPTION: For intrathecal (IT) Methotrexate plus Cytarabine, omit steroid prophylaxis.

Moderate Risk Chemotherapy Regimen

Preferred agents: **Dexamethasone (Decadron) 0.15** mg/kg/dose (max 8 mg) PO QD

Alternative agents: **Ondansetron (Zofran) 0.15** mg/kg/dose (max 8mg) PO QD
Promethazine (Phenergan) 0.5 mg/kg/dose (max 25 mg) PO Q6H

Low Risk Chemotherapy Regimen

Preferred agents: No routine prophylaxis is recommended.

Alternative agents: **Promethazine (Phenergan) 0.5** mg/kg/dose (max 25 mg) PO Q6H
Lorazepam (Ativan) 0.01 to 0.05 mg/kg/dose (max 2 mg) PO Q6H

**In fractionated chemotherapy regimens (divided daily doses), divide the total antiemetic doses to be given prior to each dose of chemotherapy.*
**In high-risk, multiple-day regimens, the combination of a serotonin antagonist plus a steroid is preferred, due to increasing incidence of dystonic reactions with multiple-day use of a dopamine antagonist, especially in younger patients. (ASCO guidelines, 1999 [4]).*
**Dexamethasone is not to be used as an antiemetic for brain tumor patients unless approved by the attending. Usage may be excluded by protocol.*

Recommended Agents for Prevention of Delayed-Onset N/V due to Cisplatin or Melphalan

Very High Risk Chemotherapy Regimen

Preferred agents: **Dexamethasone (Decadron)** 0.1 mg/kg/dose (max 2 mg) PO/IV TID x 3 days

Alternative agents: **Dexamethasone (Decadron)** 0.1 mg/kg/dose (max 4 mg) PO/IV Q6H x 3 days **plus**
Metoclopramide (Reglan) 1-2 mg/kg/dose (max 10 mg) PO/IV Q6-8H x 3 days

* pretreat with Diphenhydramine 1 mg/kg/dose PO/IV Q6H to decrease the risk of extrapyramidal reactions

Recommended Agents for Treatment of Active N/V (Rescue)

Preferred agents: **Promethazine (Phenergan)** 0.5 mg/kg/dose (max 25 mg) PO/IV Q4-6H prn
Lorazepam (Ativan) 0.01 to 0.05 mg/kg/dose (max 2 mg) PO/IV Q6H prn

Alternative agents: **Dexamethasone (Decadron)** 0.15 mg/kg/dose (max 8 mg) PO/IV Q12H prn *not to exceed 16 mg/day
Diphenhydramine (Benadryl) 1mg/kg/dose (see chart below) PO/IV Q6H prn

Children 2 - < 6 years	6.25 mg/ dose
Children 6 - < 12 years	12.5 mg/ dose
Children > 12 years	25 mg/ dose

**Dexamethasone is not to be used as an antiemetic for brain tumor patients unless approved by the attending. Usage may be excluded by protocol.*

CHEMOTHERAPY NOTES – PEDIATRICS (≤ 12 years)

NOTE: Dosing of antineoplastics for pediatric patients is age and weight dependent. If a patient is < 2 year old and/or weight 8 – 12kg, dosing should be on a mg/kg basis, NOT a mg/m^2 basis. Refer to a pediatric hematologist/oncologist if protocols not written accordingly.

Chemotherapy Dosing Weight:

Dosing weight is to be based on actual weight, unless the actual is > 130% of ideal in which case an adjusted weight is to be used. When calculating the adjusted weight, use the formula:

Adjusted weight: IBW + [Total – Ideal] x 0.25

Busulfan Dosing (COBLT Protocol):

Oral:

< 3 months	20mg/m^2/dose Q6H PO
3 months – 6 years	40mg/m^2/dose Q6H PO
≥ 6 years	1mg/kg PO Q6H

Intravenous (Busulfex®)

≤ 4 years	Initial dose at 1mg/kg actual body weight
> 4 years	Initial dose at 0.8mg/kg actual body weight

Cyclophosphamide Dosing (COBLT Protocol):

If the patient's weight is ≥ 125% of ideal body weight, then calculate the dose of cyclophosphamide according to adjusted IBW. Adjusted weight formula to be used in this case is as follows:

Adjusted Weight = IBW + [Total – Ideal] x 0.4

Mesna:

Hyperhydration is NOT to be used in cyclophosphamide containing preparative regimens. The following schedule of mesna is to be used (irrespective of patients weight/age i.e. no conversion to mg/kg is necessary):

Mesna 360mg/m^2 prior to cyclophosphamide and then repeated at 3, 6, 9 and 12 hours post each dose of high-dose cyclophosphamide as part of a HSCT preparative regimen.

Intrathecal Injections for Pediatrics

CNS therapy should be prescribed as follows:

Age	Methotrexate (mg)	Volume Optimal (mL)	Minimum (mL)
1 – 1.99 year	8	8	5.33
2 – 2.99 year	10	10	6.7
3 – 8.99 year	12	12	8
≥ 9 year	15	15	10

The final concentration should be no greater than 1.5mg/mL for MTX. Delivery should be isovolumetric (mL CSF out = mL drug in) with patients in *lateral decubitus* position during LP. Patients should remain in prone or Trendelburg for 30 minutes post LP to facilitate drug circulation throughout the CNS.

Reference: COG protocol 9904/9905/9906.

H_2-ANTAGONISTS - PEDIATRICS

PO LIQUID Options	IV Options
Ranitidine: PO: 1.25-2.5 mg/kg/dose PO BID (max 300 mg/day)	Ranitidine: IV: 0.75-1 mg/kg/dose IV Q6-8H (max 400 mg/day)
Omeprazole **[< 3 years age only]:** 1mg/kg/day starting dose	
Lansoprazole **[> 3 years age only]:** 1mg/kg/day	

Helpful Hints:

If the patients is < 3 and they are being sent home and have Medicaid as their insurance, please note that Medicaid won't pay for omeprazole, you must use lansoprazole.

Compounded liquids do not taste nice!

If they patient must take PO and it must be a liquid, lansoprazole tastes nicer (made from powder packs 15mg and 30mg). However to get the "nice tasting" lansoprazole you must specify "powder packs" on the prescription/order or else pharmacy will send a compounded liquid.

PEDIATRIC DRUG DOSING TABLE

Pediatric Drug Dosing	
DRUG NAME	***DOSE***
ANTI-INFECTIVES	
Aminoglycosides	
Amikacin	9 mg/kg/dose IV Q6H (Q8H if on CyA or FK) (for neutropenic patients)
Gentamicin	3 mg/kg/dose IV Q6H (Q8H if on CyA or FK) (for neutropenic patients)
Tobramycin	3 mg/kg/dose IV Q6H (Q8H if on CyA or FK) (for neutropenic patients)
Antifungals	
Amphotericin B	1 mg/kg/dose IV QD
ABLC (Abelcet®) **** restricted ****	5 mg/kg/dose IV QD
Caspofungin (Cancidas®) **** restricted ****	50 mg/m^2 IV QD (prelim data from study by Walsh et al. per personal communication with Merck)
Griseofulvin	Microsize: 10-20 mg/kg/day divided QD to BID Ultramicrosize: (> 2 yrs) 5 – 10 mg/kg/day divided QD – BID
Itraconazole (Sporanox®) **** IV is restricted ****	Load: 10 mg/kg/day x 3 days Maintenance: 4-6 mg/kg/day (unlabelled use) (other sources recommend 6-7 mg/kg/day?)
Cephalosporins	
Cefazolin (Kefzol®)	75 – 100 mg/kg/day divided Q8H (max 6 gm/day) (for non-CNS infections)
Cefepime	50 mg/kg/dose IV Q8H
Cefotaxime	50 mg/kg/dose IV Q6-8H
Ceftazidime **** restricted ****	50 mg/kg/dose IV Q8H (max 6 gm/day)
Ceftriaxone	Non CNS: 50 mg/kg/dose IV QD (may increase dose if PCN-resistant Strep is a concern) CNS: 100 mg/kg/dose IV QD
Beta-Lactams, Miscellaneous	
Aztreonam	90 – 200 mg/kg/day IV divided Q6 – 8H (150-200 mg/kg/day if neutropenic)
Imipenem	60 – 100 mg/kg/day IV divided Q6H OR 3 mos – 3 yrs: 25 mg/kg/dose IV Q6H (max 2 gm/day) ≥ 3 yrs: 15 mg/kg/dose IV Q6H
Meropenem *(non-formulary)*	> 3 mos, < 50 kg: 20 mg/kg/dose IV Q8H (max 1 gm/dose); CNS: 40 mg/kg/dose IV Q8H (max 2 gm/dose) > 50 kg: 1 gm IV Q8H; CNS: 2 gm IV Q8H
Macrolides	
Azithromycin	Mycoplasma: 10 mg/kg/dose (max 500mg) PO day 1; 5 mg/kg/dose (max 250 mg) PO QD days 2-5 Pharyngitis: 12 mg/kg/dose days 1-5 (max 500 mg/day)
Clarithromycin	15 mg/kg/day PO divided BID
Penicillins	
Amoxicillin	40 mg/kg/day PO divided TID Otitis media: 90 – 100 mg/kg/day PO divided TID
Amoxicillin/Clavulanate (Augmentin®)	45 mg/kg/day (amoxicillin) PO divided BID

Oxacillin	Non-CNS: 100-200 mg/kg/day divided Q6H CNS: 200 mg/kg/day divided Q6H
Penicillin G	100,000 – 250,000 units/kg/day divided Q4H severe infections: 400,000 units/kg/day divided Q4H (max 24 million units/day)
Penicillin VK	Prophylaxis: (<5 yrs) 125 mg PO BID (≥ 5 yrs) 250 mg PO BID Treatment: (<12 yr) 25-50 mg/kg/day divided Q6-8H (max 3 gm/day) (≥ 12 yrs) 125 – 500 mg Q6-8H
Tetracyclines	
Doxycycline	≥ 8yrs, < 45 kg: 2-5 mg/kg/day divided QD-BID (max 200 mg/day) > 8yrs, > 45 kg: 100 – 200 mg/day divided QD-BID
Miscellaneous Antibiotics	
Clindamycin	PO: 10-30 mg/kg/day divided Q6H IV: 40 mg/kg/day divided Q6-8H
Metronidazole	IV: 7.5 mg/kg/dose Q6H PO: 15-35 mg/kg/day divided TID C. diff: 20 mg/kg/day PO divided Q6H (max 2 gm/day)
Quinupristin/Dalfopristin (Synercid®) *** *restricted* ***	7.5 mg/kg/dose IV Q8H
Rifampin	10-20 mg/kg/day divided QD – BID
Vancomycin	Non-CNS: 10 mg/kg/dose IV Q6H CNS: 15-20 mg/kg/dose IV Q6H
Antivirals	
Acyclovir	Prophylaxis: 125 mg/m^2 IV Q6H or 250 mg/m^2 PO Q8H Treatment: 250 mg/m^2 IV Q8H or 500 mg/m^2 PO 5 x/day (500 mg/m^2 IV in immunocompromised patient)
Cidofovir	5 mg/kg IV Q week Also: probenicid 25 mg/kg PO prior to cidofovir, then 10 mg/kg PO 2 hrs and 8 hrs after cidofovir; NS 10 ml/kg IV over 1 hr prior to and immediately following cidofovir
Foscarnet	**CMV**: Induction: 60 mg/kg/dose IV Q8H or 90 mg/kg/dose IV Q12H Maintenance: 90-120 mg/kg/dose IV QD **Acyclovir-resistant HSV:** 40 mg/kg/IV Q8-12H Dose must be adjusted based on renal function ***Note: Keep pt well-hydrated, use NS if IVF needed, avoid Lasix***
Ganciclovir	Induction: 5 mg/kg /dose IV Q12H Maintenance: 5 mg/kg/dose IV QD Dose must be adjusted based on renal function
Valacyclovir	Dosing not well-established (500 mg/dose PO TID) Dose = IV acyclovir dose divided by 0.55; give QD – TID based on indication
Fluoroquinolones	
Ciprofloxacin	PO: 30 mg/kg/day divided BID IV: 20 mg/kg/day divided BID
Sulfonamides	
Sulfamethoxazole/ Trimethoprim (SMX/TMP)	PO: 8 – 10 mg/kg/day divided BID PCP: 20 mg/kg/day IV or PO divided Q6H

Sulfones	
Dapsone	1-2 mg/kg/dose PO QD (max 100 mg/day)
BLOOD-RELATED PRODUCTS	
Aminocaproic Acid (Amicar®)	PO: 100 mg/kg/dose PO Q6-8H (max 6 gm/dose) IV: 100 mg/kg/dose bolus, then infusion of 33 mg/kg/hr (max 1 gm/hr; max 18 gm/m^2/day)
Antithrombin III (AT III)	1 unit/kg increases plasma ATIII levels by 1-2%
Enoxaparin (Lovenox®)	Dosing not established Prophylaxis: 0.75 mg/kg Q12H (< 2 months) or 0.5 mg/kg/dose Q12H (if 2 mo – 18 yrs) Treatment: 1.5 mg/kg/dose Q12H (<2 months) or 1 mg/kg/dose Q12H (2 mo – 18 yrs)
FEIBA®	25-100 factor VIII units/kg/dose
Heparin	50-100 unit/kg IV Q4H OR 50 unit/kg bolus, then 15-25 units/kg/hr CIVI
Iron Dextran	IV: total dose replacement (preferred) IM: 5-10kg: 50mg (1ml); 10-50 kg: 100 mg (2ml)
Novoseven®	90 mcg/kg/IV Q2H, with gradual taper off (to Q4H, then Q6h, Q8H, etc.)
Protamine	Depends on heparin dose; 1 mg neutralizes ~ 100 units heparin; max dose is 50mg
Warfarin (Coumadin®)	0.05-0.34 mg/kg/day PO; usual maintenance dose is ~ 0.1 mg/kg/day (> 1yr)
CARDIAC	
Atenolol	1-2 mg/kg/dose PO QD
Captopril	Infants: 0.15 – 0.3 mg/kg/dose TID; titrate 0.5 – 2 mg/kg/dose PO TID; max 6 mg/kg/day older children: 6.25-12.5 mg/dose TID; max 6 mg/kg/day (up to adult max dose)
Clonidine	5-10 mcg/kg/day divided Q8-12H; titrate by 25 mcg/kg/day to max of 0.9 mg/day (max 0.3 mg/dose)
Diazoxide	1-2 mg/kg/dose (max 150 mg) prn; max duration is 10 days
Labetalol	PO: 4 mg/kg/day divided BID (max 2400 mg/day) IV:0.3-1 mg/kg/dose intermittently; 0.4-1 mg/kg/hr continuous infusion (max 3 mg/kg/hr)
Nifedipine	Immediate release:0.25 – 0.3 mg/kg/dose PO initially; max 10 mg/dose
ANALGESICS: NSAIDS	
Ketorolac (Toradol®)	< 6yr: 1 mg/kg/dose IV/IM Q6H prn > 6yr: 0.5 mg/kg/dose IV/IM Q6H prn * max 120 mg/day, max 5 days
Naproxen	> 2yr: 2.5-7 mg/kg/dose PO Q8-12H (max 10 mg/kg/day)
ANALGESICS: OPIATES	
Codeine	Pain: 0.5 – 1 mg/kg/dose IM/PO Q4-6H (max 60 mg/dose) Cough: 1-1.5 mg/kg/day divided Q6H OR 2-6 yrs: 2.5-5mg PO Q4H prn (if normal size/weight) 6-12yrs: 5-10 mg PO Q4H prn(if normal size/weight) > 12 yrs: 10-20 mg PO Q4H prn(if normal size/weight)
Fentanyl	1-2 mcg/kg/dose IV/IM, may repeat Q30-60 min 1-2 mcg bolus, then 0.5 - 1 mcg/kg/hr CIVI

Hydromorphone	Younger children: 0.03 – 0.08 mg/kg/dose PO Q4-6H prn (max 5 mg/dose unless titrating up); 0.015 mg/kg/dose IV Q4-6H prn (older children) 1-4 mg PO Q4H prn; 0.2 – 1 mg IV Q4H prn
Methadone	PO/IM: 0.7 mg/kg/day divided Q4-6H OR 0.1-0.2 mg/kg/dose Q4-12H prn IV: 0.1 mg/kg/dose Q4H x 2-3 doses, then Q6-12H prn (max 10 mg/dose)
Morphine	0.05 – 0.2 mg/kg/dose IV/IM Q2-4H prn 0.02 – 0.07 mg/kg/hr continuous IV infusion PCA: 0.1 mg/kg loading dose; 0.01 – 0.02 mg/kg/dose PCA (demand) dose; 4 hr lockout ~ 0.08 mg/kg PO: (IR) 0.2-0.5 mg/kg/dose Q4H prn; (SR) 0.3-0.6 mg/kg Q12H ATC
Oxycodone	0.05 – 0.15 mg/kg/dose PO Q4-6H prn OR 6-12 yrs: 1.25 mg Po Q6H prn > 12 yrs: 2.5 PO Q6H prn
Naloxone (Narcan®)	0.1 mg/kg/dose, max single dose – 2 mg (for total reversal) (usual adult dose = 0.4 mg)
GI MEDICATIONS	
Diphenoxylate/Atropine (Lomotil®)	0.3-0.3 mg/kg/day divided BID-QID OR 2-5 yrs: 2mg PO TID (not recommended in < 2yrs) (if normal weight) 5-8 yrs: 2 mg PO QID(if normal weight) 8-12 yrs: 2 mg PO 5x/day(if normal weight)
Docusate (Colace®)	< 2yr: 25 mg/day PO 2-12yrs: 50 – 150 mg/day PO > 12 yrs: 50 – 300 mg/day PO divided QD – TID
Loperamide (Imodium®)	2-6 yrs: 1 mg PO TID in 1st day, then 0.1 mg/kg/dose (max 1 mg) prn 6-8 yrs: 2 mg PO BID in 1st day, then 0.1 mg/kg/dose (max 2 mg) prn 8-12 yrs: 2 mg PO TID in 1st day, then 0.1 mg/kg/dose (max 2 mg) prn Chronic diarrhea: 0.08-0.24 mg/kg/day divided BID-TID; max 2 mg/dose
Simethicone	20-40 mg PO prn
Magnesium Citrate	< 6yrs: 0.5 ml/kg/dose PO 6-12yrs: 80 – 120 ml/dose PO > 12 yrs: 120 – 240 ml/dose PO
Magnesium Oxide	400-800 mg PO Qd-QID
Magnesium Sulfate	25 – 50 mg/kg IV Q6H as needed 100-200 mg/kg/dose PO QID (diarrhea may be greater vs. mag oxide)
Metoclopramide	0.1-0.2 mg/kg/dose up to QID (max 0.5 mg/kg/day)
Octreotide	Not clearly defined 1 – 10 mcg/kg IV/SC Q12H; titrate 0.3 mcg/kg/dose at 3 day intervals
Omeprazole	Not clearly defined 0.6 – 0.7 mg/kg/day, titrate up to 3.5 mg/kg/day; normal dose is 1 – 1.5 mg/kg/day
Ondansetron	0.15 mg/kg/dose IV OR 4-8 mg PO
Pantoprazole	Not clearly defined (1 mg/kg/dose PO/IV QD?)
Promethazine	0.25-1 mg/kg/dose IV/PO Q4-6H prn
Ranitidine	PO: 1.25-2.5 mg/kg/dose PO BID (max 300 mg/day) IV: 0.75-1 mg/kg/dose IV Q6-8H (max 400 mg/day)

Senna	For kids > 27 kg Tabs: 1 tab QD, max 2 tabs BID Syrup: 1mo-1yr: 1.25 – 2.5 ml QHS, max 2.5 ml BID 1-5 yrs: 2.5-5 ml QHS, max 5 ml BID 5-15 yrs: 5-10 ml QHS, max 10 ml BID
Ursodiol (Actigall®)	10-20 mg/kg/day PO divided Q8-12H
IMMUNOSUPPRESSIVES	
ATG	Atgam®: varies; 10-30 mg/kg/dose; requires test dose Thymoglobulin®: varies; 1.5 mg/kg/dose
Cyclosporine	PO: 3 mg/kg/dose Q8H IV: 1 mg/kg/dose Q8H
Daclizumab (Anti-IL2)	1 mg/kg IV days 1, 4, 8, 15, 22 of therapy
Infliximab (Anti-TNF) **** restricted ****	Dose/Use not well-established
Mycophenolate mofetil (CellCept®)	600 mg/m^2/dose PO or IV Q12H
Tacrolimus (FK506)	PO: 0.04 mg/kg/dose Q8H (may be Q12H if > 8 yrs) IV: 0.04 mg/kg/day continuous infusion
ANTICONVULSANTS	
Carbamazepine	10 – 40 mg/kg/day PO divided Q6-8H **Note: Start low, titrate dose based on serum concentrations**
Gabapentin (Neurontin®)	< 12 yrs: 30-60 mg/kg/day PO divided Q8H ≥ 12 yrs: 900 – 3600 mg/day PO divided Q8H *Note: Start at low dose, increased Q 3 days by 10 mg/kg/day; may be less effective in children; may be associated with behavioral changes*
Phenytoin (Dilantin®)	Loading dose: 20 mg/kg/dose 10 days – 3 yrs: 8 – 10 mg/kg/day IV/PO divided Q6H 3-10 yrs: 7.5 mg/kg/day IV divided Q8H (or PO divided Q12H if >5 yrs) > 10 yrs: 6 mg/kg/day IV divided Q8H or PO divided Q12H **Note: if <5 yrs, daily PO dose may be higher than daily IV dose**
Valproic Acid	40 – 60 mg/kg/day PO divided Q6-8H
MISCELLANEOUS MEDICATIONS	
Acetaminophen	10-15 mg/kg/dose PO/PR Q4-6H PRN
Acetazolamide (Diamox®)	5 mg/kg PO/IV QD OR 150 mg/m^2 PO/IV QD
Diphenhydramine	1 mg/kg/dose PO/IV Q6H prn OR 2-6 yrs: 6.25 mg/dose PO/IV Q6H prn (if normal weight for age) 6-12 yrs: 12.5-25 mg/dose PO/IV Q6H prn(if normal weight for age) > 12 yrs: 25-50 mg/dose PO/IV Q6H prn(if normal weight for age)
Lorazepam	0.05 mg/kg/dose PO/IV Q4H prn (max 2 mg/dose)

Note: Above doses may not necessarily apply to the neonatal population (≤ 2 months). Doses for this population should be verified prior to prescribing.

Prepared 5/10/02 L.E. Wiggins, PharmD, BCOP

GVHD PROPHYLAXIS - PEDIATRICS

Allogeneic (Matched Related, Matched Unrelated, Related Mismatched):
If not otherwise specified by protocol, tacrolimus (IV/PO as Prograf®) will be used for GVHD prophylaxis along with mini-dose Methotrexate. Tacrolimus will be given as a continuous intravenous infusion beginning on day -3 (or on date designated by protocol) at a dose adjusted to achieve whole blood concentration of 10 to 20 ng/ml (See table below).

Cords
GVHD prophylaxis as outlined in the COBLT protocol will be administered consisting of cyclosporine and corticosteroids.
Cyclosporine A: begins Day –3 to –1, with at least a dose of 3mg/kg/day in 2 divided doses (1.5mg/kg each) 12 hours apart and infused over a period of 4 hours or by continuous IV infusion. Trough levels of 200ng/mL by TDX if given by bolus or levels of 400ng/mL if given by continuous IV infusion should be present in Day 0 and thereafter until a taper is initiated. This is to be continued until 6 months post transplant. Thereafter if there are no signs and symptoms of GVHD and the patient is not receiving corticosteroids, the dose of CyA may be tapered by 5% per week (aim to DC by 12 months).
Corticosteroids: Methylprednisolone will be given at a dose of 1mg/kg (0.5mg/kg BID) on Day +1 to Day +4, and 2mg/kg (1mg/kgBID) beginning on Day +5 until Day +19 or until the first day ANC's reach $\geq$ 500/mm^3. After ANC's have reached $\geq$ 500/mm^3, steroids should be tapered by 0.2mg/kg/week.

Mini-Dose Methotrexate (MTX):
Methotrexate 5 mg/m^2 IV on day's +1, +3, +6, +11
For pediatric (age<12, < 40kg) protocols that mandate MTX, consider deleting Methotrexate if SCr is greater than twice normal for age. Approach on a case-by-case basis, and discuss with attending.

Leucovorin
Leucovorin 5 mg PO/IV q6h x 4 doses will be given beginning 24 hours following Methotrexate doses on Day +3, +6, and +11 in all patients receiving methotrexate. Do not give leucovorin after the Day +1 methotrexate.

Cyclosporine & Tacrolimus PEDIATRICS

Drug	Initial Dose	Target Range	Dosage Forms
Cyclosporine (CSA)	> 40kg: 2.5 mg/kg IV q12h (administered over 2 hours) < 40kg: 2.5mg/kg IV q8h (1:3 conversion to PO CSA) 4.5 mg/kg PO q12h	150-450 ng/ml	Injection: Sandimmune® 50mg Oral capsules: Gengraf®, Neoral® 25 mg, 100mg caps Oral liquid: 100 mg/ml liquid (Neoral®, Sandimmune®)
Tacrolimus (FK-506)	0.04 mg/kg IV as continuous infusion (1:4 conversion to PO FK506) 0.16mg/kg/day PO peds	10-20 ng/ml	Injectable mixed as 0.02 mg/ml in D5W or NS Oral: Prograf® 0.5mg, 1 mg, 5 mg capsules only; a liquid formulation (0.5mg/mL) can be compounded. Topical ointment: for localized skin GVHD use a topical tacrolimus preparation: Protopic® 0.03% and 0.1%, 30g and 60g

NORMALS FOR AGE

Age	Weight	Pulse	Respiratory Rate
0-3 months	3-6 kg	100-180	30-60
3-6 months	6-7 kg	100-160	30-60
6-12 months	7-10 kg	80-110	30-60
1-2 years	10-12 kg	80-110	24-40
2-4 years	12-16 kg	70-110	22-34
4-6 years	16-20 kg	70-110	18-30
6-8 years	20-24 kg	65-110	18-30
8-12 years	24-40 kg	65-110	18-30
12-15 years	40-46 kg	60-90	12-16

While young patients can be quite tachypneic by adult standards they should not have any signs of distress: grunting respiration's, nasal flaring, retractions or other accessory muscle use

Blood Pressure Limits

Hypotension

0 – 1 month: BP should be > 60 systolic
1-12 months: BP should be > 70 systolic
> 1 year old: systolic BP should be at least 70 + (age x 2)

Hypertension

< 5 years: systolic > 110, diastolic > 70
5-10 years: systolic > 120, diastolic > 80
10-18 years: systolic > 130, diastolic > 90

Calculating CrCl

Estimation of creatinine clearance using serum creatinine and body length. NOTE: this formula may not provide an accurate estimation of creatinine clearance for infants younger than 6 months of age and for patients with severe starvation or muscle wasting.

CL_{cr} = K x L/SCr where,

CL_{Cr} = creatinine clearance in mL/min/1.73m^2
K = constant of proportionality that is age specific

Age	K
Low birth weight $\leq$ 1 year	0.33
Full-term $\leq$ 1 year	0.45
2 – 12 year	0.55
13 – 21 year female	0.55
13 – 21 year male	0.70

L = length in centimeters
S_{Cr} = serum concentration in mg/dL
[Reference: *Ped Clin N Amer* 1987; 34:571 – 90].

Other Formula:

$$CrCl = \frac{0.48x(height)}{SerumCreatinine}$$

PEDIATRIC FLUID MANAGEMENT

Consider:

Growth
Fluid requirements
Assessment of hydration status
Expected weight gain
How to estimate maintenance fluid requirements
Physical assessment/ normal urine output

Growth:

- Normal infants lose 10% of their birth weight in the first 3 days of life
- Regain birth weight by 10 – 14 days
- Double birth weight by 5 months ($\pm$ a month)
- Triple birth weight by 1 year
- After 1st year, gain about 5 pounds a year until the pre-adolescent growth spurt
- Infants: expected weight gain of 10 – 30 grams per day

Estimation of Maintenance Fluid Requirements:

Infants have higher metabolic rates and evaporative losses

First 10kg – 100 cc/kg/day
Second 10kg – 50 cc/kg/day
Each additional kg – 20 cc/kg/day

This takes into account normal urinary losses and insensible loss (i.e. water lost through the skin and lungs).

This does not take into account losses through stool or emesis.

Losses through the skin and lungs will increase with fever and tachypnea.

The "typical" pediatric maintenance fluid is D51/4NS with 10 – 20 mEq KCl per liter (Dextrose 10% gives more calories).

A "typical" pediatric fluid bolus is 20cc/kg.

Examples:

Calculate Baby S's maintenance fluid requirements (weight 6.4kg)

First 10kg: 100cc/kg/day = 640 cc/24 hours = about 27 cc/hour

Calculate Baby J's maintenance fluid requirements (weight = 11.6kg)

First 10kg: 100 cc/kg/day = 1000cc plus

Second 10kg: 50 cc/kg/day = 1.6 x 50 = 80 cc
Total = 1080 cc/24 hours = about 45 cc/hour.
Dr Z ordered a maintenance fluid rate of 125 cc/hour on a 5-year-old child weighing 20kg. What percent of maintenance is this rate?

First 10kg: 100 cc/kg/day = 1000 cc plus
Second 10kg: 50 cc/kg/day = 10 x 50 = 500 cc
Total = 1500 cc/24 hours = about 63 cc/hour
Therefore the rate ordered is twice the usual maintenance rate.

Normal Urine Output:

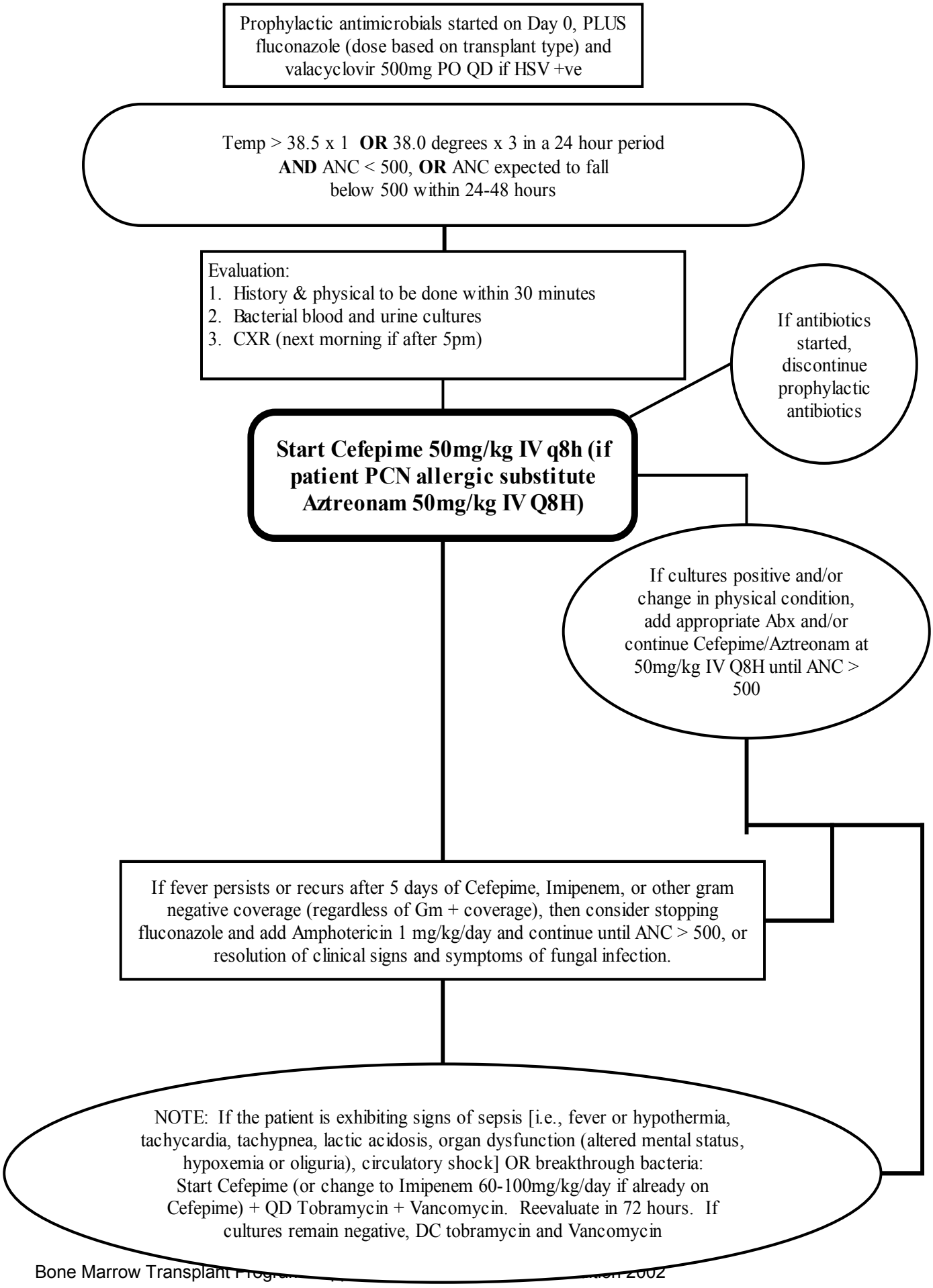
2 – 4 cc/kg/hour
Oliguria in children = 2 cc/kg/hour over 8 hours
Severe oliguria = < 1 cc/kg/hour

Evaluation of Dehydration:

Exam	**Mild**	**Moderate**	**Severe**
Skin turgor	NL	Sl tenting	Tenting
Skin touch	NL	Dry	Clammy
Mouth	Moist	Dry	Parched
Eyes	NL	Deep set	Sunken
Tears	+	Reduced	None
Fontanelle	NL	Flat	Sunken
HR	NL to mild ↑	Mild to moderate ↑	Tachycardic
UOP	More conc.	Decreased	Oliguric
Sensorium	Consolable	Irritable	Decreased
BP			Decreased
Perfusion	NL	> 2 sec	>> 2 sec

NL = normal

PEDIATRIC FEBRILE NEUTROPENIA ALGORITHM



PCA (Patient Controlled Analgesia)				
Titrate to pain relief; monitoring for side effects; start with lower dose and increase.	**Usual Doses**			
	Loading and Basal ♦ *Basal infusion not recommended for opioid naïve patients.*	**PCA Dose**	**Delay**	**Hour Limit**
Morphine Sulfate *Standard concentration = 1 mg/ml*	Loading Dose: 0.1 mg/kg; repeat PRN ♦Basal Rate: 0.01 mg/kg/hour	0.02 – 0.03 mg/kg*	6 - 10 minutes delay	0.08 mg/kg
Hydromorphone *Standard concentration = 0.2 mg/ml*	Dilaudid® Loading Dose: 0.01 mg/kg, repeat PRN ♦Basal Rate: 1 mcg/kg/hour	1-2 mcg / kg	6 - 10 minutes delay	
Fentanyl *Standard concentration = 50 mcg/ml*	Loading Dose: 1-2 mcg/kg; repeat PRN ♦Basal Rate: 0.1 mcg/kg/hour	0.1 – 0.2 mcg / kg	6 - 10 minutes	

Pediatric BMT Antimicrobial Prophylaxis

Patient Type	*Start Date*	*Drug*	*Dose/Route/ Frequency*	*Stop Date*
Allogeneic BMT	Day 0	PENICILLIN	250mg PO BID	ANC > 250
Autologous BMT	Day 0	RIFAMPIN	10 – 20mg/kg/day	ANC > 250
Allogeneic BMT	Day 0	FLUCONAZOLE (Diflucan®)	3 – 6mg/kg/day	ANC > 250 or when Amphotericin started
Autologous BMT	Day 0	FLUCONAZOLE (Diflucan®)	3 – 6mg/kg/day	ANC > 250 or when Amphotericin started
All Patients (unless sulfa-allergic)	Begin weekend following engraftment	TRIMETHOPRIM/ SULFAMETHOXAZOLE (Septra®)	5 – 10mg/kg/day divided BID 3 days a week (maximum 160mg TMP per dose)	Day +180
Sulfa-Allergic Patients	Begin weekend following engraftment	DAPSONE or PENTAMIDINE	2mg/kg PO QD (maximum 100mg) (Pent: 300mg inh qmonth; 9mg/kg/dose for $\leq$ 5 years; 300mg if > 5)[#]	Day +180
HSV positive Patients	Day 0	ACYCLOVIR (Zovirax®)	600 - 1000mg/m^2/d (divided into 3 doses) or 250mg/m^2 IV q8h (Dose based on IBW)	ANC > 250
Patients with CMV + blood cultures	Day of CMV + culture	GANCICLOVIR (Cytovene®)	5 mg/kg q12h x 2 weeks and then 5 mg/kg five times weekly (Dose based on IBW)	At completion of 3 weeks Rx is antigen negative

[#] Administer once a month using a Respigard II nebulizer.

Pediatric Dosage Guidelines for Renal Insufficiency

DRUG	CREATININE CLEARANCE (mL/min)*			
	≥ 80	50-79	10-49	< 10
Acyclovir	250-500 mg/m^2 q8h	250-500 mg/m^2 q8h	250-500 mg/m^2 q12-24h	250 mg/m^2 q24h
Aztreonam	90 – 120mg/kg q6–12h	90 – 120mg/kg q6–12h	45 – 60mg/kg q6–12 h	22.5 – 40mg/kg q6-12h
Cefepime	50 mg/kg q8h	50 mg/kg q8h	50 mg/kg q12h (30-60)	50 mg/kg q24h (<10)
Famotidine	0.6 mg/kg q12h	0.6 mg/kg q12h	0.6 mg/kg q24h (30-50)	0.6 mg/kg q36-48 (<30)
Fluconazole	3-12 mg/kg q24h	3-12 mg/kg q24h	3-12 mg/kg q48h	3-12 mg/kg q72h
Ganciclovir	5 mg/kg q12h	2.5 mg/kg q12h	2.5 mg/kg q24h (CrCl 25-49)	1.25 mg/kg q24h (CrCl < 25)
Imipenem	15-25 mg/kg q6h (up to 500mg q6h)	15-25mg/kg q6-8h (30-70)	15-25 mg q8-12h (20-30)	15 mg/kg q12h (5-20)
Penicillin	25,000 U/kg q4h	25,000 U/kg q4h	25,000 U/kg q6-8h (10-50)	25,000 U/kg q12h
Ticarcillin/clavulanate	200-300mg/kg/day (divided into q4-6h)	q4-6h	q6-8h	q12h
Tobra/Gent	3mg/kg q8h**	3mg/kg q12**	***	***
Vancomycin	10/kg q6h	10/kg q8h	***	***

*For calculation of Creatinine Clearance in children (ml/min):

*Obtain peak and trough levels after third dose of aminoglycoside.Pharm.D. will evaluate levels and make recommendations for future dosing regimens.

Obtain Vancomycin trough only after fifth dose (if continued beyond 48hr). ***Dose based on drug levels. Give single dose (Vanc 10/kg; aminoglycoside 3mg/kg). Consult Pharm.D. for recommendations regarding timing of drug levels and further dosing recommendations.

PEDIATRIC GANCICLOVIR AND VALGANCICLOVIR DOSING

Renal Function	IV treatment dose (equivalent to 5mg/kg/dose IV q12h)	PO Valcyte treatment dose (equivalent to 5mg/kg/dose IV BID ganciclovir) **GIVE WITH FOOD or drug will not absorbed**	IV prophylaxis dose (equivalent to 5mg/kg/day)	PO Valcyte Prophylaxis dose (equivalent to 5mg/kg/dose IV q24h ganciclovir) **GIVE WITH FOOD or drug will not be absorbed**
➢ **70 ml/min**	**5 mg/kg q12h**	**12.75 mg/kg bid** (max 900mg bid)	**5 mg/kg q24h**	**12.75 mg/kg q24h** (max 900mg q24h)
50-69 ml/min	**2.5 mg/kg q12**	**6.375 mg/kg bid** (max 450mg bid)	**2.5 mg/kg q24h**	**6.375 mg/kg q24h** (max 450mg q24h)
25-49 ml/min	**2.5 mg/kg q24h**	**6.375 mg/kg q24h** (max 450mg q24h)	**1.25 mg/kg q24h**	**3.1875 mg/kg q24h** (max 225mg q24h or 450mg q48h)
10-24 ml/min	**1.25 mg/kg q24h**	**3.1875 mg/kg. q24h** (max 225mg q24h or 450mg q48h)	**0.625 mg/kg q24h**	**1.59 mg/kg q24h** (max 112.5mg q24h or 225mg q48h or 450mg 2/week)
< 10 ml/min	**1.25 mg/kg/dose 3x/week**	**3.1875 mg/kg 3x/week** (max 225mg/dose)	**0.625 mg/kg/dose 3x/week**	**1.59 mg/kg 3x/week** (max 112.5mg 3x/week or 225mg q3-4 days)

Prepared by: Debbie Kahler, Pharm.D. July 2002.

PEDIATRIC ELECTROLYTE BOLUS GUIDE (<40KG) - GUIDELINES BASED ON **PLASMA** SAMPLE RESULTS

	Potassium		Calcium		Magnesium		Phosphate	
Abnormality	Hypokalemia	Hyperkalemia	Hypocalcemia	Hypercalcemia	Hypomagnesemia	Hyper-magnesemia	Hypo-phosphatemia	Hyper-phosphatemia
Plasma Level	< 3.3 mEq/L	> 4.6 mEq/L	< 8.4 mg/dL	Ca > 10.2 mg/dL	< 1.8 mEq/L	> 2.8 mEq/L	< 2.5 mg/dL	> 4.5 mg/dL
Symptoms	Fatigue; weakness in legs; cramps	Vague muscular weakness; flaccid muscle paralysis in legs; paresthesias of face, tongue, feet, and hands	Numbness & tingling of fingers, circumoral region, and toes; muscle cramps, spasms, tremors, twitching; convulsions; depression; emotional instability; anxiety; psychosis	Muscle weakness; confusion; emotional instability; anxiety; psychosis; lethargy; coma	Muscle weakness; muscle twitching & cramps; paresthesias; depression; agitation; confusion; psychosis; anorexia; nausea; vomiting	Drowsiness; muscle weakness; coma	Paresthesias; muscle weakness (hand grasp, speech difficulty); muscle pain & tenderness; confusion; apprehension; delirium; coma; seizures	Tetany; tingling of fingertips, circumoral region, and toes; numbness; muscle spasms
Action	If K^+ 3.0 – 3.2 and no symptoms, then give KCl 0.5 mEq/kg PO with next dose of oral medications, if able to tolerate oral. If unable to tolerate oral, please give 0.5mEq/kg IV. If K^+ 3.0 - 3.2 and symptoms present, or K^+ 2.7 – 2.9, then give KCl 0.5 - 1 mEq/kg IV and repeat K^+within 1 hour of completion of infusion. If repeat level still < 3.0 then call H.O. If K^+ < 2.7mEq/L or dysrhythmia, give KCl 1mEq/kg IV. Repeat K^+within 1 hour of completion of infusion. If repeat level still < 2.7 then call H.O.	If K^+ > 5.1, then obtain EKG and call H.O.	If total serum Ca < 8.4, then calculate corrected serum calcium: $Ca_{corrected}$ = total serum calcium + [0.8 x (4.0-measured albumin)] If $Ca_{corrected}$ 8.1-8.5 and no symptoms, then give Calcium Carbonate 10 mg/ kg q6h x 4 - repeat Ca level in 24hr. If $Ca_{corrected}$ 8.1-8.4 and symptoms present or $Ca_{corrected}$ < 8.1, then give Calcium Gluconate 100 mg/kg IV now and repeat level. If still < 8.1 call H.O.	If total serum calcium > 11, then call H.O.	If Mg^{++} 1.4 - 1.8 and no symptoms, then give Mg Oxide 30mg/kg PO with the next dose of oral medication. If unable to tolerate oral, give $MgSO_4$ 25mg/kg IV. Repeat Mg within 1 hour of completion of IV replacement. If Mg^{++} > 1.4mg/dL and pt symptomatic without life-threatening conditions, give $MgSO_4$ 25mg/kg IVPB. Repeat Mg within 1 hour of completion. If Mg^{++} 1.1 – 1.4, give $MgSO_4$ 25mg/kg IV. Repeat Mg within 1 hour of completion. If Mg^{++} < 1.1, give $MgSO_4$ 50mg/kg	If Mg^{++} > 3.0 then call H.O.	If serum phosphorous $\geq$ 1 - 2.5 mg/dL give IV PO_4 at dose of 0.08 mmol/kg of PO_4. If serum phosphorous is 0.5 – 1mg/dL, give IV PO_4 0.20 mmol/kg of PO_4. Draw a repeat PO_4 level, and if PO_4 level still < 1.0, then call H.O. If PO_4 < 0.5mg/dL, give 0.36mmol/kg IV PO_4 over 6 hours Phosphate is administered in the form of NaPhos or KPhos. If Na low (normal 130-140), then give as NaPhos. If K low (normal 3.5-5.0), then give as KPhos.	If serum phosphorous > 6.0, then call H.O.

IV Administration	Max rate: 0.5mEq/kg/hr without cardiac monitor or 1 mEq/kg/hr with monitor [40mEq/hour maximum]		Maximum concentration 20mg/mL *peripherally*; maximum concentration 50mg/mL *centrally*. Infuse no faster than 120 – 240mg/kg/hour.		Do not exceed 125mg/kg/hour.		Dilute every 3 mM phosphate in 25 ml for central lines and 60 ml for peripheral lines. Give no faster than 0.05 mM/kg/hr	

ELECTROLYTE BOLUS GUIDE (<40KG) GUIDELINES BASED ON SERUM SAMPLE RESULTS

	Potassium		Calcium		Magnesium		Phosphate	
Abnormality	Hypokalemia	Hyperkalemia	Hypocalcemia	Hypercalcemia	Hypomagnesemia	Hyper-magnesemia	Hypo-phosphatemia	Hyper-phosphatemia
Serum Level	< 3.5 mEq/L	> 5.0 mEq/L	< 8.4 mg/dL	Ca > 10.2 mg/dL	< 1.8 mEq/L	> 2.8 mEq/L	< 2.5 mg/dL	> 4.6 mg/dL
Symptoms	Fatigue; weakness in legs; cramps	Vague muscular weakness; flaccid muscle paralysis in legs; paresthesias of face, tongue, feet, and hands	Numbness & tingling of fingers, circumoral region, and toes; muscle cramps, spasms, tremors, twitching; convulsions; depression; emotional instability; anxiety; psychosis	Muscle weakness; confusion; emotional instability; anxiety; psychosis; lethargy; coma	Muscle weakness; muscle twitching & cramps; paresthesias; depression; agitation; confusion; psychosis; anorexia; nausea; vomiting	Drowsiness; muscle weakness; coma	Paresthesias; muscle weakness (hand grasp, speech difficulty); muscle pain & tenderness; confusion; apprehension; delirium; coma; seizures	Tetany; tingling of fingertips, circumoral region, and toes; numbness; muscle spasms

Action	If K^+ 3.1 - 3.5 and no symptoms, then give KCl 0.5 mEq/kg PO with next dose of oral medications, if able to tolerate oral. If unable to tolerate oral, please give 0.5mEq/kg IV. If K^+ 3.1 - 3.5 and symptoms present, or K^+ < 3.1, then give KCl 0.5-1 mEq/kg IV and repeat K^+within 1 hour of completion of infusion. If repeat ~~level still < 3.1 then~~ call H.O. If K^+ < 3.1 mEq/L or dysrhythmia, give KCl 1mEq/kg IV. Repeat K^+within 1 hour of completion of infusion. If repeat level still < 2.7 then call H.O.	If K^+ > 5.5, then obtain EKG and call H.O.	If total serum Ca < 8.4, then calculate corrected serum calcium: $Ca_{corrected}$ = total serum calcium + [0.8 x (4.0-measured albumin)] If $Ca_{corrected}$ 8.1-8.5 and no symptoms, then give Calcium Carbonate 10 mg/ kg q6h x 4 - repeat Ca level in 24hr. If $Ca_{corrected}$ 8.1-8.4 and symptoms present or $Ca_{corrected}$ < 8.1, then give Calcium Gluconate 100 mg/kg IV now and repeat level. If still < 8.1 call H.O.	If total serum calcium > 11, then call H.O.	If Mg^{++} 1.4 - 1.8 and no symptoms, then give Mg Oxide 30mg/kg PO with the next dose of oral medication. If unable to tolerate oral, give $MgSO_4$ 25mg/kg IV. Repeat Mg within 1 hour of completion of IV replacement. If Mg^{++} > 1.4mg/dL and pt symptomatic without life-threatening conditions, give $MgSO_4$ 25mg/kg IVPB. Repeat Mg within 1 hour of completion. If Mg^{++} 1.1 – 1.4, give $MgSO_4$ 25mg/kg IV. Repeat Mg within 1 hour of completion. If Mg^{++} < 1.1, give $MgSO_4$ 50mg/kg	If Mg^{++} > 3.0 then call H.O.	If serum phosphorous $\geq$ 1 - 2.5 mg/dL give IV PO_4 at dose of 0.08 mmol/kg of PO_4. If serum phosphorous is 0.5 – 1mg/dL, give IV PO_4 0.20 mmol/kg of PO_4. Draw a repeat PO_4 level, and if PO_4 level still < 1.0, then call H.O. If PO_4 < 0.5mg/dL, give 0.36mmol/kg IV PO_4 over 6 hours Phosphate is administered in the form of NaPhos or KPhos. If Na low (normal 130-140), then give as NaPhos. If K low (normal 3.5-5.0), then give as KPhos	If serum phosphorous > 6.0, then call H.O.
IV Admini-stration	Max rate:0.5mEq/kg/hr without cardiac monitor or 1mEq/kg/hr with monitor [40mEq/hour maximum]		Maximum concentration 20mg/mL *peripherally*; maximum concentration 50mg/mL *centrally*. Infuse no faster than 120 – 240mg/kg/hour.		Do not exceed 125mg/kg/hour.		Dilute every 3 mM phosphate in 25 ml for central lines and 60 ml for peripheral lines. Give no faster than 0.05 mM/kg/hr	

SHANDS

at the University of Florida
PHYSICIAN'S ORDERS

DATE	TIME	PHYSICIAN'S ORDERS (Provider ID # Required)	SMS #
		CRYOPRESERVED STEM CELL INFUSION ORDERS	
		□ PBSC's □ BM (check correct box)	
		Allergies: _____	
		1. Infuse cryopreserved stem cells on ____/____/____ .	
		2. Physician (or designee) must be present during the stem cell infusion.	
		3. Patient must be on a CR monitor and continuous 0_2 SAT monitor throughout	
		infusion and one hour post infusion.	
		4. **Epinephrine (1:1000, 1mg/mL)** (for pts >20kg) and **diphenhydramine** at	
		Bedside	
		5. **Epinephrine (1:2000, 0.5mg/mL)** (for pts ≤ 20kg) and vial of **diphenhydramine**	
		at bedside.	
		6. For cryopreserved stem cells infusion:	
		A. IV Hydration:	
		i. Start D5 ½ NS + 20mEq KCl/L at _____mL/hr (2x maintenance) 12 hours prior to	
		PBSC infusion (at ____ on ___/___/___) & continue for 12 hrs post last infusion.	
		ii. **Hold** IVF during PBSC infusion.	
		B. Premedications to be given 30 mins - 1 hr prior to infusion:	
		i. Acetaminophen mg PO (10 - 15 mg/kg/dose; MAX = 650mg)	
		ii. Diphenhydramine _____mg IV (1mg/kg/dose; MAX = 50mg)	
		iii. Hydrocortisone _____mg IV (1mg/kg/dose; MAX 100mg)	
		iv. 25% Mannitol _____ g IV over 15 minutes (0.2g/kg/dose)	
		C. Once the contents of the bag are thawed, hang utilizing standard IV tubing with	
		a 170 micron filter (platelet infusion set) and rapidly infuse each bag	
		according to the transplant infusion protocol over a period not to exceed	
		20 minutes.	
		7. Observations with infusion:	
		A. V/S at beginning of the infusion, 5 mins into infusion, then Q15mins during	
		infusion, then Q 30 mins for 1 hour post-infusion.	
		B. Accurate I & O's for 24 hours & if output is < ___ mL (4mL/kg) in a 4 hour	
		period please notify BMT team (or resident if after hours).	
		C. Monitor urine color and heme test Q void x24 hours. May see red urine after	
		infusion due to RBC lysis from freezing process.	
		D. RN should stay with patient for 1 hour post-infusion.	

Rev 8/00 15-0610-1

DO NOT WRITE BELOW THIS LINE

SHANDS
at the University of Florida

PHYSICIAN'S ORDERS

DATE	TIME	PHYSICIAN'S ORDERS (Provider ID # Required)	SMS #
		FRESH ALLOGENEIC BONE MARROW OR PBSC PRODUCT	
		□ PBSC □ BM (check correct box)	
		Allergies:	
		1. Infuse marrow on ____/____/____ at approximately ~_____.	
		2. Physician (or designee) must be present during the marrow infusion.	
		3. Patient must be on a CR monitor and continuous 0_2 SAT monitor throughout	
		infusion, and for one hour post infusion.	
		4. Epinephrine (1:1000, 1mg/mL) and diphenhydramine at bedside	
		5. Epinephrine 1:2000 (0.5mg/mL) (for patients ≤ 20 kg) and vial of diphenhydramine	
		at bedside.	
		6. Start IVF: D5 ½ NS + 20mEq KCl/L at _____ mL/hr (1.5X Maintenance)	
		Start at 2300 on Day -1 (____/____/____) and continue through 2300 on Day 0	
		(____/____/____).	
		7. Infusion of Allogeneic stem cells:	
		A. Premedicate with:	
		i. Acetaminophen _____ mg PO (10 - 15 mg/kg/dose; MAX 650mg)	
		ii. Diphenhydramine ____mg IV (1 mg/kg/dose; MAX 50mg)	
		iii. Hydrocortisone ____mg IV (1mg/kg/dose; MAX 100mg)	
		B. Stem cells should be hung utilizing standard IV tubing. Infuse cells slowly at	
		First; rate may be increased slowly if tolerated to infuse over a period of 2 – 4 hours	
		(maximum rate = 10mL/kg/hour)	
		C. Flush transfusion bag and tubing with NS at end of marrow infusion.	
		D. HOLD IVF during marrow infusion.	
		8. Observation with infusion:	
		A. V.S. at beginning of infusion, 5 min into infusion, then Q 15mins during	
		infusion, then Q 30 mins until 1 hr after infusion complete.	
		B. Monitor I & Os for 12 hrs after infusion. If urine output is < _____mL (4mL/kg)	
		in a 4 hour period (<1 mL/kg/hr), notify BMT team (or resident after hours).	
		C. Monitor urine color and heme test Q void for 12 hours after marrow infusion.	
		D. RN should stay with patient throughout the infusion.	

Rev. 8/00 **DO NOT WRITE BELOW THIS LINE** 15-0610-1

POST-TRANSPLANT CHEMOTHERAPY

1. Acute Lymphoblastic Leukemia

Intrathecal therapy (applies to both pediatric and adult populations):

A. CR1 patients who are taken to HSCT prior to completing CNS therapy (e.g., after only 2 cycles of chemotherapy): 5 doses of IT chemotherapy post-HSCT

B. CR1 with a history of treatment for CNS disease AND all those beyond CR1: IT therapy as tolerated. Patients who have difficulty tolerating it should be taken off therapy.

C. CR1 who received prophylactic cranial radiation as part of pre-HSCT and those who had TBI in the preparative regimen should not have post-HSCT IT therapy: risk of leukoencephalopathy outweighs the potential benefits.

Choice of Therapy:

Pediatrics: Intrathecal Methotrexate dose is adjusted according to patient age, see page **.
Administer IT therapy every month (total number of injections listed above)
Calcium leucovorin 5mg PO x 4 doses, starting 24 hours after IT injection

Philadelphia Chromosome positive ALL:

Patients with Philadelphia chromosome positive ALL are also to receive imatinib (Gleevec®) upon stable engraftment and stabilization of the immunoprophylaxis (IP) regimen.

2. Chronic Myeloid Leukemia

Patients who have a history of, or who are transplanted in accelerated phase or in blast crisis are to start imatinib (Gleevec®) upon stable engraftment and stabilization of the immunoprophylaxis (IP) regimen.

Dose: see Dr Mogul

PEDIATRIC LEUKEMIA/SOLID TUMOR PROTOCOLS

<table>
<tr><th>IRB number/
COG number</th><th>Study Title</th><th>Eligible Patients (Disease criteria – refer to protocol for organ function criteria)</th><th>Age Cut-off</th></tr>
<tr><td colspan="4">ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)</td></tr>
<tr><td>IRB 318-00
POG 9904</td><td>Protocol for patients with newly diagnosed low risk ALL – evaluation of the augmented BFM regimen: A Phase III study</td><td>Patients must have been registered on the POG 9900 Classification Study with a confirmed diagnosis of B-Precursor ALL
<u>Low-risk (POG 9904</u>): Standard consensus risk category (WBC < 50,000/ul, age 1.001 – 9.999 years), lack adverse translocations [E2A-PBX1, t(1;19) or BCR/ABL, t(9;22); and MLL rearrangements], lack CNS 3 disease (do not have CSF WBC ≥ 5/ul with blasts present), lack testicular disease, and have at least 1 of the following: (a) TEL/AML1, t(12;21) (according to New Mexico reference laboratory results) or (b) simultaneous trisomy of chromosomes 4 and 10 (per NM)</td><td>1.001 – 21.999 years at diagnosis</td></tr>
<tr><td>IRB 317-00
POG 9905</td><td>Protocol for patients with newly diagnosed standard risk ALL (as above)</td><td>Patients must have been registered on the POG 9900 Classification Study with a confirmed diagnosis of B-Precursor ALL
<u>Standard risk (POG 9905)</u>: These patients will be defined by elimination (not low, high, or very high risk)</td><td>1.001 – 21.999 years at diagnosis</td></tr>
<tr><td>IRB 319-00
POG 9906</td><td>Protocol for patients with newly diagnosed high risk ALL (as above)</td><td>Patients must have been registered on the POG 9900 Classification Study with a confirmed diagnosis of B-Precursor ALL
<u>High risk (POG 9906):</u> Patients must not be very high risk and meet on of the following: (a) patients with CNS 3 (blasts and ≥ 5/ul), testicular leukemia, or with MLL gene rearrangement will be considered high risk regardless of any other factors; (a2) (3 conditions to be met) pt doe not have simultaneous trisomy 4 and 10, patient does not have TEL/AML1 gene (per NM), and age and white count must fall in the following ranges:
<table>
<tr><th colspan="2">Girls</th><th colspan="2">Boys</th></tr>
<tr><th>Age (rounded down)</th><th>WBC</th><th>Age (rounded down)</th><th>WBC</th></tr>
<tr><td>ANY</td><td>>100K</td><td>ANY</td><td>>100K</td></tr>
<tr><td>16+</td><td>ANY</td><td>12+</td><td>ANY</td></tr>
<tr><td>15</td><td>>20</td><td>11</td><td>>20</td></tr>
<tr><td>14</td><td>>40</td><td>10</td><td>> 40</td></tr>
<tr><td>13</td><td>>60</td><td>9</td><td>> 60</td></tr>
<tr><td>12</td><td>>80</td><td>8</td><td>> 80</td></tr>
</table></td><td>1.001 – 21.999 years at diagnosis</td></tr>
</table>

IRB number	Study Title	Eligible Patients (Disease criteria – refer to protocol for organ function criteria)	Age cut-off
COG A ALL00P2	(Modified BFM ± Compound 506U78)	Newly diagnosed T-cell ALL (with > 25% marrow blasts (M3), per local institutional criteria No prior therapy other than steroids or emergency XRT to mediastinum in pts in respiratory distress. Patients must have registered on POG 9900 no greater than 8 days prior to registration on AALL00P2.	> 1.00 and < 21.99 years
IRB 524-99 POG 9673		Patients with recurrent or refractory T-cell malignancies (acute lymphoblastic leukemia or non-Hodgkin's lymphoma) Patients are assigned to one of four strata: 01 T-cell ALL or NHL in 1st relapse (>25% bone marrow blasts, with or without concomitant extramedullary relapse – other than CNS) 02 T-cell ALL or NHL in 2nd or later relapse (>25% bone marrow blasts, with or without concomitant extramedullary relapse – other than CNS) 03 T-cell ALL or NHL with positive bone marrow and CSF (> 5% bone marrow blasts and CNS 2 or 3 involvement) 04 Extramedullary relapse and < 25% blasts in the bone marrow (excluding isolated CNS relapse) Patients with isolated CNS relapse are NOT eligible.	≤ 21 years of age at time of initial diagnosis
ACUTE MYELOID LEUKEMIA (AML), including APL			
IRB 031-02 CALGB/COG 9710	Concurrent tretinoin + chemo with or without As_2O_3 as initial consolidation therapy followed by maintenance therapy with intermittent tretinoin versus intermittent tretinoin plus 6-MP and MTX for patients with untreated APL	Eligibility criteria are patient-specific criteria. Patients must have a diagnosis of APL with proof of APL morphology (FAB M3) confirmed by RT-PCR assay. A patient may be entered prior to completion of RT-PCR studies, but a patient ho is subsequently found to be PML-RAR-α negative and RARα-PML negative will be removed from protocol treatment	Not listed in protocol. Entry criteria listed as patient-specific criteria

IRB number	Study Title	Eligible Patients (Disease criteria – refer to protocol for organ function criteria)	Age cut-off
IRB 415-00 POG 9720	Idarubicin and cladribine in recurrent and refractory AML	Diagnosis is AML (FAB M0 – M7) or secondary AML in first relapse or primary induction failure, and myelodysplastic syndrome (not related to Down's syndrome) are eligible.	< 21 years of age at the time of initial diagnosis
IRB 259-01 COG ADVL0022	A phase II study of gemcitabine in children with relapsed ALL or AML	Relapsed ALL or AML Must have verification of the relapse as defined by M3 marrow ($\geq$ 25% blasts in BM aspirate)	< 21 at time of original diagnosis
SOLID TUMORS			
IRB 493-01 COG ADVL0017	Phase I study of flavopiridol in patients with relapsed or refractory pediatric solid tumors or lymphomas	Must have histologic verification of the malignancy at the original diagnosis (excluding brain stem tumors)	< 22 at time of entry onto protocol
IRB 416-00 COG 9963	A Phase II trial of rebeccamycin analogue in children with solid tumors	Solid tumors (histological or cytologic diagnosis) including: neuroblastoma, Ewing's sarcoma/PNET; osteosarcoma; rhabdomyosarcoma; NHL; other solid tumors refractory to conventional therapeutic modalities CNS (brain) tumors (histologically documented who exhibit recurrent or refractory tumor growth.	$\leq$ 21.99 years
IRB 481-01 AEWS0031	Trial of chemotherapy intensification through interval compression in Ewing's sarcoma and related tumors.	Ewing's sarcoma or PNET of the bone or soft tissues, excluding the central nervous system are eligible. Paraspinal tumors of extra-dural origin will be considered outside the CNS and are therefore eligible for this study	< 50 years at diagnosis

APPENDIX

BSA Calculation Sheet
GVHD Assessment Guide
Dermatomes
Peripheral Nerves
Discharge Summary Format
Karnofsky Score and Lansky Score
Diagnosis of Hematological Malignancies
Prognostic Tables and Graphs
ALL
IPI
Hodgkin's Disease
MDS
IPI for MDS
Cytogenetics
Adult ALL
Adult AML
Lymphomas
Selected Immunohistologic Tumor Markers
Flow Cytometry
IBMTR/ABMTR Staging and Response Codes
VF/VT Algorithm
Tachcardia Algorithm
Bradycardia Algorithm

Shands Hospital at
The University of Florida
Bone Marrow Transplant Program

BSA CONFIRMATION SHEET

Patient Name: _____ **MRN:** _____

Date: ____ / ____ / ____ **NURSING**

Measurement No. 1

HEIGHT: _____ (cm)

_____ (inches)

WEIGHT: _____ (kg)

RN/PCA Signature: _____

Measurement No. 2

HEIGHT: _____ (cm)

_____ (inches)

WEIGHT: _____ (kg)

RN/PCA Signature: _____

Physician/Physician's Assistant/Pharmacist:

IDEAL BODY WEIGHT (IBW)

ADULTS:

Males: 50kg + (2.3 x inches of 5 feet) = _____ kg
Females: 45.5 kg + (2.3 x inches over 5 feet) = _____ kg

CHILDREN: (Under age 12 years)

A. 1 – 12 Years: IBW (kg) = _____ $\frac{\text{height}^2\text{(cm)} \times 1.65}{1000}$

B. 5 Feet and Taller:
Males: 39 kg + (2.27 x inches over 5 feet) = _____ kg
Females: 42.2 kg + (2.27 x inches over 5 feet) = _____ kg

*** IBW derived from pediatric formulas should be compared to growth charts**

BODY SURFACE AREA (BSA):

BSA (m^2) = $\sqrt{\frac{\text{Height (cm)} \times \text{Weight (kg)}}{3600}}$

BSA based on Actual Body Weight: _____
BSA based on Ideal Body Weight: _____

BSA used to calculate chemotherapy doses: _____
(Use ideal or actual, whichever is less)

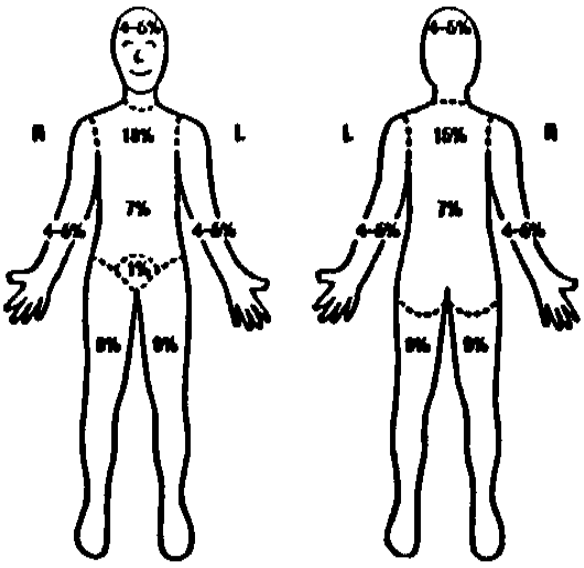
Calculator's Signature: _____

Patient height and weight shall be obtained by 2 medical staff performing 2 separate measurements. Measurements should be taken when patients are in stocking feet and light street clothes or scrubs. Patients shall have voided prior to measurements if possible.

Graft Versus Host Disease Assessment Guide

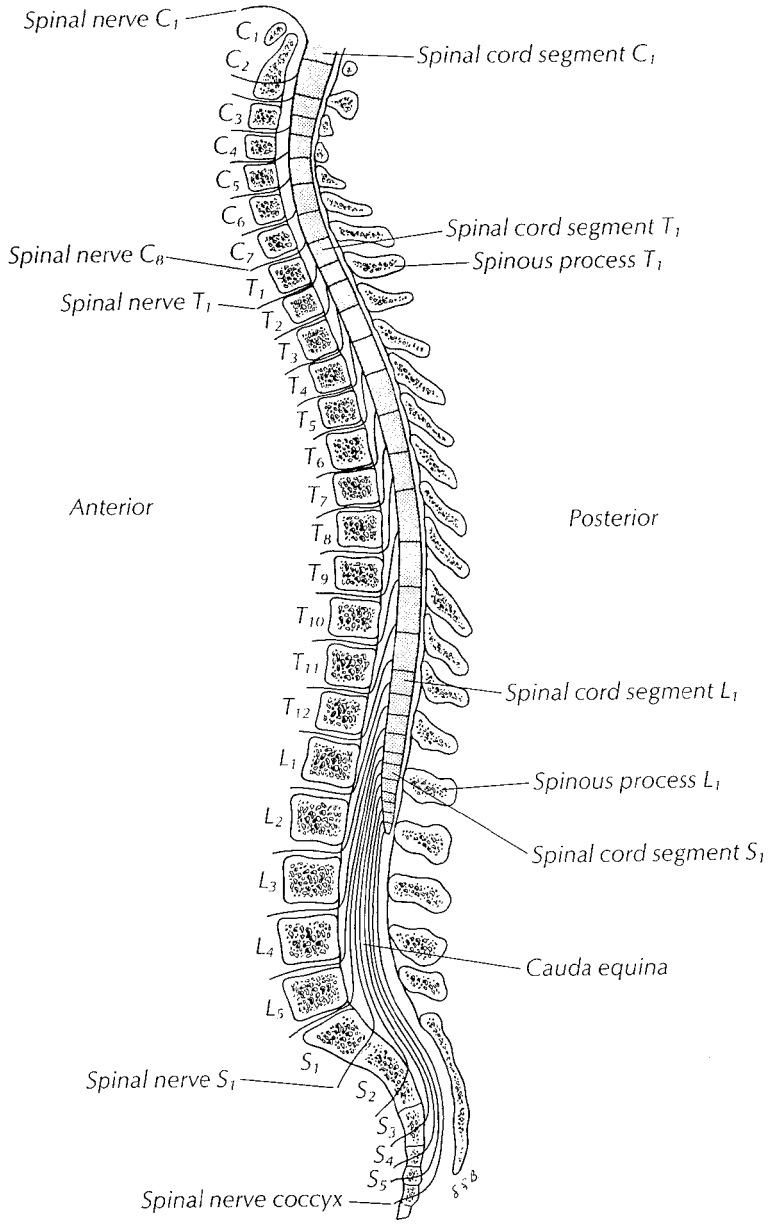
Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
Skin:				
□ no rash	□ Maculopapular rash, <25% of body surface	□ Maculopapular rash, 25-50% of body surface	□ Generalized erythroderma	□ Generalized erythroderma with bullae formation and desquamation
Intestinal tract (use ml/day for adult patients and ml/m^2/day for pediatric patients):				
□ No diarrhea □ Diarrhea ≤500ml/day or <280 m/m^2/day	□ Diarrhea >500 but ≤1000 ml/day or 280-555 ml/m^2/day	□ Diarrhea >1000 but ≤1500 ml/day or 556-833 ml/m^2/day	□ Diarrhea >1500 ml/day or >833 ml/m^2/day	□ Severe abdominal pain, with or without ileus
Liver:				
□ Bilirubin <2.0 mg/dL	□ Bilirubin 2.0-3.00 mg/dL	□ Bilirubin 3.1-6.0mg/dL	□ Bilirubin 6.1-15.0 mg/dL	□ Bilirubin >15.0mg/dL

% of Body

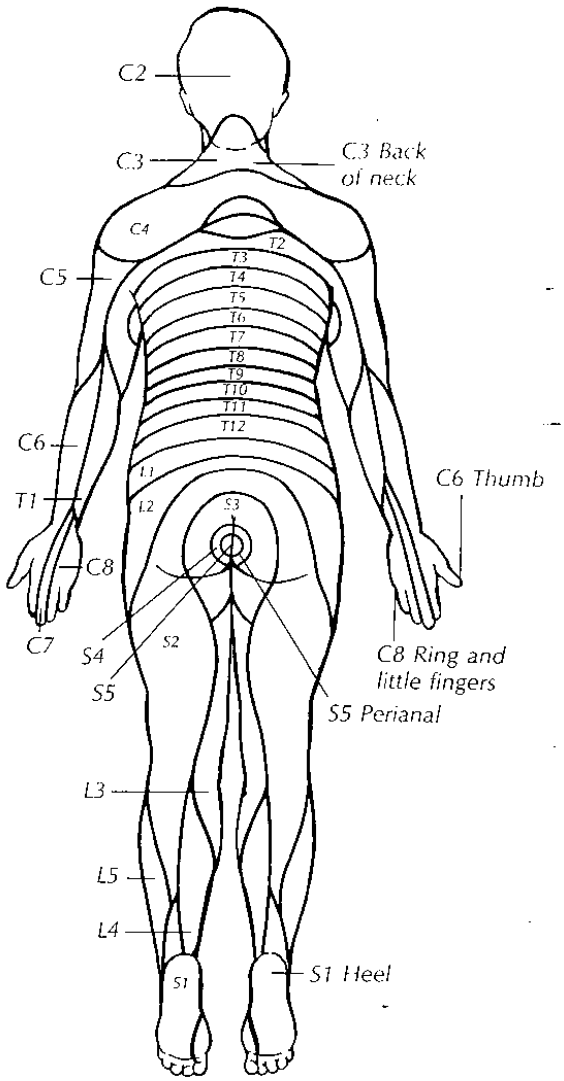


Overall Grade of Acute GVHD By Organ Stage

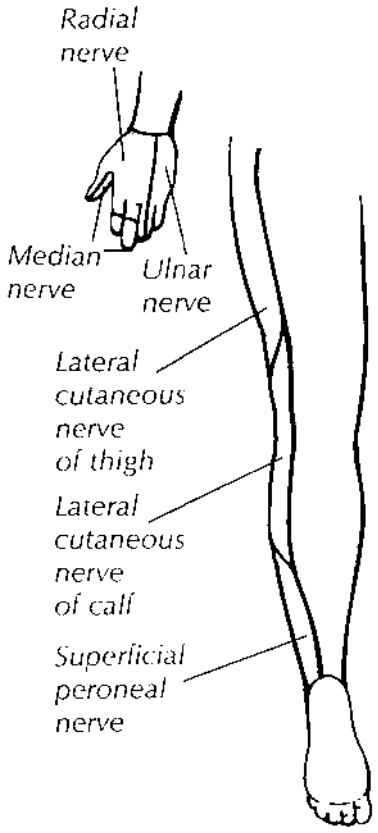
Grade	Skin	Liver	GI
I	1-2	0	0
II	0	0-1	1
	0	1	0-1
	1-3	0-1	1
	1-3	1	0-1
	3	0	0
III	0-3	2-3	0-2
	0-3	0-3	2-3
	0-3	4	0-3
IV	0-3	0-4	4
	4	0-4	0-4



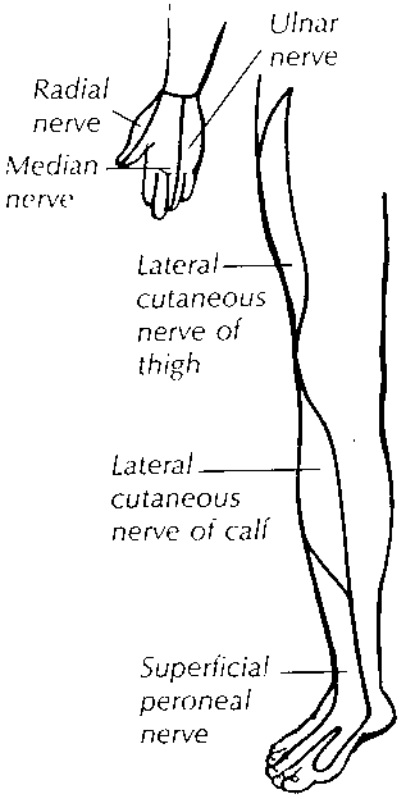
THE SPINAL CORD, LATERAL VIEW



DERMATOMES INNERVATED BY POSTERIOR ROOTS



AREAS INNERVATED BY PERIPHERAL NERVES



AREAS INNERVATED BY PERIPHERAL NERVES

BMTU DISCHARGE SUMMARY FORMAT

Patient Name
Medical Record Number
Patient Age and Sex
Admitting Diagnosis
Discharge Diagnosis
Procedures/Consultations
Viral Titers (CMV, HSV, HEP, EBV, VZ…)
Stem Cell Source:
Allo (PBSC)
Allo (Bone Marrow)
Auto (PBSC)
MUD (PBSC)
MUD (Bone Marrow)
UCB
HLA Typing
Donor Name
Medical Record Number
Donor Age and Sex
Blood Type
Viral Titers (CMV, HSV, HEP, EBV, VZ, Blood Type…)
Relation to Patient
HLA Typing
Brief History of Present Illness, *including admission physical exam*

1. ***List all Protocols Patient*** *is enrolled in.*
2. ***Conditioning Regimen.*** *Include chemotherapy agents used, dose, infusion information and dosing weight either actual or ideal body weight. (Look at Pharmacy orders). Include TBI and Splenic RT when applicable.*
3. ***Bone Marrow Transplant.*** *Include date of BMT, cell dose and any complications.*
4. ***Engraftment.*** *Include the day Patient's AGC <500 (day+1, -2, etc…), the day the Patient's AGC>500 Any growth factors used and the day they started. Also include frequency of PRBC and PLT infusions at time of discharge, and any other related engraftment problems.*
5. ***Infectious Disease.*** *A.) Fever of Unknown Origin* *B.) Bacterial Infections* *C.) Fungal Infections* *D.) Viral Infections – CMV status of the donor and recipient include.* *Include for all of the above, day of initial fever spike management taken, antibiotics used, positive cultures, date of completion of therapy and status at time of D/C.*
6. ***Graft vs. Host Diseases.*** *Include date of onset, manifestation (skin, liver, or gut, biopsies). Grade at diagnosis, management and response. Include overall stage and meds. Important to include any prophylaxis that was used. Note the number of MTX doses and if any dose reductions*
7. ***Toxicities:*** *Include date of onset, grade of disease, management and status at time of D/C. Mucositis, Pulmonary (ARDS), Cardiac, Psychiatric, Neurologic, Gastrointestinal, Hepatic (VOD), Renal and Social.*
8. ***Fluids, Electrolytes and Nutrition.*** *Include if the patient required TPN, dietary supplements, or maintenance fluids. Mention if patient requires electrolyte replacement and how often and anyremaining nutritional problems. Include D/C weight!*
9. ***Discharge Laboratory Data.*** *10.* ***Discharge Medications.*** *11.* ***Discharge Disposition. Must include any labs, X-rays, tests that need to be followed up on. Include all follow up Clinic visit, appointment dates/times.***

Please Dictate STAT w/in 24 hrs. Call transcriptions @ 44816. Inform them that dictation is needed ASAP.

KARNOFSKY AND LANSKY SCALES

KARNOFSKY SCALE > 16 years	LANSKY SCALE < 16 years
Check the phrase in the Karnofsky Scale which best describes the activity status of the recipient: **Able to carry on normal activity; no special care is needed** 1 □ 100 Normal: no complaints; no evidence of disease 2 □ 90 Able to carry on normal activity 3 □ 80 Normal activity with effort **Unable to work; able to live at home, cares for most personal needs; a varying amount of assistance is needed** 4 □ 70 Cares for self; unable to carry on normal activity or to do active work 5 □ 60 Requires occasional assistance but is able to care for most needs 6 □ 50 Requires considerable assistance and frequent medical care **Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly** 7 □ 40 Disabled; requires special care and assistance 8 □30 Severely disabled; hospitalization indicated although death not imminent 9 □ 20 Very sick; hospitalization necessary 10 □ 10 Moribund; fatal process progressing rapidly	Select the phrase in the Lansky Play-Performance Scale which best describes the activity status of the recipient: **Able to carry on normal activity; no special care is needed** 1 □ 100 Fully active 2 □ 90 Minor restriction in physically strenuous play 3 □ 80 Restricted in strenuous play, tires more easily, otherwise active **Mild to moderate restriction** 4 □ 70 Both greater restrictions of, and less time spent in, active play 5 □ 60 Ambulatory up to 50% of time, limited active play with assistance/supervision 6 □ 50 Considerable assistance required for any active play; fully able to engage in quiet play **Moderate to severe restriction** 7 □40 Able to initiate quiet activities 8 □ 30 Needs considerable assistance for quiet activity 9 □ 20 Limited to very passive activity initiated by others (e.g. TV) 10 □ 10 Completely disabled, not even passive play

DIAGNOSIS OF HEMATOLOGICAL MALIGNANCIES

Acute lymphoblastic leukemia

Precursor B-cell ALL:	Typical immunophenotype CD19+, CD20-, CD22+. CD79a+, sIg-, cIg±, CD34+, TdT+, CD10+
Mature B-cell ALL: (Burkitt-ALL)	Typical immunophenotype: CD19+, CD20+, CD22+, CD79a+, sIg+, cIg±, CD34-, TdT-, CD10±
Precursor T-cell ALL:	Typical Immunophenotype CD19-, CD20-, CD22-, CD79a-, CD7+, cCD3+, sCD3±, CD4±, CD5+, CD8±, CD34+, TdT+

CHRONIC LYMPHOCYTIC LEUKEMIA

B-CLL:
- Absolute lymphocytosis > $5x10^9$/L
- Mature lymphocytes
- Characteristic immunophenotype CD19+, CD20+, CD5+, CD23+, weak surface immunoglobulin

T-CLL:
- Absolute lymphocytosis > $5x10^9$/L
- Mature lymphocytes
- Characteristic immunophenotype CD7+, CD2+, CD3+, CD5+, CD4+, CD8+

PLL:
- CD19+, CD20+, CD22+, CD5+, often expression of T-cell markers
- 80% B-PLL, 20% T-PLL
- Usually hepatosplenomegaly

JUVENILE MYELOMONOCYTIC LEUKEMIA (JMML)

A diagnosis of JMML is confirmed only if the following criteria for JMML are met:

ALL of the following:	Absence of t(9;22) or bcr/abl by PCR Absolute monocyte count > 1000 (1 x 10^9/L) < 20% bone marrow blasts
At least 2 of the following:	↑ F hemoglobin Myeloid precursors in PB WBC > 10,000 (10 x 10^9/L) GM-CSF hypersensitivity

PROGNOSTIC TABLES/GRAPHS

Breast Cancer Risk Estimates for Family Members at Risk*

A. High-Risk Families

Genetic Alteration	Sex	Breast Cancer Risk†	Other Considerations
BRCA 1	F	87%	Increased risk for bilateral breast cancer and ovarian cancer; slightly increased risk for colon cancer
BRCA 1	M	Negligible	Slightly increased risk for colon and prostate cancer
BRCA 2	F	87%	Moderately increased risk for ovarian cancer
BRCA 2	M	6% (by age 70 years)	Risk for other cancers has not been evaluated

B. Moderate-Risk Families‡

Affected Relative	Age of Affected Relative (years)	Cumulative Breast Cancer Risk by age 80 years (%)
One first-degree	< 50 ≥ 50	13-21 9-11
One second-degree	<50 ≥ 50	10-14 8-9
Two first-degree	Both < 50 Both ≥ 50	35-48 11-24
Two second-degree§	Both < 50 Both ≥ 50	21-26 9-16

*Persons shown to be mutation noncarriers have a cancer risk equivalent to that of the general population.

† Expressed as cumulative lifetime risk to age 80 years, except where noted

‡ Risk estimates are derived by including age extremes from the risk tables calculated by Claus. For example, for affected relatives younger than 50 y, the lower limit is the calculated risk for a relative in the 20- to 29- year age group. Thus, these figures represent the range of risk based on age and are not confidence intervals.

§ Both paternal or both maternal.

Adapted from *MKSAP Hematology* 2nd edition

Prognosis in Acute Lymphoblastic Leukemia

Unfavorable	Favorable
Advanced age	Younger Age
High leukocyte count at diagnosis	Low leukocyte count at diagnosis
Presence of myeloid antigens	Absence of myeloid antigens
Late achievement of CR	Early achievement of CR
Chromosomal abnormalities: †(9:22)(q34:q11) †(4;11)(q21;q23) †(8;14)(q24;q32) †(1;19)(q23;p13)	Chromosomal abnormalities: Hyperdiploidy (50-60 chromosomes) †(12;21)
CR= complete remission.	

Prognosis in Acute Myeloid Leukemia

Unfavorable	Favorable
Advanced age	Younger age
High leukocyte count at diagnosis	Low leukocyte count at diagnosis
MDR-1 positive	MDR-1 negative
Prior myelodysplasia	No previous hematologic disorder
Chromosomal abnormalities: see below	Chromosomal abnormalities: see below

Adapted from *Hematology MKSAP* 2ND edition

SWOG and MRC cytogenetic risk category definitions

Risk Status	SWOG coding	N (n = 609)	MRC coding	N (n = 609)
Favorable	inv(16)/t(16;16)/del(16q), t(15;17) with/without secondary aberrations; t(8,21) lacking del(9q) or complex karyotypes	121 (20%)	inv(16)/t(16;16)/del (16q), t(15;17), t(8;21) with/without secondary abnormality	130 (21%)
Intermediate	Normal, +8, +6, -Y, del(12p)	278 (46%)	Normal, 11q23 abnormality, +8, del(9q), del(7q), +21, +22, all others	375 (62%)
Unfavorable	del(5q)/-5, -7/del(7q), abn 3q, 9q, 11q, 20q, 21q, 17p, t(6;9), t(9;22) and complex karyotypes (≥ unrelated abnormalities)	184 (30%)	del(5q)/-5, -7, abnormality (3q), complex karyotypes (≥ 5 unrelated abnormality) t(9;22) and t(6;9)[#]	104 (17%)
Unknown	All other abnormalities	26 (4%)	Category not recognized	

[#] Risk status for t(6;9) or t(9;22) is not defined by MRC criteria, presumably due to a lack of these low-frequency aberrations in their cohort.

Reference: Slovak ML, et al. *Blood* 2000; 98(13): 4075 – 83.

International Prognostic Index

Parameter	Criteria	Score*
Age	≤ 60 years	0
	> 60 years	1
Ann Arbor stage	I – II	0
	III – IV	1
Serum Lactate Dehydrogenase	Normal	0
	High	1
Performance status	0 – 1	0
	> 1	1
Extranodal sites	0 – 1	0
	> 1	1

*Total score; 0 or 1 = low risk;
2 = low intermediate risk;
3 = high intermediate risk;
4 or 5 = high risk

*Blood*1997; 89(6): 2079-2088

Table 4. Outcome According to Risk Group Defined by the International Index and the Age-Adjusted International Index.

Risk Group	No. of Risk Factors	Distribution of Patients (%)	Complete Response			Survival	
			Rate (%)	Relapse-free survival		2-yr rate (%)	5-yr rate (%)
				2-yr rate (%)	5-yr rate (%)		
International index, all patients (n = 2031)*							
Low	0 or 1	35	87	79	70	84	73
Low intermediate	2	27	67	66	50	66	51
High intermediate	3	22	55	59	49	54	43
High	4 or 5	16	44	58	40	34	26
Age-adjusted index, patients ≤60 (n = 1274)†							
Low	0	22	92	88	86	90	83
Low intermediate	1	32	78	74	66	79	69
High intermediate	2	32	57	62	53	59	46
High	3	14	46	61	58	37	32
Age-adjusted index, patients >60 (n = 761)†							
Low	0	18	91	75	46	80	56
Low intermediate	1	31	71	64	45	68	44
High intermediate	2	35	56	60	41	48	37
High	3	16	36	47	37	31	21

*The total of patients includes the 1385 in the training sample and the 646 in the validation sample.

†The total of the patients in the two analyses with the age-adjusted index includes four more patients than the total in the analysis with the international index because all the data necessary for these four patients to be included in the age-adjusted analyses (which evaluated fewer variables) were available.

Engl J Med 1993; 329: 987-94

Prognostic System for Hodgkin's Disease (HD)

Factor	Log Hazard Ratio	P Value	Relative Risk	Points
Serum albumin, < 4 g/dl	0.40 ± 0.10	<0.001	1.49	1
Hemoglobin, < 10.5 g/dl	0.30 ± 0.11	0.006	1.35	1
Male sex	0.30 ± 0.09	0.001	1.35	1
Stage IV disease	0.23 ± 0.09	0.011	1.26	1
Age, ≥ 45 yr	0.33 ± 0.10	0.001	1.39	1
White-cell count, ≥ 15,000/mm^3	0.34 ± 0.11	0.001	1.41	1
Lymphocyte count, < 600/mm^3 or < 8% of white-cell count	0.31 ± 0.10	0.002	1.38	1
* Hazard ratios and relative risks are for freedom from progression of disease in patients with the factors as compared with those without the factors. Plus-minus values are rate estimates ± SE (approximate 95 percent confidence intervals can be calculated as the rate estimates ± 2 SE).				

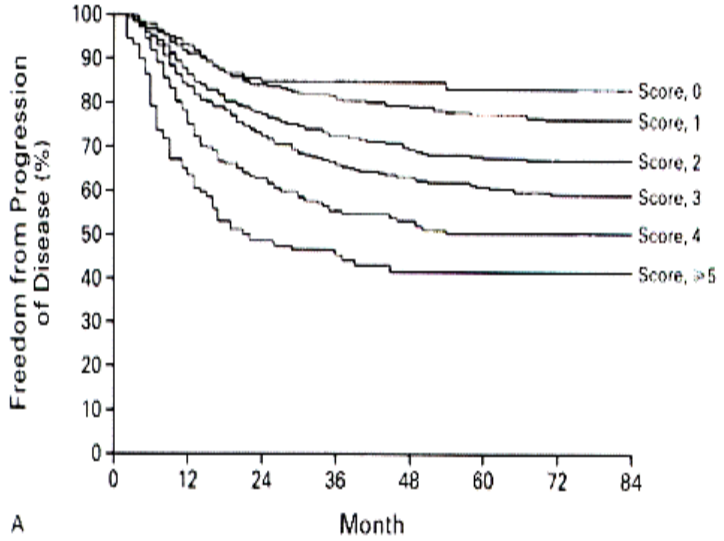
Prognostic Score	No. of Patients (%)	Rate of Freedom from Progression	Rate of Overall Survival
		Percent	
Individual			
0	**115 (7)**	84 ± 4	89 ± 2
1	**360 (22)**	77 ± 3	90 ± 2
2	**464 (29)**	67 ± 2	81 ± 2
3	**378 (23)**	60 ± 3	78 ± 3
4	**190 (12)**	51 ± 4	61 ± 4
≥ 5	**111 (7)**	42 ± 5	56 ± 5
Grouped			
0 or 1	**475 (29)**	79 ± 2	90 ± 2
≥ 2	**1143 (71)**	60 ± 2	74 ± 2
0-2	**939 (58)**	74 ± 2	86 ± 2
≥ 3	**679 (42)**	55 ± 2	70 ± 2
0-3	**1317 (81)**	70 ± 2	83 ± 1
≥ 4	**301 (19)**	47 ± 2	59 ± 2

N Eng J Med 1998; 339: 1506-1514

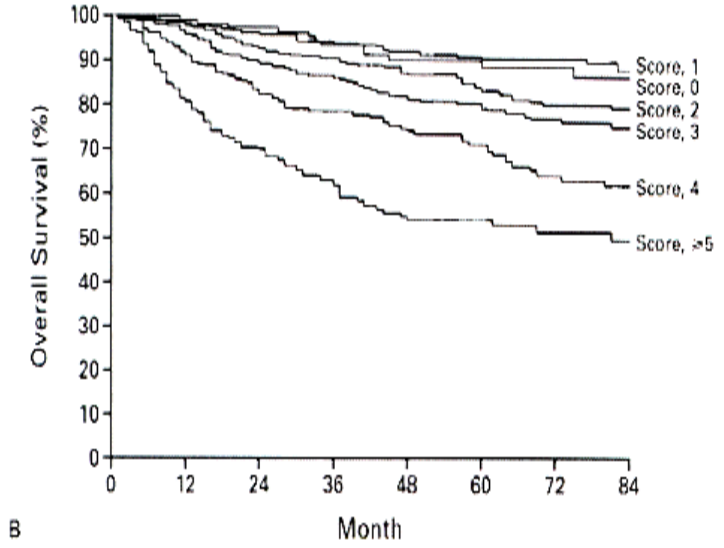
Figure 1: Use of the Prognostic Score to Predict Rates of Freedom from Progression of Disease (Panel A) and Overall Survival (Panel B) in 1618 Patients with Advanced Hodgkin's Disease.

The number and percentage of patients with each score were as follows: a score of 0, 115 patients (7 percent); 1, 360 (22 percent); 2, 464 (29 percent); 3, 378 (23 percent); 4, 190 (12 percent); and 5 or higher, 111 (7 percent).

Panel A:



Panel B:



N Eng J Med 1998; 339: 1506-1514

Myelodysplastic Syndrome (MDS)

Classification of MDS by the FAB Cooperative Group

Classification	% Marrow Blasts	% Peripheral Blood Blasts	Ringed Sideroblasts > 15% of BM	Monocytes > 1000/μL
Refractory anemia	< 5	$\leq$ 1	-	-
Refractory anemia with ringed sideroblasts	< 5	$\leq$ 1	+	-
Refractory anemia with excess blasts	5-20	< 5	-/+	-
Refractory anemia with excess blasts in transition	20-30	> 5	-/+	-/+
Chronic myelomonocytic anemia	$\leq$ 20	< 5	-/+	+

International Prognostic Scoring System for Myelodysplasia*

Parameter	**Criteria**	**Score**
Marrow blasts	<5% 5-10% 11-20% 21-30%	0 0.5 1.5 2.0
Karyotype	Normal 46 XY, -Y, $5^{-}q$, 20^{-q} Other At least 3 abnormalities, Chromosome 7 abnormalities	0 0.5 1.0
Cytopenias (hemoglobin <10g/dL, platelet count < 100,000/μL, neutrophil count < 1500/μL)	None or one Two or three	0.5
*Total score 0= low risk group; 0.5-1.0 = intermediate-1risk group; 1.5-2.0 = intermediate-2 risk group; >2.0 = high risk group.		

Adapted from *Hematology MKSAP* 2ND edition

CYTOGENETICS

Adult ALL

Cytogenetics	% of Patients	CR(%)	Long-term Prognosis
Normal	20-30	90	Good
Ph^+	15-20	50-65	Poor
†(8;14), †(8;2), †(8;22)	<10	65 (with conventional therapy)	Poor, but changing with new therapy
6q-, 14q+	5	55-60	?
Hyperdiploid	10	85	Good
Hypodiploid	<5	60	Poor
†(4;11)	<2	?	Poor
†(1;19)	<2	?	Poor
Insufficient metaphases	20-30	75	Good
ALL = acute lymphocytic leukemia; CR= complete response.			

Abnormality	Genes Involved	Associated Phenotype
T(1;19)	E2A-PBX1	Pre-B ALL
T(4;11)	AF4-MLL	CD 10 neg, B ALL
T(8;14)	Myc-IG	B cell, L3 (100%)
T(9;22)	BCR-ABL	Mixed lineage ALL
T(12;21)*	TEL-AML1	Pre-B ALL
+4; +10*	unknown	Pre-pre B, hyperdiploid
T(1;14)	TAL1-T cell receptor delta	T cell

***confers a good prognosis**

AML

Abnormality	Genes Involved	Associated phenotype
T(15;17)	PML-RAR	M3 (100%)
Inv(16) or t(16;16)	CBFB-MYH11	M4E (100%)
T(8;21)	AML-ETO	M2
+8	Unknown	AML
T(9;22)*	BCR-ABL	M1, M2, post CML
Del 5 or del 7*	Unknown	Secondary AML
11q23*	MLL	Secondary AML
Complex*	various	Secondary AML

*difficult to treat

UF Hematopathology Course 2000

Lymphomas

Cell Type	Phenotype	Typical Cytogenetic Abnormalities	Molecular Abnormality
Follicle center lymphoma	SIG+, CIG-, CD5, CD10+, CD23-/+, CD43-/+	†(14;18)	BCL-2 rearrangement
Burkitt's lymphoma	SIG+,CD5+, CD23-, CD10+, CD5-, CD43	†(8;14) (q24;q32); †(8;22) (q24;q11); †(2;8) (p12;q24)	MYC rearrangement or overexpression
B-cell CLL/SLL	SIG+, CD5+, CD10, CD23+, CD43+	Trisomy 12 (30%)	
Immunocytoma	SIG+, CIG+, CD5-, CD10-, CD23-, CD43 -/+	†(9;14) (p13;32q32)	?
Mantel cell lymphoma	SIG+, CIG-, CD5+, CD10-, CD23-,CD43+	†(11;14)	BCL-1 (PRAD-1 or cyclin D1) rearrangement
Monocytoid B-cell	SIG+, CD5-, CD10-, CD23	Trisomy 3, trisomy18, rearrangement of 1q21 or 1p34	
Splenic marginal zone lymphoma	SIG+, CD5-, CD10-, CD23-/+, CD43-/+	Chromosome 3 abnormalities	?
Primary extranodal diffuse large cell lymphoma	B cell	3q27 rearrangements with 14q23, 22q11, 2p12	BCL-6 rearrangement
Ki-1 anaplastic large cell lymphoma (ALCL)	CD30+, CD15-, CD3+ T cell or Null cell	†(2;5) (p23;q35)	ALK fusion gene NPM-ALK1
Malt Lymphoma	SIG=, CD5-, CD10-, CD23-/+, CD43-/+	Trisomy 3 and 18; changes in 1q21 and 1p34; †(11;18) (q21q21)	?
CLL= chronic lymphocytic leukemia; MALT= mucosa associated lymphoid tissue; SLL =small lymphocytic lymphoma.			

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SELECTED IMMUNOHISTOLOGIC TUMOR MARKERS

Detectable Antigen	Tumor Type
Alpha-fetaprotein (AFP)	Germ cell and trophoblastic tumors, hepatocellular carcinoma
Beta-1-antitrypsin	Hepatocellular carcinoma
Carcinoembryonic antigen(CEA)	Gut, pancreas, cervix, uteri, lung, ovary, breast, urinary tract
Chromogranin	NET
Collagen, type IV; laminin	Sarcomas (neurogenic, smooth muscle)
Cyclin D	Mantle cell lymphoma
Cytokeratin	Nonspecific; broad range of carcinomas and sarcomas
CD68	Macrophages
Desmin	Sarcomas (smooth or skeletal muscle, glomus tumor); corpus uteri (connective tissue part)
Factor VIII; CD31, CD34	Sarcomas (vascular)
Gross cystic disease fluid protein (GCDFP-15)	Breast
Hormones, specific	Endocrine gland, gut, or pancreatic tumors
Human chronic gonadotropin (hCG)	Trophoblastic, breast, and other tumors
Human placental lactogen	Trophoblastic tumors
Ki67	Proliferation antigen
Immunoglobulin molecules	Lymphomas/leukemias
Involucrin	Squamous epithelia
Leukocyte common antigen (LCA)	Lymphomas/leukemias, histiocytic tumors
Lymphoid cell epitopes and activation markers	Lymphomas/leukemias
Milk fat globules	Breast(nonspecific)
Muramidase (lysozyme); CD68	Histiocytic tumors, myelogenous leukemia
Myelin basic protein	Sarcomas (neurogenic)
Myoglobin	Sarcomas (neurogenic, skeletal muscle), corpus uteri
Muscle-specific actin	Sarcomas (leiomyosarcoma, MFH)
Neurofilaments	NET; lung (small cell carcinoma)
Neuron-specific enolase	NET; lung (small cell carcinoma); breast carcinoma (some); melanoma
NKI/C3 or MB-5	Melanoma
Pancreatic carcinoma antigen	Pancreas, gut
Prostate-specific acid phosphatase, prostate-specific antigen (PAP, PSA)	Prostate
S-100 protein	Melanoma; sarcomas (neurogenic, cartilage); histiocytic tumors
Thyroglobulin	Thyroid
Vimentin	Sarcomas (muscle, cartilage, vessels, bone synovial, epitheloid, MFH); renal cell carcinoma; lymphomas/leukemias; melanoma
MFH, Malignant fibrous histiocytoma; NET, neuroendocrine tumors (neuroblastic, Merkel cell, and ca tumors; paragangliomas; pheochromocytoma).	

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FLOW CYTOMETRY

T-lymphocyte markers

CD1 (common thymocyte)
CD2 (E-rosette-forming T cell)
CD3 (immunocompetent T cell)
CD4 (helper T cell)
⇓ in HIV infection
⇑ in Sézary syndrome
⇓ in T-cell-directed immunosuppression
CD5 (mature T cell)
Aberrantly expressed in CLL/mantel cell
CD7 loss of CD7 in Mycosis Fungoides
CD8 (suppressor T-cell)

B-lymphocyte markers

CD10 (Common All-associated Antigen (CALLA)
Often expressed in bilineage lymphoblastic leukemia/NHL
CD19 (pan-B-cell)
Virtually always expressed in CLL
Commonly expressed in ALL and intermediate-and high-grade lymphomas; used as target for immunotherapy and immunotoxins
CD20 (pan-B-cell): used in Rituxan therapy
CD22 (resting B-cell)
CD23 (activated B-cell): negative in mantel /(+) CLL
IgG (surface or cytoplasmic)
IgM (surface or cytoplasmic; usual in CLL)
κ chains (surface or Cytoplasmic)
λ chains (surface or Cytoplasmic)
CD79a (B lineage pan B)

Myelomonocytic markers

CD11C (on monocytes, macrophages, and NK cells)
CD13 (monocytes, granulocytes)
CD14 (monocytes)
CD15 (granulocytes)—Reed Sternberg cells, also

NK-cell markers

CD16 (NK cells and granulocytes)
CD56 (NK cells)
CD57 (NK cells and T and B lymphocytes)

Miscellaneous markers

CD25 (Hairy cell, Transformed of Mycosis Fungoides)
CD30 (Reed-Sternberg cell)
CD34 (myeloid progenitors) (immature marker)
CD38 (activated T cells, plasma cells)
CD45 (all leukocytes)
CD61 (platelets, megakaryocyes)
Recognizes glycoprotein IIIa
Ckit (stem cell receptor: myeloidblasts)
HLA-DR (immture myeloids and lymphoid)
Glycophorin (erythrocytes)
Tdt (lymphoblast)
CD103;11c:Hairy cell

Adapted from Hematology MKSAP 2nd edition

IBMTR/ABMTR STAGING AND RESPONSE CODES

MULTIPLE MYELOMA STAGING

STAGE I requires ***ALL*** of the following criteria:

- Hemoglobin >10 g/dL
- Serum Calcium < 12 mg/dL
- Normal bones on radiographs, or solitary plasmacytoma
- IgG <5 g/dL
- IgA < 3g/dL
- Urine light chains < 4 g/24 hours

Stage II

- Fitting ***NEITHER*** Stage I or Stage III criteria

Stage III requires ***ONE OR MORE*** of the following criteria:

- Hemoglobin < 8.5 g/dL
- Serum calcium > 12 mg/dL
- Advanced lytic bone lesions (> 3 lytic lesions)
- IgG > 7 g/dL
- IGA > 5 g/dL
- Urine light chain excretion > 12 g/24 hours

A=Relatively normal renal function (Creatinine < 2 mg/dL)
B=Abnormal renal function (Creatinine $\geq$ 2 mg/dL)

MULTIPLE MYELOMA RESPONSE CODES

CR=Complete Response. CR requires ***all*** of the following:

- Absence of the original monoclonal paraprotein in serum and urine by electrophoresis and immunofixation for at least 6 weeks
- < 5% plasma cells in a bone marrow aspirate and also on trephine bone biopsy, if biopsy performed (repeat biopsy after at least 6 weeks is needed in non-secretory myeloma only)
- No increase in size or number of lytic bone lesions; no new lesions
- Disappearance of soft tissue plasmacytomas

CCR=Continuing Complete Response. CR continuing from CR prior to this line of therapy.

PR=Partial Response. PR requires ***all*** of the following:

- ≥ 50% reduction in serum paraprotein levels for at least 6 weeks
- Reduction in 24 hour urinary light chain excretion either by ≥ 90% or to < 200 mg/24hr maintained for at least 6 weeks
- No increase in the size or number of lytic bone lesions; no new lesions
- ≥ 50% reduction in size of soft tissue plasmacytomas (by radiographs or exam)
- For non-secretory myeloma only, ≥ 50% reduction in plasma cells in a bone marrow aspirate and on trephine biopsy, if biopsy is performed, maintained for at least 6 weeks

MR=Minimal Response. MR requires ***all*** of the following:

- 25-49% reduction in serum paraprotein levels for at least 6 weeks
- 50-89% reduction in 24 hour urinary light chain excretion, which still exceeds 200 mg/24hrs for at least 6 weeks
- No increase in the size or number of lytic lesions
- 25-49% reduction in size of soft tissue plasmacytomas (by radiographs or exam)
- For non-secretory myeloma only, 25-49% reduction in plasma cells in a bone marrow aspirate and on trephine biopsy, if biopsy performed, for at least 6 weeks

NR/SD=No Response/Stable Disease.

- Not meeting criteria for minimal response or progressive disease.

PROG=Progressive disease. PROG includes ***any*** of the following:

- > 25% increase in the level of serum monoclonal paraprotein, which must be an absolute increase of 5g/L above baseline and confirmed by at least 1 repeated evaluation
- > 25% increase in 24hr urinary light chain excretion from a minimum baseline amount of at least 500 mg/24 hour on 2
- > 25% increase in plasma cells in a bone marrow aspirate or on trephine biopsy from a minimum baseline of 5%
  - Increase in number and/or > 25% increase in size of plasmacytoma
  - Development of new bone lesions or soft tissue plasmacytomas
  - Development of hypercalcemia

REL from CR=Relapse from CR includes ***any*** of the following:

- Reappearance of serum or urinary paraprotein on electrophoresis or immunofixation, confirmed by at least one repeated evaluation
  - Reappearance or development of hypercalcemia
  - ≥ 5% plasma cells in a bone marrow aspirate or on trephine biopsy
- Development of new lytic bone lesions or > 25% increase of existing lesions
  - Development of new soft tissue plasmacytomas

PLATEAU

Stable values (within 25% above or below value at the time response is assessed) maintained for ≥ 3 months.

LYMPHOMA STAGING

Stage I

- Involvement of a single lymph node region or a single extralymphatic organ or site

Stage II

- Involvement of two or more lymph node regions on same side of diaphragm or localized involvement of extralymphatic organ or site and one or more lymph node regions on same side of diaphragm

Stage III

- Involvement of lymph node regions on both sides of diaphragm, which may also be accompanied by localized involvement of extralymphatic organ or site, or the spleen, or both

Stage IV

- Diffuse or disseminated involvement of one or more extralymphatic organs in tissues with or without associated lymph node enlargement

A=No unexplained weight loss, fevers or night sweats
B=Unexlpained weight loss > 10% body weight in six months before treatment; unexplained fever > 38 C; or, night sweats

LYMPHOMA RESPONSE CODES

CR=Complete Remission

- Complete disappearance of all known disease for ≥ 4 weeks.

CRU=Complete Remission Undetermined

- Complete disappearance of known disease for ≥ 4 weeks with the exception of persistent scan abnormalities of unknown significance.

PR=Partial Remission

- ≥50% reductions in greatest diameter of all known sites of disease and no new sites.

NR/PROG=No resonse/Progression

- < 50% reduction in greatest diameter of all known sites of known disease or increase in size of known disease or new sites of disease.

LYMPHOMA REMISSION STATE CODES

(USED TO DETERMINE STATUS OF DISEASE IMMEDIATELY PRIOR TO CONDITIONING)

PIF res=Primary induction failure-resistant

- Never in complete remission but with stable or progressive disease on treatment

PIF sen=Primary induction failure-sensitive

- Never in complete remission but with partial remission on treatment

PIF unt=Primary induction failure-untreated

PIF unk=Primary induction failure-unknown sensitivity

CR1=1st complete remission

- No bone marrow or extramedullary relapse prior to transplant

CR2=2nd complete remission

CR3+=3rd or subsequent complete remission

REL1 unt=1st relapse-untreated

- includes either bone marrow or extramedullary relapse

REL1 res=1st relapse-resistant

- stable or progressive disease with treatment

REL1 sen=1st relapse-sensitive

- partial remission

REL1 unk=1st relapse-sensitivity unknown

REL2 unt=2nd relapse-untreated

- includes either bone marrow or extramedullary relapse

REL2 res=2nd relapse-resistant

- stable or progressive disease with treatment

REL2 sen=2nd relapse-sensitive

- partial remission

REL2 unk=2nd relapse-sensitivity unknown

REL3+ unt=3rd or subsequent relapse-untreated

- includes either bone marrow or extramedullary relapse

REL3+ res=3rd or subsequent relapse-resistant

- stable or progressive disease with treatment

REL3+ sen=3rd or subsequent relapse-sensitive

- partial remission

REL3+ unk=3rd relapse-sensitivity unknown

ACUTE LEUKEMIA RESPONSE CODES

PIF=Primary induction failure

1st CR=first complete remission (no prior marrow or extramedullary relapse)

2nd CR=Second complete remission

≥3rd CR=Third complete remission and beyond

1st REL=First relapse

2nd REL=Second relapse

≥3rd REL=Third relapse and beyond

CML STATUS CODES

(USED TO DETERMINE STATUS OF DISEASE JUST PRIOR TO CONDITIONING)

1st Chronic Phase (no previous transplant)

Accelerated Phase (no previous transplant)

Second or greater Chronic Phase (no previous transplant)

Blastic Phase (no previous transplant)

Chronic Phase (following previous transplant)

Accelerated Phase or Blast Phase (following previous transplant)

CHRONIC LYMPHOCYTIC LEUKEMIA STAGING

Rai Stage

Stage 0
- Lymphocytosis only

Stage I
- Lymphocytosis plus lymphadenopathy

Stage II
- Lymphocytosis plus lymphadenopathy and/or splenomegaly (with or without lymphadenopathy)

Stage III
- Lymphocytosis plus anemia (Hemoglobin < 11g/dL)

Stage IV
- Lymphocytosis plus thrombocytopenia (platelet count < 100 x 10^9/L)

Binet Stage

Stage A
- < 3 lymphoid sites involved (areas of involvement include cervical, axillary, and inguinal nodes, spleen, liver) and hemoglobin > 10 g/dL, platelets > 100 x 10^9/L

Stage B
- ≥ 3 lymphoid sites involved, and hemoglobin > 10 g/dL, platelets > 100 x 10^9/L

Stage C
- hemoglobin < 10 g/dL and/or platelets < 100 x 10^9/L, independent of lymphoid sites involved

A=No unexplained weight loss, fevers or night sweats
B=Unexlpained weight loss > 10% body weight in six months before treatment; unexplained fever > 38 C; or, night sweats

CLL RESPONSE CODES

CR=Complete Remission
- No lymphadenopathy; no organomegaly; neutrophils > 1.5 x 10^9/L; platelets > 100 x 10^9/L; hemoglobin > 11 g/dL; lymphocytes < 4 x l0^9/L ; bone marrow < 30% lymphocytes; absence of constitutional symptoms

PR=Partial Remission
- Change from Binet Stage C to Stage A or B; change from Binet Stage B to A

SD=Stable disease
- No change in Binet stage of disease

PROG=Progression
- Change from Binet Stage A to Stage B or C; or from Binet Stage B to C

NEUROBLASTOMA STAGING

INSS Staging System

Stage 1

- Localized tumor with complete gross excision, with or without microscopic residual disease; representative ipisilateral lymph nodes negative for tumor microscopically (nodes attached to and removed with the primary tumor may be positive).

Stage 2A

- Localized tumor with incomplete gross excision; representative ipsilateral nonadherent lymph nodes negative for tumor microscopically.

Stage 2B

- Localized tumor with or without complete gross excision, with ipisilateral nonadherent lymph nodes positive for tumor. Enlarged contralateral lymph nodes must be negative microscopically.

Stage 3

- Unresectable unilateral tumor infiltrating across the midline (1) , with or without regional lymph node involvement; or localized unilateral tumor with contralateral regional lymph node involvement; or midline tumor with bilateral extension by infiltration (unresectable) or by lymph node involvement

Stage 4

- Any primary tumor with dissemination to distant lymph nodes, bone, bone marrow, liver, skin, and/or other organs (except as defined for stage 4S)

Stage 4S

- Localized primary tumor (as defined for Stage 1, 2A or 2B), with dissemination limited to skin, liver, and/or bone marrow (2) (limited to infants < 1 year of age).

(1) The midline is defined as the vertebral column. Tumors originating on one side and crossing the midline must infiltrate to or beyond the opposite side of the vertebral column.

(2) Marrow involvement is Stage 4S should be minimal, i.e., < 10% of total nucleated cells identified as malignant on bone marrow biopsy or on marrow aspirate. More extensive marrow involvement would be considered to be stage 4. The MIBG scan (if performed) should be negative in the marrow.

POG Staging System

Stage A

- Complete gross excision of primary tumor, margins histologically negative or positive. Intracavitary lymph nodes not intimately adhered to and removed with resected tumor must be histologically free of tumor. If primary is in abdomen or pelvis, liver must be histologically free of tumor.

Stage B

- Incomplete gross resection of primary. Lymph nodes and liver must be histologically free of tumor.

Stage C

- Complete or incomplete gross excision of primary. Intracavitary nodes (cavity of primary) histologically positive for tumor. Liver histologically free of tumor.

Stage D

- Disseminated disease beyond intracavity nodes in bone marrow, bone, liver, skin or lymph nodes beyond cavity containing primary tumor.

Evans Group Staging System

Stage I

- Tumor confined to organ structure of origin

Stage II

- Tumors extending in continuity beyond the organ or structure of origin but not crossing the midline. Regional lymph nodes on the homolateral side may be involved.

Stage III

- Tumors extending in continuity beyond the organ or structure of origin but not crossing the midline. Regional lymph nodes bilaterally may be involved.

Stage IV

- Remote disease involving skeleton, soft tissues, distant lymph node groups, etc.

Stage IV-S

- Patient with local stage I or II disease but who have remote disease confined to one or more of the following: liver, skin, bone marrow (with no evidence of bone metastases on complete skeletal survey).

NEUROBALSTOMA RESPONSE CODES

CR=Complete Remission

- No primary tumor
- No metastatic tumor sites; catecholamines normal

VGPR=Very Good Partial Remission

- Primary tumor size decreased by 90– 99%
- No metastatic tumor sites; catecholamines normal; residual ^{99}Tc bone changes allowed

PR=Partial Response

- Primary tumor size decreased by > 50%
- All measurable sites decreased by > 50%.
- Bones and bone marrow: number of positive bone sites decreased by > 50%, no more than 1 positive bone marrow site allowed (1 positive marrow aspirate or biopsy allowed for PR if this represents a decrease from the number of positive sites at diagnosis)

MR=Minimal Response

- No new lesions; > 50% reduction of any measurable lesion (primary or metastases) with < 50% reduction in any other; < 25% increase in any existing lesion

NR=No Response

- No new lesions; <50% reduction but <25% increase in any existing lesion

PD=Progressive Disease

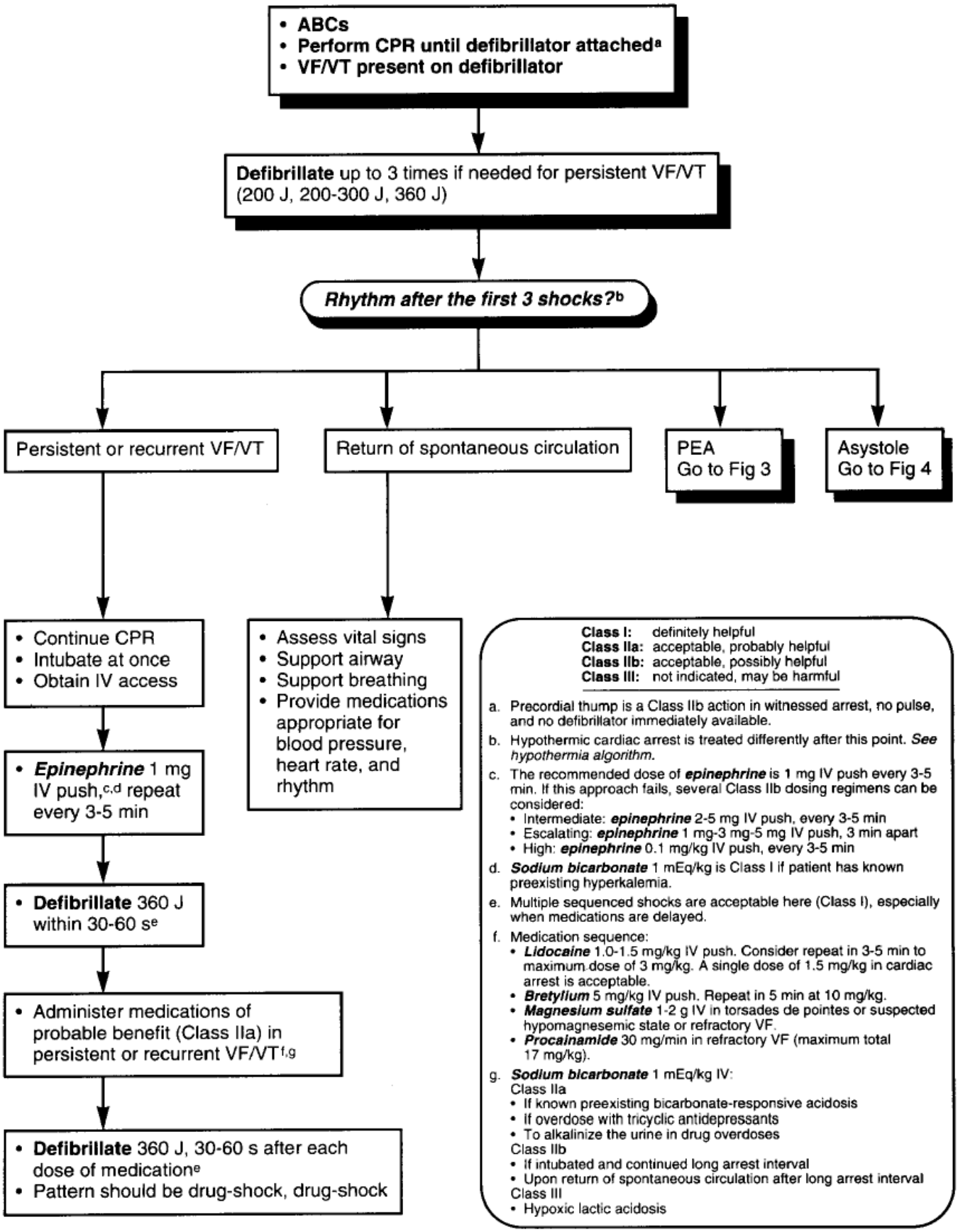
- Any new lesion; increase of any measurable lesion by > 25%; previous negative marrow positive for tumor

NE=Not Evaluable

NE=Not tested; unknown

Ventricular Fibrillation/Pulseless Ventricular Tachycardia (VF/VT) Algorithm

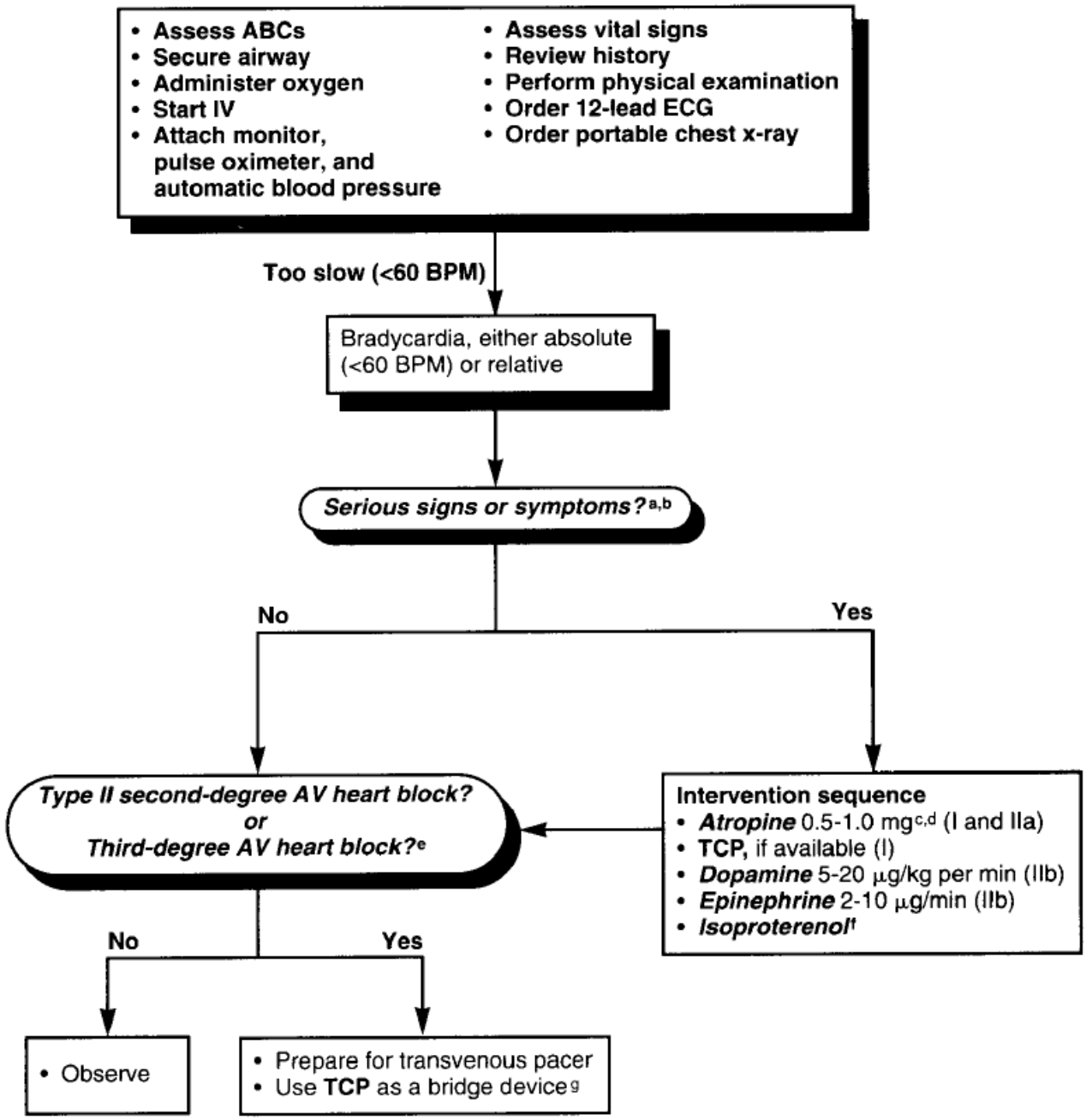
Figure 2



Bradycardia Algorithm

(Patient is not in cardiac arrest)

Figure 5



a. Serious signs or symptoms must be related to the slow rate. Clinical manifestations include
   - Symptoms (chest pain, shortness of breath, decreased level of consciousness)
   - Signs (low BP, shock, pulmonary congestion, CHF, acute MI)

b. Do not delay TCP while awaiting IV access or for ***atropine*** to take effect if patient is symptomatic.

c. Denervated transplanted hearts will not respond to ***atropine.*** Go at once to pacing, ***catecholamine*** infusion, or both.

d. ***Atropine*** should be given in repeat doses every 3-5 min up to total of 0.03-0.04 mg/kg. Use the shorter dosing interval (3 min) in severe clinical conditions. It has been suggested that ***atropine*** should be used with caution in atrioventricular (AV) block at the His-Purkinje level (type II AV block and new third-degree block with wide QRS complexes) (Class IIb).

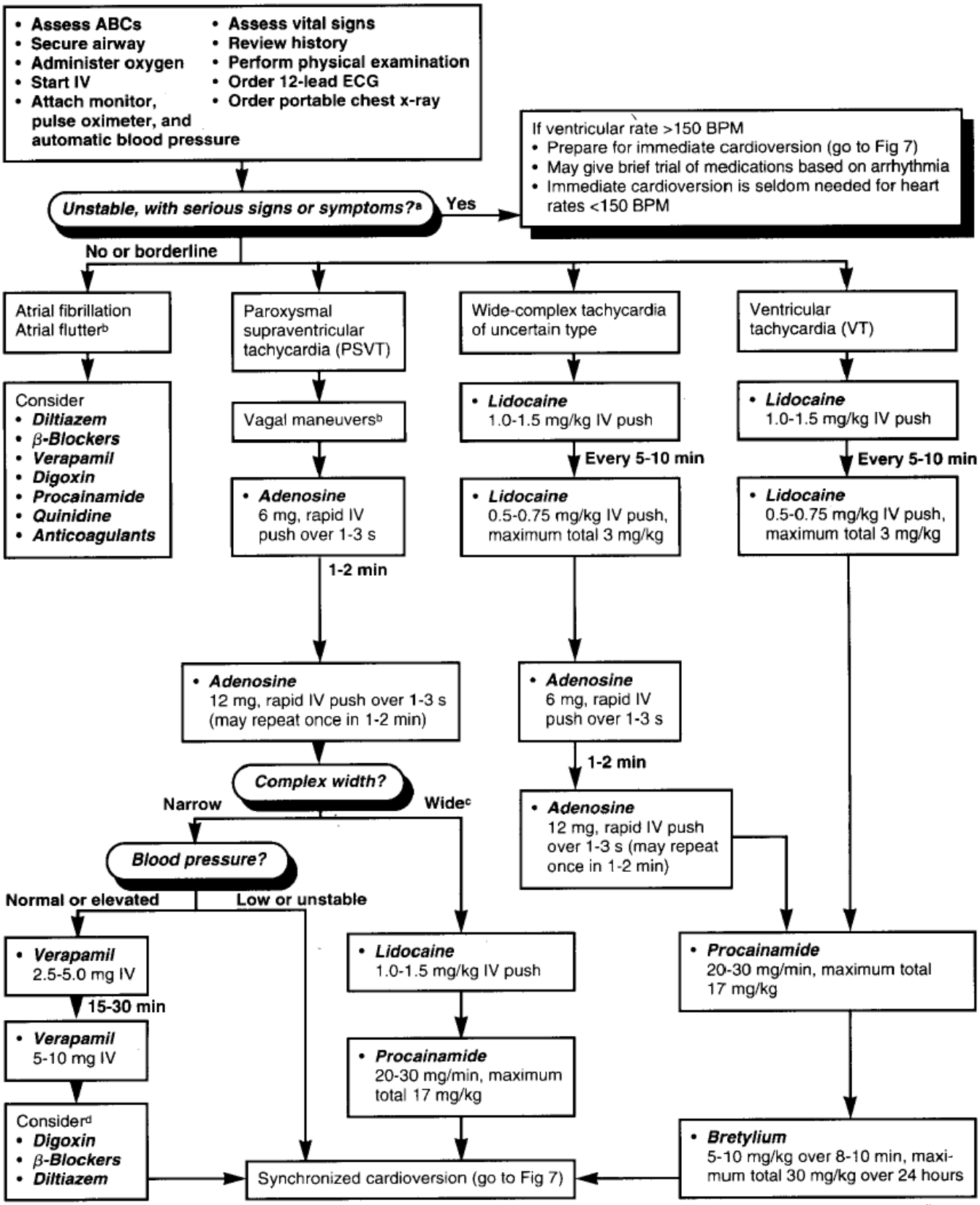
e. Never treat third-degree heart block plus ventricular escape beats with ***lidocaine.***

f. ***Isoproterenol*** should be used, if at all, with extreme caution. At low doses it is Class IIb (possibly helpful); at higher doses it is Class III (harmful).

g. Verify patient tolerance and mechanical capture. Use analgesia and sedation as needed.

Tachycardia Algorithm

Figure 6



a. Unstable condition must be related to the tachycardia. Signs and symptoms may include chest pain, shortness of breath, decreased level of consciousness, low blood pressure (BP), shock, pulmonary congestion, congestive heart failure, acute myocardial infarction.

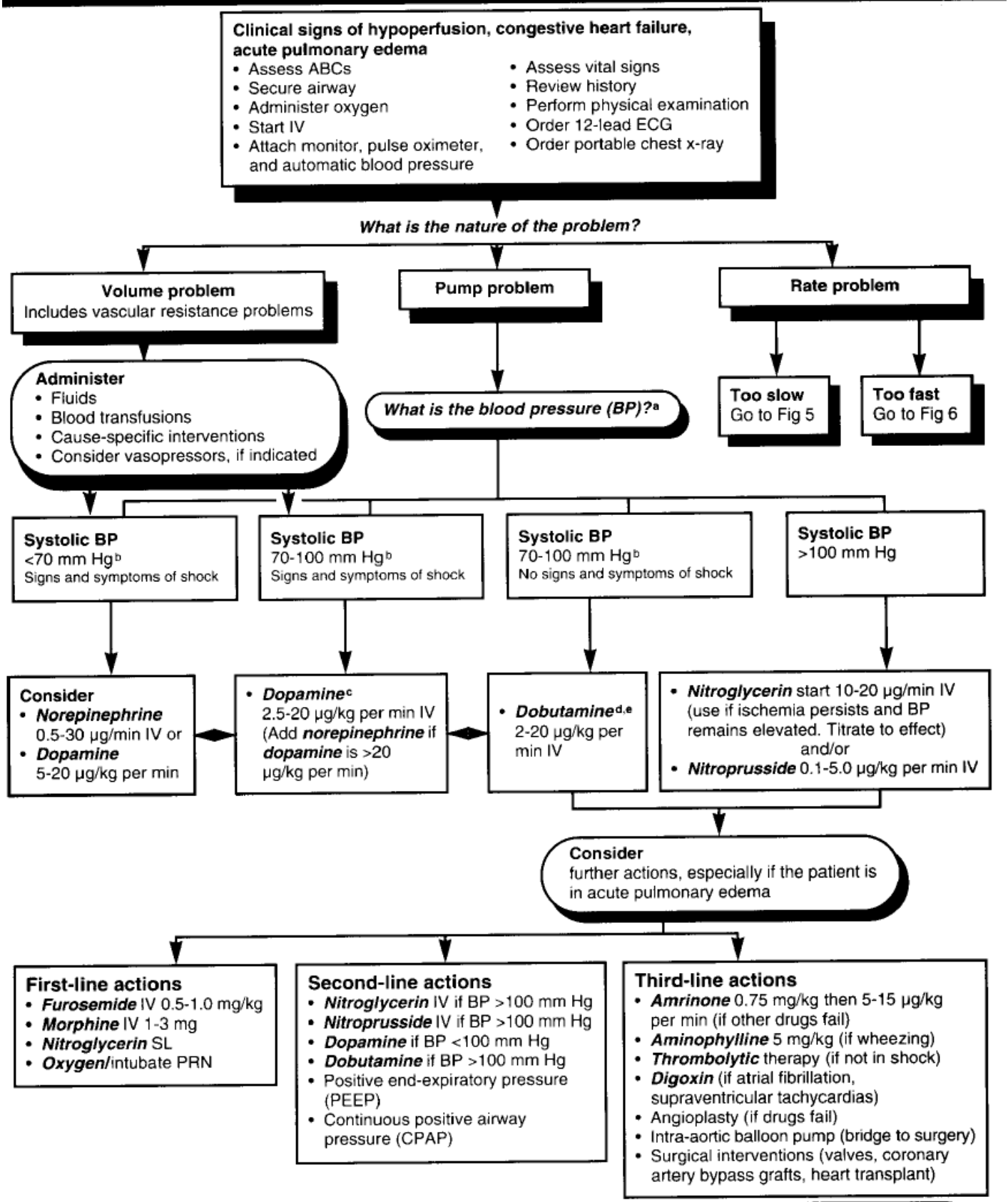
b. Carotid sinus pressure is contraindicated in patients with carotid bruits; avoid ice water immersion in patients with ischemic heart disease.

c. If the wide-complex tachycardia is known with certainty to be PSVT and BP is normal/elevated, sequence can include ***verapamil.***

d. Use extreme caution with β-blockers after ***verapamil.***

Acute Pulmonary Edema/Hypotension/Shock Algorithm

Figure 8



a. Base management after this point on invasive hemodynamic monitoring if possible. Guidelines presume clinical signs of hypoperfusion.
b. Fluid bolus of 250-500 mL normal saline should be tried. If no response, consider sympathomimetics.
c. Move to ***dopamine*** and stop ***norepinephrine*** when BP improves. Avoid ***dopamine*** (consider ***dobutamine***) if no signs of hypoperfusion.
d. Add ***dopamine*** (and avoid ***dobutamine***) if systolic BP drops below 90 mm Hg.
e. Start with ***nitroglycerin*** if initial blood pressures are in this range.