Tool Book

medicina fortis

Omnia venenum sunt: nec sine venenoquicquam existit. Dosis sola facit, ut venenum non sit. Quod quecunque uspiam tandem in eam assumam, arcanum omnino in se contineant, quod pro contrario expellendo facit. Porro autem etiam notate, qualiter procedam. Quod arcanum non est, separo ab eo, quod arcnum est, & arcano ipsi definitam suam dosin assigno. Iam ergo est certum, me mea Recepta abunde saris defendisse. Hoc autem sciendum vobis est, venemum id minime esse, quod in hominis bonum vergit. Id enim saltem venenum est, quod in detrimentum

Drug Dosing and Usage Guidelines Eleventh Edition July 2013

Department of Pharmacy
Barnes-Jewish Hospital
Washington University
Medical Center
St. Louis, Missouri

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2013

About the cover

Medicina Fortis (Strong Medicines)

“In all things there is a poison, and there is nothing without poison. It depends only upon the dose whether a poison is poison or not. I separate that which does not belong to the arcanum from that which is effective as the arcanum, and I prescribe it in the right dose […] then the recipe is correctly made. That which redounds to the benefit of man is not poison; only that which is not of service to him, but which injures him is poison.”

From: Jolande Jacobi translation of selected quotations from the Paracelsus: Selected Writings, The Third Defense: Description of New Recipes. Available at the Rare Book Room, Becker Medical Library, Washington University School of Medicine. The editors would like to thank Lilla Vekerdy, Rare Book Librarian, for her assistance with the cover and its translation.

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THE TOOL BOOK

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ANTICOAG

ANTICOAGULATION THERAPY

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NATIONAL LEADERS IN MEDICINE

ACTIVATED FACTOR VIIa (rFVIIa, NOVO-SEVEN)

Barnes-Jewish Hospital Anticoagulation Subcommittee, February 2013

TABLE 1	DOSING
Indication	Dose [1]
Intracranial hemorrhage (warfarin related)	See CONSIDERATIONS below
Bleeding/surgery with hemophilia A/B, acquired factor VIII inhibitor	90 mcg/kg every 2 hours until bleeding controlled
Bleeding/surgery with congenital factor VII deficiency	15-30 mcg/kg every 4-6 hours until hemostasis achieved
Refractory Bleeding After Cardiac Surgery (non-hemophiliac patients)	Not well established; 10-70 mcg/kg [2]
Bleeding due to novel oral anticoagulants (dabigatran, rivaroxaban, apixaban)	Not proven to be effective

1 Reconstituted product must be used within 3 hours
2 May repeat dose in 2 hours if bleeding continues

CONSIDERATIONS FOR WARFARIN REVERSAL

1. CHEST, American Heart Association, and American Society of Hematology no longer routinely recommend rFVIIa for warfarin reveral
2. Dose is not well established. Doses as high as 100 mcg/kg have been utilized, but lower doses (10-20 mcg/kg) are preferred due to risk of thrombosis with higher doses
3. IV vitamin K is the mainstay treatment for warfarin reversal and should always be administered in addition to rFVIIa
4. Duration of INR correction is dose dependent, transient, and does not reflect efficacy
5. There is a risk of thrombotic complications with the use of rFVIIa. This risk may be increased with concomitant use of prothrombin complex concentrates.

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2. Freeman WD, et al. Mayo Clin Proc 2004;79:1485-500.
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4. Morgenstern, et al. AHA Guidelines for Management of Spontaneous Intracerebral Hemorrhage. Stroke 2010;41:2108-29.
5. Holbrook A, et al. Evidence-based management of anticoagulant therapy. CHEST 2012;141(2)(Suppl):e152S-e184S.
6. Rosovsky RP and Crowther MA. Hematology Am Soc Hematol Educ Program 2008;36-38.

TABLE 1	DRUGS IN THESE GUIDELINES	
Drugs	Generic	Tradename
Antiplatelet agents	Aspirin (ASA) ASA 25 + dipyridamole 200 Cilostazol Clopidogrel Prasugrel Ticagrelor Ticlopidine	Many Aggrenox Pletal Plavix Effient Brilinta Ticlid
Heparins	Enoxaparin Unfractionated heparin	Lovenox Many
Pentasaccharide	Fondaparinux	Arixtra
Vitamin K antagonist	Warfarin	Coumadin Jantoven
Direct thrombin inhibitors	Bivalirudin Argatroban Dabigatran	Angiomax Argatroban Pradaxa
Factor Xa inhibitor	Apixaban Rivaroxaban	Eliquis Xarelto

MONITORING REQUIREMENTS FOR ANTICOAGULANT THERAPY

To reduce patient harm associated with anticoagulation therapy, BJH has developed a set of requirements for the safe initiation and maintenance of therapeutic enoxaparin (Lovenox), heparin infusions, and warfarin (Coumadin). Prescribers can avoid delays in anticoagulant therapy by becoming aware of the following lab requirements:

Warfarin	Baseline: CBC, PT/INR, PTT in past 48h Maintenance: CBC and PT/INR q72h
Enoxaparin	Baseline: CBC, PT/INR, PTT, serum creatinine in past 48h Maintenance: CBC and serum creatinine q72h
Heparin infusion	Baseline: CBC, PT/INR, PTT in past 48h Maintenance: PTT q6h until therapeutic x2, then qday, CBC q72h

Adapted from BJH Organizational Policy and Procedures, Medication Management, Therapeutic Anticoagulation, http://bjhnet.carenet.org/pandp/default.aspx

TABLE 1	ATRIAL FIBRILLATION, VTE PROPHYLAXIS	
Disease	First line therapy	Alternative
Atrial fibrillation	See $CHADS_2$ score	
VTE prophylaxis	VTE risk factors for immobile and operative patients • Estrogen replacement therapy • Contraception containing estrogen • Pregnant or postpartum within 6 weeks • BMI > 25 • Previous DVT/PE • Family history of DVT/PE • Thrombophilia (congenital or acquired) • Cardiac dysfunction (heart failure, arrhythmia, MI) • Chronic lung disease • Malignancy • Inflammatory disorder (IBD, SLE, RA, etc) • Swollen legs or varicose veins • Active collagen-vascular disorder • Ischemic stroke • Acute respiratory failure • Serious infections • ICU admission • Burn greater than 20% BSA • Indwelling central venous catheter • Surgery • Trauma • Spinal cord injury • Fracture	
• No VTE risk factors	Ambulation ± ES	—
• With VTE risk factors, Non-ambulatory	• < 100 kg:UFH 5000 units sq bid or tid[1] • > 100 kg: UFH 7500 units sq tid[1]	Not considered first-line therapy at BJH: • Enoxaparin 40 mg sq q24h[2] • Fondaparinux 2.5 mg sq q24h[3]
• Trauma patients	Enoxaparin 30 mg sq q12h[2]	—
• Orthopedic patients	• Enoxaparin 30 mg sq bid[2] • Warfarin INR 1.8-2.2 (2-2.5 with additional VTE risk factors) • ≤ 50 kg: UFH 5000 units sq bid	• Rivaroxaban: See monograph for prescribing details • ASA 325 mg bid

1 Standard heparin tid times: 0600, 1300, and 2100
2 If > 100 kg and BMI ≥ 40: 40 mg sq q12h
If CrCl 10-30 ml/min: 30 mg sq q24h (can consider 40 mg sq q24h if >100 kg& BMI ≥ 40)
3 Contraindicated if weight < 50 kg or CrCl <30. Use with caution if CrCl 30-50

TABLE 2	VTE TREATMENT, ISCHEMIC STROKE, POST-MI	
Disease	First line therapy	Alternative
Post-MI	See Chest Pain or Ischemic Symptoms monograph	
VTE treatment, acute	• Enoxaparin 1 mg/kg sq q12h • Enoxaparin: See monograph for prescribing details	• IV UFH see Heparin Nomogram • or Enoxaparin 1.5 mg/kg sq q24h • Enoxaparin: See monograph for prescribing details • Rivaroxaban: See monograph for prescribing details
	For bridge therapy with enoxaparin/heparin administration **ONLY**: Initiate warfarin therapy together and continue injection for at least 5 days and until INR ≥ 2 for at least 24 hours	
Ischemic stroke	**Secondary prophylaxis**	
• Typical patient	Duration: lifelong • Clopidogrel 75 mg qday, or • ASA 25-Dipyridamole 200 mg bid	ASA 81 mg q day, or cilostazol 100 mg bid
• Cardioembolic stroke, mitral stenosis or h/o Afib	• Warfarin: INR 2-3 or, • Dabigatran: See monograph for prescribing details • Rivaroxaban: See monograph for prescribing details • ASA 81 mg qday plus clopidogrel 75 mg qday	

TABLE 3	HEART VALVE REPLACEMENT	
Disease	First line therapy	Alternative
Bioprosthetic	• Mitral: warfarin: INR 2-3 for 3 months, then change to ASA 81mg q24h • Aortic: ASA 81 mg q24h • Any with history of systemic embolism or known atrial thrombus: warfarin INR 2-3 for at least 3 months or until clot resolution documented	Warfarin INR 2-3 long-term with bioprosthetic valves and additional risk factors including atrial fibrillation, hypercoagulable state, or low ejection fraction
	Addition of ASA 81mg qday if history of atherosclerotic vascular disease without contraindications	

Mechanical	• Bileaflet or tilting disk in aortic position: warfarin INR 2-3 • All others or bileaflet or tilting disk in mitral position: warfarin INR 2.5-3.5	Warfarin: INR 2.5-3.5 for any with risk factors for thromboembolism such as atrial fibrillation, anterior apical STEMI, left atrial enlargement, hypercoagulable state, or low ejection fraction
	Addition of ASA 81mg qday if atrial fibrillation, hypercoagulable state, low ejection fraction, or history of atherosclerotic vascular disease without contraindications	

CONSIDERATIONS

1. Prolonged or lifelong therapy should be considered for all patients with unprovoked VTE (DVT and/or PE) and patients with recurrent DVT or PE.
2. Dosing of LMWH in obese patients has not been well studied. Consider anti-factor Xa level monitoring. See Therapeutic Enoxaparin monograph.
3. LMWH, FOND, and UFH should be used with caution within 24 hrs (before and after) of spinal/epidural procedures
4. ASA 75-150 mg has a similar efficacy yet lower bleeding risk than higher daily doses; in combination with clopidogrel, ASA dose < 100 mg/day has been associated with lower bleeding risk

REFERENCES

1. Tables adapted from: 9th ACCP Consensus Conference, FDA, and Chest Supplement, Feb 2012.
2. Wann LS, et al. JACC 2011;57(11).

APIXABAN (ELIQUIS)

Barnes-Jewish Hospital Anticoagulation Subcommittee, February 2013

INDICATIONS

1. FDA approved: prevention of stroke/systemic embolism in non-valvular atrial fibrillation
2. Non-FDA approved: orthopedic surgery VTE prophylaxis, extended treatment of VTE/PE

TABLE 1	**DOSING FOR ATRIAL FIBRILLATION**
Patient Characteristics	Dose
Most patients	5 mg po bid
Patients with ≥ 2 of the following: • age ≥ 80 years • body weight ≤ 60 kg • serum creatinine ≥ 1.5 mg/dL	2.5 mg po bid
Coadministration with strong dual 3A4 and P-glycoprotein inhibitors [1]	2.5 mg po bid [2]
Coadministration with strong dual 3A4 and P-glycoprotein inducers [3]	Avoid use
Creatinine clearance < 25 mL/min	Avoid use
Child Pugh class C or D	Avoid use

1 Examples: ketoconazole, itraconazole, ritonavir, clarithromycin, conivaptan
2 If already on 2.5 mg dose for age/weight/renal criteria above, avoid combination
3 Examples: rifampin, carbamazepine, phenytoin, St. John's Wort

TABLE 2	**PHARMACOKINETICS**
Parameter	Value
Time to peak therapeutic levels	3-4 hrs after dose
Half-life (steady state)	2.5 mg dose: 8 hours 5 mg dose: 12-15 hours

MONITORING

There is no way to effectively quantify the effects of apixaban. PT/INR and aPTT may be elevated due to factor Xa inhibition, but elevations may be small and are subject to a high degree of variability. Anti-Xa monitoring may be useful in the future; assays with standard apixaban calibration/controls are currently under development.

TRANSITIONING FROM WARFARIN TO APIXABAN

Discontinue warfarin and initiate apixaban once the INR falls below 2.0.

TRANSITIONING FROM APIXABAN TO WARFARIN

- Discontinue apixaban. In 12 hours, initiate dual anticoagulation therapy with a parenteral anticoagulant and warfarin bridge.
- NOTE: Apixaban affects the INR due to factor Xa inhibition, but the effects are variable. The INR will better reflect the effect of warfarin after apixaban has been stopped for at least 2 days.

TABLE 3	TRANSITIONING FROM IV/SQ ANTICOAGULANT TO APIXABAN
Anticoagulant	When to start apixaban
SQ agents (enoxaparin, etc.)	Discontinue the SQ agent. Give the first dose of apixaban when the next dose of the SQ agent would have been due
Infusions (heparin, bivalirudin etc.)	As soon as the first dose of apixaban is given, discontinue the iv infusion

TRANSITIONING FROM APIXIBAN TO IV/SQ ANTICOAGULANT
Discontinue apixaban. In 12 hours, initiate IV/SQ anticoagulant.

TABLE 4	BLEEDING AND REVERSAL
Bleeding	Discontinue apixaban and institute supportive measures (mechanical compression, surgical hemostasis, red blood cell transfusions, fresh frozen plasma, etc).
Reversal	• No reliable reversal agent has been identified. Activated charcoal is most effective in absorbing apixaban if given within 2 hours of apixaban ingestion, but some continued absorption may be observed up to 6 hours. • **Note: vitamin K, protamine, and dialysis are not effective for reversing apixaban effects**

SURGICAL MANAGEMENT
At steady state, the half-life of apixaban is approximately 12-15 hours (8 hours if 2.5 mg dose). Approximately 75% of active drug is removed from circulation in 24 hours. In patients with a high risk of bleeding or undergoing a high-risk surgery, may consider holding apixaban for 5 half-lives (~2.5-3 days).

REFERENCES
1. Eliquis [package insert]. Princeton, NJ: Bristol-Myers Squibb and Pfizer; 2012.
2. Furie KL, et al. Stroke 2012;43:3442-53.

$CHADS_2$ SCORE

Barnes-Jewish Hospital Anticoagulation Subcommittee, June 2013

TABLE 1	SCORING SYSTEM	
C	Heart failure	Patient receives one point for each of the following
H	Hypertension	
A	Advanced age (> 75 yo)	
D	Diabetes	
S	Previous ischemic stroke or transient ischemic attack	Two points

RISK OF STROKE WITH ATRIAL FIBRILLATION			
$CHADS_2$ Score	Stroke rate [1]	95% CI	Recommended therapy [2]
0	1.9	1.2-3.0	• Preferred: no therapy • Alternative: aspirin 81-325 mg qday
1 [3]	2.8	2.0-3.8	• Preferred ✓ Warfarin with INR goal 2-3, or ✓ Dabigatran CrCl >30 mL/min: 150 mg bid CrCl 15-30 mL/min: 75 mg bid • Alternative for patients that are not anticoagulation candidates for reasons other than bleeding risk: aspirin 81 mg daily + clopidogrel 75 mg daily • Alternative for patients at high risk for bleeding: aspirin 81 to 325 mg
2	4.0	3.1-5.1	
3	5.9	4.6-7.3	
4	8.5	6.3-11.1	
5	12.5	8.2-17.5	
6	18.2	10.5-27.4	

1 Expressed as rate per 100 person years
2 Therapy is lifelong unless contraindications exist
3 For patients with $CHADS_2$ score of 1, additional risk factors for stroke (female gender, vascular disease, or age 65-74) should be considered

REFERENCES

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2. You JJ, et al. Chest 2012;141(Suppl):e531S-e575S.

DABIGATRAN (PRADAXA)

Barnes-Jewish Hospital Anticoagulation Subcommittee, June 2013

INDICATIONS

1. FDA approved: prevention of stroke/systemic embolism in non-valvular atrial fibrillation
2. Non-FDA approved: treatment and prevention of venous thromboembolism

CONSIDERATIONS

Dabigatran capsules should never be opened, crushed, chewed, or given per tube. Tampering with the delivery system increases the oral bioavailability of dabigatran by up to 75% and may increase bleeding risk. The efficacy of dabigatran may be reduced with concomitant use of P-gp inducers (e.g., carbamazepine, rifampin, trazodone, St. John's Wort). Coadministration of dabigatran with any inducers should be avoided.

TABLE 1	**DOSING FOR ATRIAL FIBRILLATION**
Estimated CrCl (mL/min)	Dose
> 30	150 mg po bid [1]
15-29	75 mg po bid [2]
< 15 or hemodialysis	Not recommended

1 If estimated CrCl is 30-50 mL/min and patient is on dronedarone or ketoconazole, dose should be 75 mg po bid

2 If estimated CrCl is 15-30 mL/min and patient is on a P-gp inhibitor, dabigatran use should be avoided. Some examples of P-gp inhibitors: amiodarone, dronedarone, ketoconazole, quinidine, ranolazine, verapamil.

TABLE 2	**PHARMACOKINETICS**
Parameter	Value
Time to peak therapeutic levels	1-4 hrs after dose
Half-life (at steady state, CrCl >50)	12-17 hrs (15-34 hrs with renal impairment)

MONITORING

In general, no monitoring of anticoagulant effect is required. Activated partial thromboplastin time (aPTT) may estimate anticoagulant effect but is unreliable at higher concentrations (mild aPTT elevations may correlate with significant drug levels). Thrombin time (TT) is sensitive to very low drug concentrations and may be used to confirm if dabigatran is present in circulation.

TRANSITIONING FROM WARFARIN TO DABIGATRAN

Discontinue warfarin and initiate dabigatran once the INR falls below 2.0.

TRANSITIONING FROM DABIGATRAN TO WARFARIN

Recommendations are based on renal function. Of note, dabigatran may contribute to an elevated INR due to a lab interaction. The INR will better reflect the effect of warfarin after dabigatran has been stopped for at least 2 days.

CrCl (mL/min)	When to start warfarin
> 50	Start warfarin 3 days before discontinuing dabigatran
31-50	Start warfarin 2 days before discontinuing dabigatran
15-30	Start warfarin 1 day before discontinuing dabigatran
< 15	No recommendations

TRANSITIONING FROM IV/SQ ANTICOAGULANT TO DABIGATRAN

Anticoagulant	When to start dabigatran
SQ agents: Enoxaparin Fondaparinux	Discontinue the sq agent. Give the first dose of dabigatran ≤ 2 hrs before the next dose of the sq agent would have been due
Infusions (heparin, bivalirudin etc.)	As soon as the first dose of dabigatran is given, discontinue the iv infusion

TRANSITIONING FROM DABIGATRAN TO IV/SQ ANTICOAGULANT

CrCl (mL/min)	When to start IV/SQ anticoagulant
≥ 30	Discontinue dabigatran. Start iv infusion or give first sq dose 12 hrs after the last dose of dabigatran.
< 30	Discontinue dabigatran. Start iv infusion or give first sq dose 24 hrs after the last dose of dabigatran.

BLEEDING AND REVERSAL

Bleeding	Discontinue dabigatran and institute supportive measures (mechanical compression, surgical hemostasis, red blood cell transfusions, fresh frozen plasma, etc). In patients with normal renal function, approximately 50% of active drug is removed from circulation within 12 hrs.
Reversal	No reliable reversal agent has been identified. Hemodialysis is effective in removing ~60% of drug at 2 hrs and ~70% at 4 hrs after dosing. Activated charcoal is effective if given within 1-2 hours of dabigatran ingestion. A single 4-factor prothrombin complex concentrate (PCC) product (only 3-factor products are available in the US) was found to have no effect on dabigatran reversal in healthy males. See PCC monograph. **Note: Vitamin K is not effective for reversing dabigatran effects**

SURGICAL MANAGEMENT

	Recommended timing of discontinuation of dabigatran prior to surgery or invasive procedure	
CrCl (mL/min)	High risk of bleeding	Standard bleeding risk
> 50	2-4 days	24 hrs
30-50	4 days	At least 48 hrs
≤ 30	> 5 days	2-5 days

Surgery should be delayed in patients with high risk of bleeding if the thrombin time (TT) is elevated. Examples of high bleeding risk: cardiac surgery, neurosurgery, abdominal surgery, surgeries involving a major organ, spinal anesthesia, advanced age, co-morbidities, concomitant antiplatelet therapy.

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THERAPEUTIC ENOXAPARIN

Barnes-Jewish Hospital Anticoagulation Subcommittee, June 2013

TABLE 1	ENOXAPARIN PRODUCT FORMULATIONS		
Concentration	Syringe type	Syringe markings	Available doses
100 mg/mL	Prefilled	Non-graduated	30 mg, 40 mg
100 mg/mL	Prefilled	Graduated	60 mg, 80 mg, 100 mg
150 mg/mL	Prefilled	Graduated	120 mg, 150 mg

TABLE 2	CONSIDERATIONS
Body weight	• Use actual body weight for all patients, including pregnant women
Rounding doses	• For all ACS patients, doses should be rounded **down** to nearest 10 mg • All other patients, round dose to nearest 10 mg
Maximum doses	• For STEMI patients, the initial maximum dose should be 75 mg or 100 mg, depending on patient age (see detailed dosing for STEMI below) • Maximum doses for other indications have not been well established. There are limited data and clinical experience available for patients weighing > 150 kg or using >150 mg per dose. • Some patients (pregnant or morbidly obese) may require >150 mg per dose, but dosing should be titrated based on anti-Xa levels • For patients weighing >100kg, q 12h dosing is recommended over q24h dosing (see Table 3 below and Morbid Obesity sections below)
Renal dysfunction	• Enoxaparin is not recommended in patients with estimated CrCl <10 mL/min or requiring dialysis

TABLE 3	NON-ACS INDICATIONS	
Indication	Estimated CrCl (ml/min)	Dosing
Atrial fibrillation DVT/PE	> 30	• 1 mg/kg sq q12h • Alternative for DVT/PE: 1.5 mg/kg sq q24h • BJH lung transplant patients: 0.8 mg/kg sq q12h
	10-30	• 1 mg/kg sq q24h • BJH lung transplant patients: 0.8 mg/kg sq q24h
Periprocedural cardiac ablation at BJH	> 30	• Commonly used: 0.5 mg/kg sq q12h • Alternative: 1 mg/kg sq q12h
	10-30	• Commonly used: 0.5 mg/kg sq q24h • Alternative: 1 mg/kg sq q24h

TABLE 4	ACUTE CORONARY SYNDROMES (ACS)		
Indication	Estimated CrCl (ml/min)	Dosing Note: round **down** to nearest 10 mg for ACS	
Non ST-elevation MI (NSTEMI)	> 30	1 mg/kg sq q12h	
	10-30	1 mg/kg sq q24h	
ST-elevation MI (STEMI)	> 30	Age < 75 y	• 30 mg iv bolus x 1 • With 1 mg/kg sq q12h x 2 doses. Max of 100 mg/dose for the first two doses • Then 1 mg/kg sq q12h
		Age ≥ 75 y	• **No iv bolus** • 0.75 mg/kg sq q12h x 2 doses. Max of 75 mg/dose for the first two doses • Then 0.75 mg/kg sq q12h
	10-30	Age < 75 y	• 30 mg iv bolus x 1 • With 1 mg/kg sq x 1 • Then 1 mg/kg sq q24h
		Age ≥ 75 y	• **No iv bolus** • 1 mg/kg sq q24h

MORBID OBESITY(BMI>40 kg/m^2)

- Anticoagulation dosing in patients with morbid obesity is uncertain. A small retrospective cohort study performed in morbidly obese patients at BJH (n=26, median weight of 162 kg (range 106–243), median BMI of 49.5 kg/m^2 (range 40.1–98.1)) demonstrated that the median dose to achieve goal anti-Xa levels was 0.73 mg/kg twice daily (range 0.51–1, absolute dose range 80-150 mg). No bleeding events occurred in patients achieving goal anti-Xa levels versus 4/10 (40%) with high anti-Xa levels (p= 0.033).
- Based on this experience, consider a starting dose of 0.75 mg/kg sq q12h in patients with morbid obesity (BMI>40) and normal renal function. Regardless of starting dose, anti-Xa monitoring is recommended in this patient population.

ANTI-Xa MONITORING

- Routine monitoring of anti-Xa levels is not required/recommended for most patients
- Anti-Xa monitoring may be considered in the following situations: pregnancy, renal insufficiency, and morbid obesity (BMI > 40)
- Draw peak anti-factor Xa (anti-Xa) level 4 hours after the 4th dose

TABLE 5	PEAK THERAPEUTIC ANTI-Xa TARGETS
Q12 hour dosing regimen	0.6-1 units/mL
Once daily dosing regimens	1-2 units/mL

DOSAGE ADJUSTMENTS FOR BID REGIMEN

- **Note: no validated nomogram** for dosage of enoxaparin in adult patients exists
- Recommendations are adapted from a study performed in pediatric patients and should not replace clinical judgment

TABLE 6	**TITRATING ENOXAPARIN BY ANTI-Xa LEVELS ***	
Anti-Xa level (units/mL)	Dose titration	Next anti-Xa level
< 0.35	Increase dose by 25%	4 hours after a dose (requires at least 4 doses to reach new steady state level)
0.35 – 0.59	Increase dose by 10%	
0.6 - 1	No change	If long-term therapy, may check 4 hours after a dose every 1-2 months
1.1 – 1.5	Decrease dose by 20%	4 hours after a dose (requires at least 4 doses to reach new steady state level)
1.6-2	Decrease dose by 30%	
> 2	Hold until anti-Xa is < 0.5, then decrease dose by 40%	

* Adapted from: Monagle P, et al. Antithrombotic therapy in children. Chest 2001;119:344S-70S.

REFERENCES

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HEPARIN NOMOGRAM

Barnes-Jewish Hospital Anticoagulation Subcommittee, June 2013

WEIGHT-BASED DOSING OF UNFRACTIONATED HEPARIN (UFH)		
PTT	Bolus	Infusion Rate
< 40 sec	3000 units [1]	↑ by 3 units/kg/hr
40-50 sec	2000 units [2]	↑ by 2 units/kg/hr
51-59 sec	None	↑ by 1 units/kg/hr
60-94	None	No change
95-104 sec	None	↓ by 1 units/kg/hr
105-114 sec	Hold 30 min	↓ by 2 units/kg/hr
≥ 114 sec	Hold 1 hr	↓ by 3 units/kg/hr

[1] Acute DVT/PE: higher bolus (eg, 80 units/kg) is recommended
[2] Acute DVT/PE: a higher bolus (eg, 40 units/kg) can be used

FOR PATIENTS WITH ACUTE VENOUS THROMBOEMBOLISM

Typical bolus dose is 80 units/kg with a max dose of 6000 units. For patients with a high risk of bleeding, the bolus may be reduced or omitted. The typical starting infusion rate is 18 units/kg/hr. A lower initial rate may be used if the patient's BMI is greater than 40 kg/m^2 (14 units/kg/hr) or if the patient is at a high risk of bleeding (12 units/kg/hr).

FOR PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

Typical bolus is 60 units/kg with a max dose of 4000 units. Initial infusion rate is 12 units/kg/hr with a max initial rate of 1000 units/hr.

OTHER INDICATIONS (MECHANICAL VALVE, ATRIAL FIBRILLATION)

Typical bolus is 60 units/kg with a max dose of 6000 units. For patients with a high risk of bleeding, the bolus may be reduced or omitted. The initial infusion rate is 14 units/kg/hr. For patients with a high risk of bleeding, a lower initial infusion rate (12 units/kg/hr) can be used.

MONITORING

Baseline labs include PT/INR, PTT and CBC express within 48 hours prior to the initiation of heparin. Order PTT 6 hrs after initial heparin bolus. Thereafter, order stat PTT to be drawn 6 hrs after each rate change. Once two consecutive PTTs are therapeutic (60-94 seconds), the PTT should be monitored at least once daily and 6 hours after each rate change until a therapeutic level is achieved. Also, monitor CBC express q72 hr (until iv heparin stopped).

REFERENCES

1. Adapted from: Raschke et al. Weight-based heparin dosing nomogram compared with a "standard care" nomogram. Ann Intern Med 1993;119:874-81.
2. Hirsh et al. Chest 2008;133 (suppl):67s-968s.
3. Riney JN, et al. Ann Pharmacother 2010;44:1141-51.

HIGH-DOSE SUBCUTANEOUS HEPARIN FOR VTE

Barnes-Jewish Hospital Anticoagulation Subcommittee, June 2013

1. High-dose subcutaneous heparin is a potential therapeutic option in patients where therapeutic anticoagulation is necessary, but no other treatment options are available.
2. High-dose subcutaneous heparin is listed as an equivalent alternative treatment regimen to low-molecular weight heparin or intravenous unfractionated heparin for the treatment of venous thromboembolism by the American College of Chest Physicians.
3. Heparin vial concentrations can be a source of inpatient medication errors. As such, the availability of higher concentrations (20,000 units/mL) should be limited.
4. High concentration heparin (20,000 unit/mL) should not be stored with regular stocked medications.
5. Typical dose utilized is 250 units/kg q 12 hours (17,500 units for a 70 kg patient). Subcutaneous drug administration is generally limited to a total volume of 1 mL. If single dose significantly exceeds 20,000 units (1 mL), consider dividing total daily requirement into every 8 hour administration (166 units/kg q 8 hours).
6. Doses of this product are to be drawn up for individual use by the pharmacy department (See Pharmacy Policy and Procedures)
7. No standardized format for monitoring this product exists. See Compass order set for suggested monitoring.

REFERENCES

1. Antithrombotic Therapy for Venous Thromboembolic Disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (9th Edition). CHEST 2012; 141:e419S–e494S.
2. Comparison of fixed-dose weight-adjusted unfractionated heparin and low-molecular weight heparin for acute treatment of venous thromboembolism. JAMA. 2006;296:935-942.

HEPARIN-INDUCED THROMBOCYTOPENIA

Barnes-Jewish Hospital Anticoagulation Subcommittee, June 2013

Direct thrombin inhibitors are the drug of choice for treating patients with known or suspected heparin induced thrombocytopenia (HIT). HIT occurs within 5-10 days of initiating heparin therapy in heparin naïve patients. Any form of heparin can cause HIT including DVT prophylaxis doses and flushes used for maintaining catheter patency. HIT may occur earlier in the course of therapy if the patient has been previously exposed to heparin.

DIAGNOSTIC STUDIES

1. Platelet Factor 4/Heparin ELISA
   - Performed Monday-Friday at BJH
   - Must be received in lab by noon
   - Sensitivity >90%
   - Specificity varies based on clinical patient characteristics
   - Optical density (OD) correlates with clinical probability of HIT
     ✓ Cut-off for positive result is ~0.4 with minor day-to-day variation
     ✓ The higher the OD value, the greater the likelihood of thrombotic complications
2. Platelet Serotonin Release Assay
   - Send out lab performed Monday-Friday
   - Sensitivity >90%
   - Specificity varies based on clinical patient characteristics
   - For ELISA confirmation when clinical uncertainty exists

PREDICTING HIT USING THE FOUR T'S

	Points		
Four T's	2	1	0
Thrombocytopenia	>50% ↓ from baseline	30-50% ↓ from baseline	<30% ↓ from baseline
Timing of onset of platelet fall *	Day 5-10 or < 1 day if recent heparin exposure in past 3 months	> 10 days or < 1 day with heparin exposure in last 3 months	Prior to day 4 with no previous exposure
Thrombosis/sequelae	New thrombosis, skin necrosis, acute systemic reaction to iv heparin	Progressive/ recurrent thrombosis or suspected thrombosis	None
O**T**her causes of decreased platelets	None	Possible	Definite

* First day of heparin exposure considered Day 0
Adapted from: Warkentin TE and Greinacher A. Chest 2008;133:340s-380s.

Total Points	**Probability of HIT**
6-8	High
4-5	Intermediate
0-3	Low

FORMULARY TREATMENT OPTIONS

BIVALIRUDIN (ANGIOMAX)
- Mechanism: specific and reversible direct thrombin inhibitor of both circulating and clot-bound thrombin.
- Half-life
  - ✓ Normal renal function: 25 min
  - ✓ CrCl < 30 ml/min: 57 min
- Dosing for HIT (non-FDA approved indication)
  - ✓ Normal renal function: 0.04-0.08 mg/kg/hr
  - ✓ CrCl < 30 ml/min 0.04-0.06 mg/kg/hr
- Check PTT 2 hrs after initiation and dose change
- Target PTT 1.5-2.5 times control (~45-70 sec)
- No dosing nomogram or established dosing recommendations available; consider ~40-50% dose decrease for supratherapeutic PTTs and 20% dose increase for subtherapeutic PTTs

ARGATROBAN (ARGATROBAN)
- Mechanism: reversibly binds to the active thrombin site of free and clot-associated thrombin
- Half-life: 39-51 min and undergoes hepatic elimination
- Dosing
  - ✓ Initial: 0.5-1 mcg/kg/min
  - ✓ Hepatic insufficiency start at 0.5 mcg/kg/min
- Check PTT 2 hrs after initiation and any dose change
- Target PTT 1.5-3 times control (~45-90 sec)
- No dosing nomogram or established dosing recommendations available; consider ~40-50% dose decrease for supratherapeutic PTTs and 20% dose increase for subtherapeutic PTTs
- INR may be falsely elevated due to lab assay interference with argatroban
- Conversion to oral anticoagulant
  - ✓ Loading doses of warfarin should not be used
  - ✓ Warfarin therapy should be started at the expected daily dose
  - ✓ Patients receiving up to 2 mcg/kg/min of argatroban
    Argatroban therapy can be stopped when the combined INR on warfarin and argatroban is ≥ 4. Repeat INR measurement in 4-6 hours. If INR is below therapeutic level, argatroban therapy may be restarted. Repeat procedure daily until desired INR on warfarin alone is obtained.
  - ✓ **Patients receiving ≥ 2 mcg/kg/min of argatroban**
    Reduce dose of argatroban to 2 mcg/kg/min. Measure INR for argatroban and warfarin 4-6 hrs after dose reduction. Argatroban therapy can be stopped when the combined INR on warfarin and argatroban is ≥ 4. Repeat INR measurement in 4-6 hours. If INR is below therapeutic level, argatroban therapy may be restarted. Repeat procedure daily until desired INR on warfarin alone is obtained.

TRANSITIONING TO WARFARIN THERAPY IN PATIENTS WITH HIT
- Early initiation of therapy with warfarin during acute HIT may lead to thrombotic complications
- Do not begin warfarin until platelet count recovery has occurred (≥100-150x10^9)
- Overlap the therapy of direct thrombin inhibitor AND warfarin should occur for a minimum of 5 days and until the INR is therapeutic for at least 2 consecutive days

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PROTHROMBIN COMPLEX CONCENTRATE (PCC)

Barnes-Jewish Hospital Anticoagulation Subcommittee, February 2013

TABLE 1	PCC PRODUCTS	
Category	Tradenames	Available in the US?
3-factor PCC	**Bebulin VH** Profilnine	Yes
4-factor PCC	Octaplex Beriplex P/N Cofact Kanokad	No
Activated PCC (aPCC) [3-factor + aFVIIa]	FEIBA NF	Yes

NOTE: The only product currently stocked at BJH is the 3-factor PCC product Bebulin VH. Bebulin VH contains a small amount of heparin (< 0.15 IU heparin per IU Factor IX). Three factor products contain low/negligible amounts of factor VII compared to 4 factor products. All PCC products contain similar amounts of factors II, IX, and X

TABLE 2	BEBULIN VH DOSING
Indication	Dose (units of factor IX activity)
Minor bleeding with factor IX deficiency	25-35 units/kg
Major bleeding with factor IX deficiency	60-70 units/kg
Surgery with factor IX deficiency	Raise factor IX level to 40% to ≥ 60% on day of surgery. 1 unit/kg will generally increase factor IX level by ~0.8%
Warfarin-associated hemorrhage	See Table 3
Bleeding due to rivaroxaban	Not well established; 50 units/kg of 4-factor PCC successfully reversed prothrombin time in healthy males
Bleeding due to dabigatran, apixaban	No data to support efficacy

CONSIDERATIONS FOR WARFARIN REVERSAL

1. IV vitamin K is the mainstay treatment for warfarin reversal and should always be administered in addition to any factor concentrate or FFP
2. CHEST and AHA/ASA guidelines suggest use of 4-factor PCC agents over FFP for warfarin reversal
3. PCCs are generally better tolerated than FFP due to lower fluid volumes per dose compared to FFP (typically < 100 mL vs. ~1000 mL per dose)
4. Administration rates up to 40 mL/min have been safely utilized (Ann Hematol 2010;3099-16)

TABLE 3	DOSING FOR WARFARIN-RELATED HEMORRHAGE	
Dosing is not well-established. The following regimens have been utilized.		
Dose based solely on baseline INR	INR < 2	20 units/kg
	INR 2-4	30 units/kg
	INR >4	50 units/kg
Dose based on both baseline and target INR	**STEP 1**: convert baseline and target INR to estimated % functional prothrombin complex (%)	
	INR > 5	5%
	INR 4.0-4.9	10%
	INR 2.6-3.2	15%
	INR 2.2-2.5	20%
	INR 1.9-2.1	25%
	INR 1.7-1.8	30%
	INR 1.4-1.6	40%
	INR 1.0	100%
	STEP 2: calculate dose	
	Total units of PCC needed = (Target % - current %) * weight (kg)	

ADMINISTRATION AND STORAGE

1. Infusion rate (non-urgent indications): package labeling recommends a maximum rate of 2 mL/min; however, replacement doses have been safely given at BJH which exceed this rate (~10-15 mL/min)
2. Pharmacy prepared product must be used within 3 hours
3. Vials contain approximately 500 units per 20 mL total volume (~25 units/mL). Pharmacy may adjust ordered dose by ±10% prior to compounding to account for vial size differences

REFERENCES

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6. Erenberg ES, et al. Circulation 2011;124:1573-9.
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RIVAROXABAN (XARELTO)

Barnes-Jewish Hospital Anticoagulation Subcommittee, June 2013

INDICATIONS

1. FDA approved
   a. Prevention of stroke/systemic embolism in non-valvular atrial fibrillation
   b. Prevention of DVT/PE in patients undergoing knee or hip replacement
   c. Treatment of DVT/PE
2. Non-FDA approved
   a. Secondary prevention of cardiovascular events (in combination with low dose aspirin ± thienopyridine)

      Note: Rivaroxaban was found to increase bleeding risk versus enoxaparin 40 mg once daily for the prevention of DVT/PE in patients hospitalized for acute medical illness and is not recommended for this indication.

CONSIDERATIONS

1. Avoid the use of rivaroxaban in patients with moderate to severe hepatic function (Child-Pugh B,C) or any hepatic disease associated with coagulopathy.
2. Avoid concomitant administration of rivaroxaban with combined P-gp and strong CYP3A4 inhibitors (i.e. ketoconazole, itraconazole, boosted lopinavir, ritonavir, boosted indinavir, and conivaptan) or inducers (i.e. carbamazepine, phenytoin, rifampin, St. John's Wort).
3. In tables below, IHD is intermittent hemodialysis

TABLE 1	ATRIAL FIBRILLATION
Estimated CrCl (mL/min)	Dose
> 50	20 mg po qday with evening meal
15-50	15 mg po qday with evening meal [1]
< 15 or IHD	Not recommended

1 Use rivaroxaban cautiously in patients with CrCL 15-50 mL/min who are receiving concomitant combined P-gp and weak or moderate CYP3A4 inhibitors (examples: amiodarone, diltiazem, verapamil, quinidine, ranolazine, dronedarone, felodipine, erythromycin, azithromycin). These interactions increase rivaroxaban exposure and may increase bleeding risk.

TABLE 2	DVT PROPHYLAXIS: KNEE/HIP REPLACEMENT
Estimated CrCl (mL/min)	Dose
>30	10 mg po qday with or without food
< 30 or IHD	Not recommended

TABLE 3	TREATMENT: DVT AND PE
Estimated CrCl (mL/min)	Dose
>30	15 mg twice daily with food for 3 weeks followed by 20 mg once daily with food.
< 30 or IHD	Not recommended

TABLE 4	PHARMACOKINETICS
Parameter	Value
Time to peak therapeutic level	2-4 hrs after dose
Half-life (at steady state, CrCl > 50)	5-9 hrs (11-13 hrs if age > 65 yrs)

MONITORING

There is no way to effectively quantify the anticoagulant effects of rivaroxaban. PTT and PT/INR may be elevated, but drug effects on these labs are transient and highly variable. In the future, anti-Xa monitoring may prove useful; assays with standard rivaroxaban calibration/controls are currently under development.

TRANSITIONING FROM WARFARIN TO RIVAROXABAN

Discontinue warfarin and initiate rivaroxaban once the INR falls below 3.0.

TRANSITIONING FROM RIVAROXABAN TO WARFARIN

- Discontinue rivaroxaban
- 24 hours after the final rivaroxaban dose, initiate warfarin **and** a parenteral anticoagulant (i.e. heparin infusion, enoxaparin)
- Of note, rivaroxaban may elevate the INR. The INR will better reflect the true effect of warfarin after rivaroxaban has been stopped for 1-2 days.

TABLE 5	TRANSITIONING FROM IV/SQ ANTICOAGULANT TO RIVAROXABAN
Anticoagulant	When to start rivaroxaban
Subcutaneous agents ✓ Enoxaparin ✓ Fondaparinux	• Discontinue the subcutaneous agent • Give the first dose of rivaroxaban ≤ 2 hrs before the next dose of the subcutaneous agent would have been due.
Infusions ✓ Heparin ✓ Bivalirudin, etc.	As soon as the first dose of rivaroxaban is given, discontinue the iv infusion

TRANSITIONING FROM RIVAROXABAN TO IV/SQ ANTICOAGULANT

- Discontinue rivaroxaban
- 24 hours after the final rivaroxaban dose, initiate the iv/subcutaneous anticoagulant

TABLE 5	BLEEDING AND REVERSAL
Anticoagulant	When to start rivaroxaban
Bleeding	• Discontinue rivaroxaban • Then institute supportive measures (mechanical compression, surgical hemostasis, red blood cell transfusions, fresh frozen plasma, etc).
Reversal	• A single four-factor prothrombin complex concentrate (PCC) product (only three-factor products are available in the US) has been shown to reduce/reverse rivaroxaban effects in healthy males. See PCC monograph for additional details. • **Note: vitamin K, protamine, and dialysis are not effective for reversing rivaroxaban effects**

SURGICAL MANAGEMENT

1. Rivaroxaban should be stopped at least 24 hours before a procedure when possible. In patients < 65 years of age with normal renal function (CrCl >50 ml/min), approximately 75% of active drug is removed from circulation in 24 hours.
2. If a patient is at high risk of bleeding and the goal is minimal or no residual anticoagulant effect, hold rivaroxaban for at least 48 hours (≥ 5 half-lives) prior to the procedure.
3. If age >65 and/or renal dysfunction, consider holding for a longer period of time.

REFERENCES

1. Cohen AT, et al. J Thromb Thrombolysis 2011;31:407-16.
2. Eerenberg ES, et al. Circulation 2011;124:1573-9.
3. Douketis JD. Curr Pharm Des 2010;16:3436-41.
4. Xarelto® [package insert]. Titusville, NJ: Bayer; 2011.

WARFARIN

Barnes-Jewish Hospital Anticoagulation Subcommittee, June 2013

TRADE NAMES

1. Coumadin
2. Jantoven

MECHANISM OF ACTION

Depletes functional vitamin K reserves by inhibition of the vitamin K epoxide reductase complex 1 (VKORC1). Inhibition results in reduced hepatic synthesis of vitamin K dependent clotting factors II, VII, IX, and X, as well as Proteins C and S.

TABLE 1 **CLOTTING FACTOR KINETICS**

Factor	II	VII	IX	X	Protein C	Protein S
Half-life (hours)	96	5-6	24	30-50	8-10	42-60

TABLE 2 **WARFARIN KINETICS AND DYNAMICS**

Onset of action	24-72 hrs
Peak effect	INR may increase in 36-72 hrs but full effect in 5-7 days
Duration of action	2-5 days
Half-life	20-60 hrs (highly variable among individuals)

TABLE 3 **WARFARIN DOSING**

Setting	Comments
Initiating warfarin	Dosing must be individualized
Typical starting dose →	• Warfarin 3-5 mg qday x 1-2 days • Then adjust dose based on INR results and desired target INR
Consider lower initial dose →	• Hepatic impairment, including obstructive jaundice, hepatitis, cirrhosis • Malnourished • Congestive heart failure • Elderly • Hyperthyroidism (active, untreated) • Concomitant use of medications known to significantly increase warfarin effects ✓ Amiodarone ✓ Azole antifungals ✓ Fluoroquinolones ✓ Metronidazole ✓ Trimethoprim/sulfamethoxazole
Consider higher initial dose →	• Young and otherwise healthy patients • Concomitant use of medications known to significantly decrease warfarin effects ✓ Carbamazepine ✓ Phenytoin ✓ Rifampin ✓ Ritonavir

TABLE 4	OTHER CONSIDERATIONS
Setting	Comments
Bridge therapy for DVT/PE	• Initiate warfarin on day 1-2 of heparin/low molecular weight heparin therapy • Continue both therapies for at least 5 days and until the INR is ≥ 2.0 for at least 24 hrs
Warfarin for treatment of HIT	See Heparin-Induced Thrombocytopenia monograph

TABLE 5	DRUG INTERACTIONS	
Common drugs known to **INCREASE** effect of warfarin	**Analgesics** Acetaminophen* Aspirin COX-2 Inhibitors NSAIDs **Antiarrhythmics** Amiodarone QuiniDINE **Anti-Hypertensives** Irbesartan Losartan NiCARdipine **Anti-infectives** Atazanavir Azole antifungals Cephalosporins Efavirenz Fluoroquinolones Macrolides Metronidazole Trimethoprim/sulfamethoxazole	**Cholesterol-lowering Drugs** Fenofibrate Fluvastatin Gemfibrozil Lovastatin Rosuvastatin Simvastatin **Miscellaneous** Anti-neoplastics Azathioprine Cimetidine Lansoprazole Levothyroxine Omeprazole Ranitidine Steroids Tamoxifen (contraindicated)
Common drugs known to **DECREASE** effect of warfarin	**Antiepileptics** Carbamazepine Phenobarbital Phenytoin	**Anti-infectives** Rifampin Ritonavir

* >1.3 grams acetaminophen/day for > 1 week

TABLE 6 **DIETARY / HERBAL INTERACTIONS**

May **INCREASE** warfarin effects	May **DECREASE** warfarin effects
Acute ethanol ingestion Cranberry Garlic Ginger Ginkgo biloba Glucosamine Green tea Omega-3 fatty acids Vitamin E (>800 units/day)	Chronic ethanol ingestion Coenzyme Q-10 Ginseng Vitamin K St. John's Wort

REFERENCES

1. Coumadin [package insert]. Princeton, NJ: Bristol-Myers Squibb;2011.
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HEMORR$_2$HAGES SCORE

Barnes-Jewish Hospital Anticoagulation Subcommittee, June 2013

Major bleeding rate in patients prescribed warfarin, stratified by HEMORR$_2$HAGES score:

HEMORR$_2$HAGES score *	Bleeding rate per 100 pt years warfarin (95 % CI)
0	1.9 (0.6-4.4)
1	2.5 1.3-4.3)
2	5.3 (3.4-8.1)
3	8.4 (4.9-13.6)
4	10.4 5.1-18.9)
≥5	12.3 (5.8-23.1)

* HEMORR$_2$HAGES is scored by adding 1 point for each bleeding risk factor, except a prior major bleed, which counts 2 points:

H	Hepatic or renal disease	Albumin < 3.6 g/dL, CrCl < 30 ml/min
E	Ethanol abuse	
M	Malignancy	
O	Older age	Age > 75 yrs
R	Reduced platelets or function	Platelets < 75K, concomitant ASA therapy
R	Rebleeding	2 points for prior major bleed, 1 point otherwise
H	Hypertension	SBP ≥ 160
A	Anemia	Hematocrit < 30
G	Genetic factors	
E	Excessive fall risk	
S	Stroke	

Adapted from: Gage BF, Yan Y, Milligan PE, Waterman AD, Culverhouse R, Rich MW, et al. Clinical classification schemes for predicting hemorrhage. Am Heart J. 2006;151:713-9.

WARFARIN REVERSAL

Barnes-Jewish Hospital Anticoagulation Subcommittee, June 2013

TREATMENT OF INR >4.5 OR WARFARIN INDUCED BLEEDING

Any INR < 4.5	**If NO risk factors** for bleeding exist, lower or hold next dose and monitor frequently; when INR approaches desired range, resume dosing with a lower dose
	If rapid reversal is required for surgery, give vitamin K orally 2.5 mg and hold warfarin. Expect INR to be reduced within 24 hrs; if INR is still elevated, another 2.5 mg of vitamin K orally may be given.
If 4.5 > INR < 9	**If NO risk factors** for bleeding exist, omit next one or two doses, monitor INR more frequently, and resume with an adjusted dose when INR is in desired range.
	If risk factors for bleeding exist, omit next dose and give vitamin K orally 2.5 mg; resume with an adjusted dose when INR is in desired range.
	If rapid reversal is required for surgery, give vitamin K orally 5 mg and hold warfarin. Expect INR to be reduced within 24 hrs; if INR is still elevated, another 2.5 mg of vitamin K orally may be given.
If INR > 9	Hold warfarin, give vitamin K orally 2.5-5 mg, expect INR to be reduced within 24-48 hrs, monitor INR more frequently and give additional vitamin K if necessary. Resume warfarin at an adjusted dose when INR is in desired range.
Serious or life-threatening bleeding at any INR	Hold warfarin, give FFP, PCC or rFVIIa supplemented with vitamin K 5-10 mg slow iv infusion; repeat if necessary, depending on INR. IV vitamin K may be repeated every 12 hrs.

1. Vitamin K is NOT recommended if:
   - INR < 4.5 and no active bleeding
   - INR < 4.5 and no surgery/procedure planned within 24 hrs
   - INR ≥ 4.5 and less than 9 and no risk factors for bleeding or falls
   - INR ≥ 4.5 and less than 9 and no surgery/procedure planned within 24 hrs

2. The subcutaneous route of Vitamin K administration is not recommended due to an unpredictable or delayed response.
3. If vitamin K IVPB is given, administer slowly to minimize anaphylactoid reaction.
4. Onset of action for oral vitamin K: 6-12 hrs, peak effect 24-48 hrs.
5. Onset of action for intravenous vitamin K: 1-2 hrs, peak effect 12-14 hrs.
6. Chest guidelines suggest the use of four-factor PCC (only three-factor products are available in the US) over FFP for rapid reversal of anticoagulation on the basis of small studies suggesting that PCC allows for faster correction of INR with less adverse events when compared with FFP. See PCC monograph.

REFERENCE

1. Adapted from: Holbrook A, et al. ACCP Evidence-Based Clinical Practice Guidelines. Chest. 2012;141:e152S-e184S
2. Ansell J, et al. ACCP Evidence-Based Clinical Practice Guidelines. Chest. 2008;133:160S-198S.

DRUG INFO

GENERAL DRUG INFORMATION
DOSING AND TREATMENT GUIDELINES

Section Editors: Jane Portell, PharmD
Ed Casabar, PharmD, BCPS
Eli Deal, PharmD, BCPS
James Hollands, PharmD, BCPS
Craig McCammon, PharmD, BCPS
Stephen Schafers, PharmD, BCPS
Jerrica Shuster, PharmD, BCPS
Rachel Stratman, PharmD, BCPS
Christine Swyres, PharmD

BARNES-JEWISH Hospital BJC HealthCare | Washington University in St. Louis Physicians

NATIONAL LEADERS IN MEDICINE

DRUG INFORMATION RESOURCES

Barnes-Jewish Hospital Department of Pharmacy, June 2013

The Department of Pharmacy maintains several resources of drug information. These resources include:

DRUG INFORMATION CENTER
Room B830, North Campus
Phone: 314-454-8399
Hours: M-F 07:00-16:00

PHRED: PHARMACY RESOURCES DIRECTORY
Phred is the Pharmacy Resources Directory (intranet site), a repository for all policies, procedures, committee reports and numerous other electronic documents related to the practice of pharmacy and pharmacotherapy at Barnes-Jewish Hospital. Physicians and pharmacists may access Phred on any Washington University or BJH/BJC computer connected to the BJC LAN only. Phred is not accessible outside of the BJC LAN. The URL is as follows.

https://phred.carenet.org/Default.aspx

If you are using one of the clinical computers located on any nursing division within the hospital, the quickest way to access Phred is to click on the yellow/purple "IV Guidelines" icon located on the computer's desktop, then search using the "search Phred" links located at the top of the page.

FORMULARY, MONOGRAPHS, PATIENT EDUCATION
Pharmacy subscribes to Lexi-Comp Online, an electronic list of all formulary drugs available at any BJC facility, including Barnes-Jewish Hospital. Each drug has a comprehensive monograph. Lexi-Comp Online can be accessed only on computers connected to the BJC LAN. For non-BJC computers, contact the Drug Information Center for a username and password. The URL for Lexi-Comp Online is:

http://www.crlonline.com/crlsql/servlet/crlonline

MICROMEDEX ONLINE
Micromedex is an online service which contains numerous drug monographs (both domestic and foreign) and information related to poison control, toxicology, iv compatibility, dosage form identification, patient teaching sheets and dosing tools. Two ways to access:

1. Via a BJC clinical computer at the following URL:
   http://www.micromedexsolutions.com/micromedex2/librarian

2. Via Compass, click on the Micromedex icon (4th from the right on main menu bar)

TOOL BOOK FOR TABLET DEVICES
A dedicated website is under construction from which the Tool Book can be downloaded in various formats (PDF, ePUB). See the "Tool Book for Tablet Devices" section.

http://bjhtoolbook.wustl.edu

SELECTED P&T COMMITTEE POLICIES

Barnes-Jewish Hospital Pharmacy and Therapeutics Committee, June 2013

Pharmacy policies and procedures can be found online at Phred, the Pharmacy Resource Directory (see previous page for URL). All BJH healthcare workers should be familiar with the following selected policies:

FORMULARY ADDITIONS

Attending physicians and housestaff may petition the Pharmacy and Therapeutics Committee (P&T) for the addition of new drugs to the formulary. A written request should include a justification for the addition (i.e., a discussion of the advantages over currently available formulary drugs). Requests should be directed to Jeff Blunt, PharmD or Jane Portell, PharmD at the Drug Information Center, 314-454-8399.

PHARMACEUTICAL SALES REPRESENTATIVES

Hospital policy limits the access that pharmaceutical sales representatives have to the medical center. Upon initial visit to BJH campus the pharmaceutical representative will be required to read and acknowledge the organization pharmaceutical representative policy via RepTrax. The pharmaceutical representative will log into RepTrax and obtain a badge with date and time of all appointments. RepTrax kiosks are available on both north and south campus. All guests accompanying the pharmaceutical representative must have a RepTrax badge. Sales representatives are not allowed in any patient care areas, nor are they allowed in house officer lounges, on-call rooms, operating room lounges or locker rooms. Representatives may not conduct business in corridors, the cafeteria, gift shop or other public areas. Sales representatives are allowed in hospital departmental offices, pharmacy offices and private physician offices. No food or beverages are to be furnished on the Barnes-Jewish Hospital campus for any hospital department, area, or any employee of Barnes- Jewish Hospital by a pharmaceutical representative or any employee of a pharmaceutical company. Promotional items (pens, notepads, clipboards, etc.) are not allowed on the BJH hospital campus.

DRUG SAMPLES

The distribution of drug samples is controlled by Pharmacy. Sales representatives should contact the Pharmacy for proper distribution of drug samples. Unauthorized distribution by pharmaceutical sales representatives of drug samples or other non-professional conduct within the institution is grounds for dismissal from the medical center.

RESTRICTED, NON-FORMULARY (RNF) DRUG STUDIES

All clinical trials of FDA-approved drugs which are restricted or non-formulary (RNF drugs) must be approved by P&T prior to WUMC Human Research Protection Office (HRPO) review. This policy applies to any inpatient or outpatient study being conducted within the confines of any BJH facility/area. Investigators must submit a study application form and various protocol materials to the respective Pharmacy committees. RNF antimicrobial studies are reviewed by the Antibiotic Utilization Review Subcommittee (AUR). All other RNF drug studies are reviewed by the Formulary Committee. Contact Jeff Blunt, PharmD or Jane Portell, PharmD at the Drug Information Center (314-454-8399) to obtain an application for RNF drug study review.

ACETAMINOPHEN OVERDOSE

Barnes-Jewish Hospital Pharmacy and Therapeutics Committee, June 2013

TOXICOLOGY CONSULT: 314-362-1242 (Central Paging)

INDICATIONS FOR IV ACETYLCYSTEINE TREATMENT (PREFERRED ROUTE)

- Patients with evidence of hepatotoxicity (elevated AST, ALT, total bilirubin, or INR) at time of presentation
- Patient with altered mental status and serum acetaminophen concentration above the Rumack-Matthew Nomogram at any time after 4 hours post-ingestion
- Nausea/vomiting refractory to standard antiemetics and/or nasogastric/duodenal tube administration
- Co-ingestion requiring continual gastric decontamination
- Gastrointestinal bleeding or obstruction
- Medical/surgical/neurological conditions precluding oral therapy
- Neonatal acetaminophen toxicity from maternal overdose
- Unknown ingestion time
- Chronic ingestion at risk for toxicity

Oral acetylcysteine therapy should only be considered for patients with uncomplicated acetaminophen overdose admitted to the Psychiatry Service. If IV administration is deemed necessary, the WU-BJH Toxicology and Hepatology Service recommend the following.

Acetylcysteine IV (Acetadote) will be prepared by Pharmacy using the standard concentration of 30 grams in D5W 1 liter (total volume). Utilization of IV acetylcysteine for acetaminophen toxicity requires either Toxicology or Hepatology approval prior to initiation. Depending on the time of presentation of the patient, empirical duration of therapy is recommended:

FOR PATIENTS PRESENTING IN < 8 HOURS AFTER INTOXICATION

- Administer 150 mg/kg/hr for the first hour, then
- 12.5 mg/kg/hr* for 20 hours, then
- If serum acetaminophen level is 0, LFTs are normal and patient is well, d/c infusion
- If laboratory values abnormal, continue infusion at 12.5 mg/kg/hr* until lab (approximate 50% decrease in transaminases from peak, INR < 2) and clinical improvement (no encephalopathy)

FOR PATIENTS PRESENTING > 8 HOURS AFTER INTOXICATION

- Administer 150 mg/kg/hr for the first hour, then
- 12.5 mg/kg/hr * for at least 36 hours
- If serum acetaminophen level is zero, LFTs are declining (approximate 50% decrease in transaminases from peak, INR < 2) and patient is well (no encephalopathy), then discontinue infusion
- If laboratory values abnormal, continue infusion at 12.5 mg/kg/hr* until lab and clinical improvement

* 12.5 mg/kg/hr is equivalent to the initial dosing (50 mg/kg over 4 hours) recommended by the manufacturer of Acetadote. BJH has safety data available supporting the above recommendations of not further decreasing the maintenance infusion dose.

ADMINISTRATION TIMES, STANDARDIZED

Barnes-Jewish Hospital Pharmacy and Therapeutics Committee, June 2013

STANDARD ADMINISTRATION TIMES FOR ALL MEDICATIONS	
Q 2 hours	Even hours
Q 3 hours	0300-0600-0900-1200-1500-1800-2100-2400
Q 4 hours	0400-0800-1200-1600-2000-2400
Q 6 hours	0200-0800-1400-2000
Q 6 hour nitrates	On: 0600-1200-2400 Off: 1800
Q 8 hours	0800-1600-2400
Q 12 hours	0900-2100
Q 24 hours	Based on first documented dose
Q day / Q am	0900
Q pm	2100
Daily quinolones	0600
Daily enoxaparin	2100
At bedtime	2200
Before meals	0700-1100-1600
With meals	0800-1200-1700
After meals	0900-1300-1800
BID	0900-2100
BID diuretics	0900-1700
BID quinolones	0600-1800
TID	0900-1300-2100
TID nitrates	0600-1100-1600 (remove drug at 2100)
TID heparin subcutaneous	0600-1300-2100
QID	0900-1300-1700-2100
5 x daily	0800-1200-1600-2000-2400

The first dose of medications will be given as soon as it is obtained (when appropriate, i.e., after culture is obtained, when iv has been started). **The next dose** will be given on the standard schedule. To determine the correct time to administer the second dose, see the guidelines below and the time grid.

Note for all medications ordered every 24 hours: administer the first dose as soon as it is obtained. Subsequent doses should be scheduled every 24 hours based on the first documented dose.

Antibiotics: administer the first dose as soon as it is obtained. Subsequent doses should be scheduled on a round-the-clock schedule based on the first dose. Antibiotic orders specifying time intervals that are not around-the-clock (e.g., bid, tid, qid, etc), should be converted automatically to fit a round-the-clock schedule (i.e., q12h, q8h, q6h, etc). The prescribing physician need not be contacted to make this conversion.

For all medications administered	Action	Examples
Before the halfway point between doses	Next dose will be started the earlier of the two times	Pepcid 20 mg IVPB Q12h. Dose given at 1500 and counted for 1200 dose. Next dose is due at 2400.
Exactly at the halfway point between doses	Next dose will be started the earlier of the two times	Pepcid 20 mg IVPB Q12h. Dose given at 1800 and counted for 1200 dose. Next dose is due at 2400.
After the halfway point between doses	Next dose will be started the later of the two times	Pepcid 20 mg IVPB Q12h. Dose given at 1900 and counted for 2400 dose. Next dose is due at 1200 the next day.

	TIME TO ADMINISTER SECOND/SUBSEQUENT DOSES		
	Standard intervals		
Time initial dose given	Q 6 Hour 02 08 14 20	Q 8 Hour 08 16 24	Q 12 Hour 09 21
0100	08 14 20 02	08 16 24	09 21
0200	08 14 20 02	08 16 24	09 21
0300	08 14 20 02	08 16 24	09 21
0400	08 14 20 02	08 16 24	21 09
0500	08 14 20 02	16 24 08	21 09
0600	14 20 02 08	16 24 08	21 09
0700	14 20 02 08	16 24 08	21 09
0800	14 20 02 08	16 24 08	21 09
0900	14 20 02 08	16 24 08	21 09
1000	14 20 02 08	16 24 08	21 09
1100	14 20 02 08	16 24 08	21 09
1200	20 02 08 14	16 24 08	21 09
1300	20 02 08 14	24 08 16	21 09
1400	20 02 08 14	24 08 16	21 09
1500	20 02 08 14	24 08 16	21 09
1600	20 02 08 14	24 08 16	09 21
1700	20 02 08 14	24 08 16	09 21
1800	02 08 14 20	24 08 16	09 21
1900	02 08 14 20	24 08 16	09 21
2000	02 08 14 20	24 08 16	09 21
2100	02 08 14 20	08 16 24	09 21
2200	02 08 14 20	08 16 24	09 21
2300	02 08 14 20	08 16 24	09 21
2400	08 14 20 02	08 16 24	09 21

ANTIDOTES

Barnes-Jewish Hospital Departments of Pharmacy and Emergency Medicine, June 2013

IMPORTANT CONTACTS

Toxicology Consult Pager	314-672-0284
BJH Drug Information Center	314-454-8399 Hours: M-F 7 am-4 pm

COMMON USED ANTIDOTES

Poisoning agent	Antidote	Dose
Acetaminophen	Acetylcysteine IV (Acetadote)	See separate Acetaminophen Overdose monograph
	Acetylcysteine po (Mucomyst)	• Loading dose: 140 mg/kg • Maintenance dose: 70 mg/kg every 4 hours for 17 doses • Each dose should be diluted to a final concentration of 5% with a diluent such as cola or orange juice to mask the taste. If patient vomits within 1 hour of dose, readminister.
	Monitoring	AST, ALT, bilirubin, PT, serum creatinine, BUN, serum glucose and electrolytes. Acetaminophen levels at ~4 hrs post-ingestion (to ensure peak levels have been obtained, ~8 hrs if extended release acetaminophen), and 4-6 hrs later to assess for possible hepatotoxicity
Benzodiazepine	Flumazenil (Romazicon)	**Reversal of conscious sedation and general anesthesia**: • Initial dose: 0.2 mg IV over 15 sec • If level of consciousness is not achieved, repeat 0.2 mg at 1 min intervals • Maximum total dose is usually 1 mg
	Monitoring	Monitor heart rate, blood pressure, respiratory rate. Observe patient for resedation, respiratory depression, pre seizure activity, or other residual benzodiazepine effects for an appropriate period (at least 2 hrs).

Poisoning agent	Antidote	Dose
Beta-blocker	Supportive care	For overdose. General supportive care is paramount (IV fluids, electrolyte management, vasopressors)
	Glucagon	3-5 mg IV push over 1 min, may repeat dose in 10 min, followed by 1-5 mg/hr up to 10 mg/hr in D5W continuous infusion. Taper as patient responds; may require 12-24 hours of therapy.
	Calcium	Give calcium chloride 1-2 g or calcium gluconate 3-5 g, may repeat in 1 hour
	Insulin with dextrose	High dose insulin 0.5-1 unit/kg IVP followed by an infusion of 0.5 unit/kg/hr. Titrate to hemodynamic effect. Dextrose infusions up to 10% should be titrated for normoglycemia. Consider consulting Toxicology.
	Intravenous lipid emulsion	20% lipid emulsion has been utilized for various beta blockers depending on their lipid solubility. Consider consulting Toxicology for further information.
	Monitoring	Serum glucose and potassium. Monitor heart rate and blood pressure to assess improvement of bradycardia and hypotension for beta-blocker/Ca channel blocker overdose.
Calcium channel blocker	Supportive care	For calcium channel blocker overdose. General supportive care is paramount (IV fluids, electrolyte management, vasopressors)
	Insulin/dextrose	High dose insulin 0.5-1 unit/kg IVP followed by an infusion of 0.5 unit/kg/hr. Titrate to hemodynamic effect. Dextrose infusions up to 10% should be titrated for normoglycemia. Consider consulting Toxicology.
	Intravenous lipid emulsion	20% lipid emulsion has been utilized for various calcium channel blockers depending on their lipid solubility. Consider consulting Toxicology for further information.
	Monitoring	Serum glucose and potassium. Monitor heart rate and blood pressure to assess improvement of bradycardia and hypotension for Ca channel blocker overdose.

Poisoning agent	Antidote	Dose
Heparin Enoxaparin	Protamine	**Heparin**: 1 mg protamine for approximately 100 units of heparin.
		Enoxaparin: 1 mg protamine neutralizes enoxaparin 1 mg..
		• The typical max protamine dose is 50 mg, regardless of the amount of heparin reversal required • Excessive doses (>100 mg) may worsen bleeding potential by acting as an anticoagulant • The infusion rate should never exceed 50 mg over 10 min. Faster infusion rates increase the risk of infusion reactions • Additional doses can be considered if aPTT remains elevated or patient is actively bleeding • The maximum total dose should be no more than 200 mg over 2 hrs
	Monitoring	Monitor for sign of bleeding, aPTT. Protamine dose required can decrease as time elapses since heparin dose.
Neuromuscular blocking agent, nondepolarizing	Edrophonium	10 mg IV over 30-45 sec; may repeat every 5-10 min up to 40 mg
	Atropine with neostigmine	• Atropine sulfate 0.6-1.2 mg IV immediately prior to minimize side effects • Neostigmine 0.5-2.5 mg over 1 min. Total dose not to exceed 5 mg
	Atropine with pyridostigmine	• Atropine sulfate 0.6-1.2 mg IV immediately prior to minimize side effects • Pyridostigmine 0.1-0.25 mg/kg/dose. 10-20 mg is usually sufficient. 5 mg doses can be pushed over 1 minute.
	Monitoring	Observe patient closely for cholinergic reactions, have atropine available

Poisoning agent	Antidote	Dose
Opiate	Naloxone (Narcan)	**Narcotic overdose**: an initial dose of 0.04 mg to 2 mg of naloxone hydrochloride may be administered intravenously. The goal is reverse apnea and slow respiratory rate (**not** to completely awaken the patient). If the desired degree of improvement in respiratory functions is not obtained, it may be repeated at 2 to 3 min intervals.
		For the initial reversal of respiratory depression: 0.04-0.2 mg IV at 2-3 min intervals to the desired degree of reversal, i.e., adequate ventilation and alertness without significant pain or discomfort. Mix naloxone 0.4 mg in 10 mL NS and administer in 0.04 mg (1 mL) dose increments. Larger than necessary doses of naloxone hydrochloride may result in significant reversal of analgesia and opioid withdrawal.
		If no response is observed after 10 mg of naloxone hydrochloride have been administered, the diagnosis of narcotic induced or partial narcotic induced toxicity should be questioned. Intramuscular or subcutaneous administration may be necessary if the intravenous route is not available.
	Monitoring	Sedation, pain control, respiratory rate, heart rate, blood pressure.

CHEST PAIN OR ISCHEMIC SYMPTOMS
INITIAL MANAGEMENT

Washington University Divisions of Cardiology and Emergency Medicine, June 2013

INITIAL MANAGEMENT

1. Criteria to obtain 12-lead ECG
   a. Current chest pain or ischemic symptoms
   b. History of prior MI or angina
   c. Prior CABG, pacer, or PCI
   d. Diabetes or hypertension

   If 12-lead computer interpretation is "Acute MI" or upon MI diagnosis, immediately call MI pager: 314-253-1579

2. Select one of the following diagnoses based on ECG and other presenting features.

Acute Myocardial Infarction (AMI)

✓ Initiate acute reperfusion protocol
✓ Call MI Pager: 314-253-1579
✓ Complete AMI orders

Ischemic symptoms and:
a. ST elevation > 1 mm in any 2 contiguous leads
b. OR new/unknown LBBB

Note: Isolated ST depression of > 2 mm in at least two precordial leads should prompt assessment of posterior leads V7, V8, V9

High Risk Acute Coronary Syndrome (ACS)

✓ Call ACS Research Pager: 314-360-0011
✓ Complete High/Intermediate Risk ACS orders in HMED

At least one of the following:
a. Known CAD or MI, age > 75
b. Accelerating pattern ischemic symptoms
c. Chest pain at rest > 20 min
d. New, transient ST changes > 0.5 mm
e. Elevated cardiac markers: Troponin >0.1
f. Exam: new murmur, S3 or rales, hemodynamic instability

Intermediate Risk ACS

✓ Call ACS Research Pager: 314-360-0011
✓ Complete High/Intermediate Risk ACS orders in HMED

No high risk features, but at least one of the following:
a. Cardiac, stroke or PVD history, age > 70 years, male, DM
b. Chest pain at rest > 20 min but now resolved
c. T wave inversions > 2 mm
d. Pathological Q waves

Low Risk ACS

✓ Complete Low Risk ACS orders in HMED

No high or intermediate risk features, but:

a. New onset angina in past 2 weeks but lasting less than 20 min
b. Atypical chest pain with one other risk factor other than DM
c. Normal or unchanged ECG during chest discomfort
d. Normal cardiac markers

3. Attach cardiac monitor, obtain vital signs, O2 at 2 L/min if SpO2 less than 90%. Start iv. Draw labs including troponin and myoglobin. Avoid unnecessary venipunctures, arterial gases, im injections or central lines

4. ASA 162 mg chewed (unless contraindicated) as soon as possible after presentation. If allergic or major GI intolerance to ASA, give clopidogrel (Plavix) 300 mg po x 1.

5. Nitroglycerin: If considering a SPECT scan (for low risk ACS only), hold nitroglycerin. Otherwise give sublingual, Nitropaste or intravenous infusion as ordered.

ACUTE MYOCARDIAL INFARCTION (AMI)

AMI with ischemic symptoms and 12-lead ECG revealing:

- ST elevation > 1 mm in any 2 contiguous leads
- Or new/unknown LBBB

Note: Isolated ST depression of > 2 mm in at least two precordial leads should prompt assessment of posterior leads V7, V8, and V9

1. **Aspirin** 162 mg chewed (unless contraindicated) as soon as possible after presentation. If allergic or major GI intolerance to ASA, give clopidogrel (Plavix) 300 mg po x1.

2. **Avoid** unnecessary venipunctures, arterial blood gases, IM injections or central lines

3. **Call MI Pager immediately 314-253-1579**

4. **Determine if patient will receive one of three initial reperfusion strategies.**

   a. **Primary PCI**
      1. Call 2-9300 to alert cath lab after calling MI Pager
      2. PCI preferred if cath lab is immediately available, fibrinolytic contraindicated, cardiogenic shock, late presentation, and age >70 years
      3. Goal time from symptom to cath lab: 60 min
      4. Goal time from arrival to balloon inflation: 90 min

   b. **Fibrinolytic: see fibrinolytic recommendations in following section**
      1. Goal time from arrival to lytic: 30 min
      2. Absolute contraindications for all fibrinolytics: previous hemorrhagic stroke at any time, other strokes or cerebrovascular events within 1 yr, known intracranial neoplasm, active internal bleeding (does not include menses), suspected aortic dissection.
      3. Cautions/relative contraindications: severe uncontrolled hypertension on presentation (BP> 180/110); history of prior CVA or known intracerebral pathology not covered in absolute contraindications; current use of anticoagulants in therapeutic doses (INR > 2-3); known bleeding diathesis; recent trauma (within 2-4 weeks) including head trauma or prolonged (>10 min) CPR or major surgery (< 3 weeks); noncompressible vascular puncture; recent (within 2-4 weeks) in-

ternal bleeding. For streptokinase: prior exposure (especially within 5 days-2 yrs) or prior allergic reaction; pregnancy; active peptic ulcer, history chronic severe hypertension.

c. **No initial reperfusion strategy (IRS)**
   1. Document reason why no IRS was selected

5. **Beta-blockers**, if eligible
   a. Oral beta blockade is preferred over iv beta blockage: metoprolol 25 mg po q6h. Hold if contraindications develop (see below)
      Caution: AVOID if pulmonary congestion or signs of early shock present, including:
      1. Signs of heart failure
      2. Evidence of low output state
      3. Increased risk for cardiogenic shock, including age >70 years, systolic blood pressure < 120 mm Hg, sinus tachycardia >110 bpm or heart rate < 60 bpm, STEMI with delayed presentation
      4. Other relative contraindications to beta blockade include PR interval > 0.24 seconds, second- or third-degree heart block, active asthma, or reactive airway disease

   b. IV beta blockade is reasonable, especially if the patient is hypertensive: metoprolol 5 mg ivp q 5 min x 3

6. IV nitroglycerin titrate to relieve ischemic symptoms or SBP < 100

7. **Recommend admit location**
   a. 8200 or another ICU
   b. Call CICU triage nurse 314-362-5096 for immediate admission

FIBRINOLYTIC THERAPY

- If fibrinolytic therapy is the choice for ST elevation MI, use one of the protocols listed below
- From arrival to drug time goal: < 30 min
- Administer **clopidogrel 300 mg po** if not at high bleed risk

1. **Tenecteplase (TNKase)**

   a. ***Preferred* population**: TNKase with enoxaparin, especially for age > 75 yo and/or late presentation (> 4 hours)

   b. **Tenecteplase dose**
      1. Single bolus dose based on patient's weight and administered over 5 seconds, NOT to exceed 50 mg.

Weight	Tenecteplase	Volume
< 60 kg	30 mg	6 mL
60-69 kg	35 mg	7 mL
70-79 kg	40 mg	8 mL
80-89 kg	45 mg	9 mL
> 90 kg	50 mg	10 mL

      2. Reconstitution with supplies provided in TNKase kit
      3. Incompatible with dextrose

c. **Antithrombin choices: choose only one regimen**
   1. Enoxaparin (Lovenox): AVOID if CrCl < 30 mL/min
      a. Age < 75 years: 30 mg iv bolus x 1 plus 1 mg/kg sq x 1, then 1 mg/kg sq q12h x 2 (MAX 100 mg/dose), then 1 mg/kg sq q12h
      b. Age ≥ 75 years: NO iv bolus. 0.75 mg/kg sq q12h x 2 (MAX 75 mg/dose), then 0.75 mg/kg sq q12h
   2. Unfractionated heparin **60 units/kg** iv bolus **(max 4,000 units)** followed by infusion at **12 units/kg/hr (initial max 1,000 units/hour)**. Maintain aPTT 60-94 seconds

2. **Reteplase**
   a. ***Preferred* population:** appropriate for patients who do not meet the criteria for tenecteplase/enoxaparin

   b. **Reteplase (Retavase or rPA)**
      1. 10 units iv bolus over 2 min
      2. Wait 30 min
      3. 10 units iv bolus over 2 min

   c. **Heparin**
      1. **60 units/kg** iv bolus (**max 4,000 units**) followed by infusion at **12 units/kg/hr** (**initial max 1,000 units/hr**)
      2. Maintain aPTT at 60-94 seconds
      3. Heparin and reteplase are incompatible when combined in solution. If reteplase is to be injected through an iv line containing heparin, flush with a minimum of 30-50 mL through the line prior to and following the reteplase injection.

AMI PAGER	**314-253-1579**
ACS RESEARCH PAGER	**314-360-0011**
CATH LAB	**314-362-9300**
CICU TRIAGE NURSE	**314-362-5096**

CHEST PAIN OR ISCHEMIC SYMPTOMS INPATIENT MANAGEMENT

Washington University Divisions of Cardiology and Emergency Medicine, June 2013

INPATIENT MANAGEMENT

1. Establish 2nd peripheral iv access

2. **Antithrombin**, choose one
   a. Unfractionated heparin **60 units/kg** iv bolus (**max 4000 units**), then iv infusion at **12 units/kg/hr** (**max 1000 units/hr**). Maintain aPTT at 60-94 seconds
      1. Preferred when immediate or early cardiac cath is planned
   b. OR enoxaparin 1 mg/kg sq q 12 hours, if NO cath planned within next 8 hours.
      1. Patients ≥ 75 years: reduce dose to 0.75 mg/kg q12h
      2. Preferred when medical management is planned
      3. Avoid if immediate or early cardiac cath is planned (within 12 hours) or if estimated CrCl < 30 mL/min.
   c. OR bivalirudin 0.1 mg/kg iv bolus, then iv infusion at 0.25 mg/kg/hr
      1. Option for patients with heparin-induced thrombocytopenia (HIT) or in patients at increased risk of bleeding

3. **Oral anti-platelet**
   a. Aspirin 162 mg chewed x 1, then 81 mg po daily. Document reason if no aspirin initiated
   b. **Choose ONE** of the following, if surgery (i.e. CABG) is not planned or is unlikely:
      1. Clopidogrel (Plavix)
         a. Loading dose
            1. 600 mg po x 1 for patients treated with an early invasive strategy primary (PCI)
            2. 300 mg po x 1 for patients with delayed PCI or if medical management is planned
         b. Maintenance dose: 75 mg po daily
            1. Note: can be dosed as 150 mg po daily for 6 days, then 75 mg po daily in post-PCI patients

      2. Ticagrelor (Brilinta) 180 mg po x 1, then 90 mg po twice daily
         a. Aspirin regimen should be 325 mg po on day 1, then 81 mg po daily
         b. CONTRAINDICATED in patients requiring > 100 mg of aspirin a day

      3. Prasugrel (Effient) 60 mg x 1, then 10 mg po daily: ONLY for patients treated with PCI
         a. Preferred for diabetic patients or patients presenting with STEMI who are treated with an invasive strategy (PCI) with no contraindications
         b. CONTRAINDICATED if patient has a history of stroke (ischemic or hemorrhagic) or TIA
         c. NOT RECOMMENDED in patients > 75 years of age, patients weighing < 60 kg, or patients requiring oral anticoagulant therapy (i.e. warfarin or dabigatran)

4. **Glycoprotein IIb/IIIa Inhibitor**, **CHOOSE ONE**
   NOTE: glycoprotein receptor antagonists are typically reserved for patients who have ongoing ischemic symptoms (e.g. ongoing chest pain, rising cardiac biomarkers) despite optimal medical management, including dual oral antiplatelet therapy.

   a. Eptifibatide (Integrilin) 180 mcg/kg iv bolus (max 22.6 mg for a patient weighing 125 kg), followed by iv infusion
      1. For CrCl ≥ 50 mL/min
         a. Weight ≤ 125 kg: 2 mcg/kg/min
         b. Weight > 125 kg: 15 mg/hr
      2. For CrCl < 50 mL/min
         a. Weight ≤ 125 kg: 1 mcg/kg/min
         b. Weight > 125 kg: 7.5 mg/hr
      3. CONTRAINDICATED if patient is on hemodialysis
      4. See IV Infusion Guide monograph
      5. *Preferred* if medical management planned

   b. OR tirofiban (Aggrastat) 0.4 mcg/kg/min for 30 min (concentration is 50 mcg/mL) iv then continue at 0.1 mcg/kg/min.
      1. Reduce bolus and infusion to half-dose for patients with CrCl < 30 mL/min.
      2. Consider for diabetic and female patients
      3. Preferred if medical management planned
      4. CONTRAINDICATED if patient is on hemodialysis
      5. See IV Infusion Guide monograph

5. **Beta-blockers**, if not on pre-admission beta-blocker
   a. Metoprolol 25 mg po q6h. Hold if contraindications develop, including:
      1. Signs of heart failure
      2. Evidence of low output state
      3. Increased risk for cardiogenic shock, including age >70 years, systolic blood pressure < 120 mm Hg, sinus tachycardia >110 bpm or heart rate < 60 bpm, STEMI with delayed presentation
      4. Other relative contraindications to beta blockade include PR interval > 0.24 seconds, second- or third-degree heart block, active asthma, or reactive airway disease
   b. Document reason if no beta-blocker initiated

6. **ACE inhibitor or angiotensin receptor blocker**, if SBP > 100 mm Hg and patient not on ACE-I or ARB begin:
   a. Captopril 6.25 mg po q6h
      1. Check BP q1hr x 3 after each dose
      2. Advance dose by 6.25 mg if SBP > 85 (max 50 mg)
      3. Document reason if no ACE-I/ARB initiated

7. **Aldosterone blockade**, for patients already on therapeutic doses of ACE-I/ARB, LVEF ≤ 0.40 and symptomatic heart failure or diabetes mellitus
   a. Contraindications: CrCl < 30 mL/min, Cr ≥ 2.5 mg/dL in men or Cr ≥ 2.0 mg/dL in women, or hyperkalemia (K+ ≥ 5.0 mEq/L)
      1. Eplerenone (Inspra) 25 mg/day OR
      2. Spironolactone (Aldactone) 12.5 - 25 mg/day
      3. Hold for SBP < 100 mm Hg
   b. Document reason if no aldosterone blocker initiated

8. **Nitrates** for angina/BP control
   a. Nitroglycerin (SL) 0.4 mg for active chest pain (hold if SBP <100). If pain persists, repeat every 5 minutes x 2 OR
   b. Nitroglycerin drip at 10 mcg/min. Titrate in 10 mcg/min increments to relieve ischemic symptoms or maintain SBP > 100 mm Hg OR
   c. Nitroglycerin paste (Nitropaste) ½ inch to chest wall three times a day. May increase by ½ inch increments to relieve ischemic symptoms. Remove paste for 8 hrs daily.

9. **Statin**, target dose to LDL < 70 mg/dL
   a. Lipid panel within 24 hrs of admission
   b. Document reason if no statin initiated
   c. See Hyperlipidemia monograph

CHILD-PUGH SCORE : HEPATIC DOSE ADJUSTMENTS

Barnes-Jewish Hospital Drug Information Center, June 2013

CHILD-PUGH SCORE	
Total Serum Bilirubin	Points
< 2 mg/dL	1
2 to 3 mg/dL	2
> 3 mg/dL	3
Serum Albumin	
> 3.5 g/dL	1
2.8 to 3.5 g/dL	2
< 2.8 g/dL	3
INR	
< 1.70	1
1.71 to 2.20	2
> 2.20	3
Ascites	
No ascites	1
Ascites controlled medically	2
Ascites poorly controlled	3
Encephalopathy	
No encephalopathy	1
Encephalopathy controlled medically	2
Encephalopathy poorly controlled	3

CHILD-PUGH CLASS	POINTS	COMMENTS
A	5-6	Life expectancy: 15-20 years Abdominal surgery peri-operative mortality: 10%
B	7-9	Indication for liver transplant evaluation Abdominal surgery peri-operative mortality: 30%
C	10-15	Life expectancy: 1-3 years Abdominal surgery peri-operative mortality: 82%

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5. FDA Hepatic Impairment Working Group
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CORTICOSTEROID CONVERSIONS

Barnes-Jewish Hospital Drug Information Center, June 2013

Glucocorticoid	Approximate Equivalent Dose (mg)	Relative Anti-inflammatory Potency	Relative Mineralocorticoid Potency	Pregnancy Category
Short-Acting				
Cortisone	25	0.8	2	D
Hydrocortisone	20	1	2	C
Intermediate-Acting				
MethylPREDNISolone	4	5	0	C
PrednisoLONE	5	4	1	B
PrediSONE	5	4	1	B
Triamcinolone	4	5	0	C
Long-Acting				
Betamethasone	0.6-0.75	25	0	C
Dexamethasone	0.75	25-30	0	C
Mineralocorticoids				
Fludrocortisone	-	10	125	C

ALARIS PUMP PROGRAMMING	Emergency drugs can be accessed on Alaris iv pumps using the non-critical care profile under **ZZZ drugs**

TABLE 1	**EMERGENCY DRUGS**	
Drug	Location	Concentration
Alteplase for pulmonary embolism (PE)	Contact Pharmacy if medication required	100 mg/100 mL (or 50 mg/50 mL)=1 mg/mL
	• Usual dose: 100 mg over 2 hrs (rarely 50 mg over 2 hrs for patients < 60 kg or at risk for bleeding) • Caution: increased bleeding risk with this medication. Follow recommendations of care in Compass.	
Adenosine (Adenocard)	Crash Cart, Drawer 1	6 mg/2 mL=3 mg/mL
	• Usual dose: 6 mg rapid iv bolus followed by 20 mL of NS flush • Caution: initial dose is 3 mg when given via central line	
Amiodarone (Cordarone)	• Crash Cart (Drawer 1 or 2, by indication) • Contact Pharmacy if continuous infusion needed	Concentrations by indications below
	• **Pulseless VT/VF (Drawer 1)** 300 mg/20 mL total volume in NS/D5W ivp, if pulseless VT/VF persists or recurs, consider additional 150 mg/10 mL total volume in NS/D5W in 3-5 min • **Patients with pulse (Drawer 2)** 150 mg/100 mL D5W over 10 min • **Maintenance standard admixture** 450 mg/250 mL D5W=1.8 mg/mL • **Maintenance dose** 1 mg/min for 6 hrs, then 0.5 mg/min thereafter	
Atropine	Crash Cart, Drawer 1 as prefilled syringes	1 mg/10 mL=0.1 mg/mL
	• Usual dose 0.5 to 1 mg iv every 3 to 5 min up to a total dose of 3 mg	
Calcium chloride (CaCl)	Crash Cart, Drawer 1 as prefilled syringes	1 g/10 mL= 100 mg/mL
	• Usual dose: 500 to 1000 mg (5 to 10 mL) iv over 5 min	

Drug	Location	Concentration
Dextrose and regular insulin for hyperkalemia	• Dextrose 50% in Crash Cart, Drawer 1 as prefilled syringes • Regular insulin in Pyxis	—
	To be administered concurrently • Dextrose 50%: 25-50 grams ivp • Regular insulin: 10-20 units ivp • See Insulin, Subcutaneous monograph	
DiphenhydrAMINE (Benadryl)	Crash Cart, Drawer 1	50 mg/mL
	Usual dose: 25-50 mg slow iv push	
DOBUTamine (Dobutrex)	• ICU Pyxis only • Contact Pharmacy if continuous infusion needed	500 mg/100 mL NS = 5000 mcg/mL
	• Drip rate (drip only, no bolus): usually starting at 3 mcg/kg/min	
DOPamine (Intropin)	Crash Cart, Drawer 2 as premixed bag	• 400 mg/250 mL = 1600 mcg/mL (premixed) • Diluent: NS, D5W
	• Drip rate (drip only, no bolus): usually starting at 3 mcg/kg/min	
EPINEPHrine	• **Usual dose**: Crash Cart, Drawer 1 as prefilled syringe • **High dose**: crash cart drawer 1 as vial • **EpiPen for anaphylaxis**: crash cart, drawer 2	• EpiPen 1:1000=1 mg/mL • Continuous infusion: 2 mg/100 mL = 20 mcg/mL
	• **Cardiac arrest (iv push)** Usual dose: 1 mg q3-5 min High dose: 3 mg x 1, then 5 mg q3-5 min • **Pressor support (continuous iv infusion)** Diluent: NS Initial rate: 1 mcg/min, titrate to desired hemodynamic response (2-20 mcg/min) • **Anaphylaxis (subcutaneous or im)** 0.3 mg injected in the thigh (0.3 mL of 1:1000 or 1 mg/mL solution as EpiPen). EpiPen located in Crash Cart, Drawer 2.	
Flumazenil (Romazicon)	Crash Cart, Drawer 1	1 mg/10 mL=0.1 mg/mL
	• Usual dose: 0.2 mg iv over 15 sec, repeat at 2 min intervals until response • Usual total dose is 1 mg or less except in benzodiazepine overdose ingestions where higher doses may be required	

Drug	Location	Concentration
Fosphenytoin (Cerebyx)	Pyxis refrigerator	• Vials 500 mg PE/10 mL =50 mg PE/mL • IV dose is diluted with equal volume of NS for final concentration of 25 mg PE/mL • Diluent: NS (preferred) or D5W
	• Doses, concentrations, etc are expressed as phenytoin equivalents (PE) • Usual loading dose: 15-20 mg PE/kg iv administered at 100-150 mg PE/min. DO NOT PUSH. May be given im if no iv available.	
Glucagon (GlucaGen) for beta-blocker overdose	Pyxis	Reconstitute 1 mg vial with 1 mL sterile water
	Bolus: 3-10 mg iv push over 1 min, may repeat dose in 10 min	
Hydrocortisone	Crash Cart, Drawer 1	100 mg/2 mL vial=50 mg/mL
	Usual dose: 50-100 mg iv	
Levophed	See norepinephrine	
Lidocaine	• Prefilled syringe: Crash Cart, Drawer 1 • Premixed bag: Crash Cart, Drawer 2	• Prefilled syringe: 100 mg/5 mL = 20 mg/mL • Premixed bag: 2000 mg/250 mL = 8 mg/mL • Diluent: D5W
	• Loading dose: 1-1.5 mg/kg iv once • Load can be followed by 0.5-0.75 mg/kg iv, maximum 3 mg/kg	
Lorazepam (Ativan)	Pyxis	2 mg/mL
	• Usual dose: 4 mg iv push ever 3-5 min • Max total dose: 0.1 mg/kg	
Magnesium sulfate	Crash Cart, Drawer 1	1 g/2 mL vial = 500 mg/mL
	• Usual dose 1-4 g • **Cardiac arrest**: dilute 2 g with at least 10 mL D5W. Can administer over 5-10 min. • **Stable patients**: dilute 2 g in 250 mL D5W. Administer over 60 min.	
Metoprolol (Lopressor)	Crash Cart, Drawer 1	5 mg/5 mL=1 mg/mL
	• Usual dose: 5 mg slow iv push at 5 min intervals up to a total dose of 15 mg	

Drug	Location	Concentration
Naloxone (Narcan)	Crash Cart, Drawer 1	0.4 mg/mL
	• Usual dose: 0.4 mg iv, repeat at 2 min intervals until desired response • Most patients respond to doses of 1.6 mg or less	
Neo-synephrine	See phenylephrine	
Nitroglycerin (Tridil) Drip only, no bolus	Pyxis	• 50 mg/250 m = 200 mcg/mL • Diluent: D5W • Special nitroglycerin bottles and bags only
	• Initial dose angina:10-20 mcg/min • Initial dose for hypertension: 25-50 mcg/min	
Norepinephrine (Levophed)	Crash Cart, Drawer 1	• 8 mg/250 mL D5W = 32 mcg/mL • Diluent: D5W (preferred) or NS
	Usual starting dose: 2-10 mcg/min	
Phenylephrine (Neo-Synephrine)	• Neo-Sticks as provided by Anesthesia or local ICU • Not available in adult crash carts or Pyxis	500 mcg/5 mL syringe = 100 mcg/mL
	• Bolus dosing from Neo-stick only • Usual dose for hypotension/shock: 100-500 mcg over 1-2 min ivp. Can repeat every 10-15 min.	
Sodium bicarbonate	Crash Cart, Drawer 1 as prefilled syringe	50 mEq in 50 mL =1 mEq/mL
	Usual dosage: 50 mEq iv over 5 min	
Vasopressin	Crash Cart, Drawer 1	• **VF/VT without pulse:** 20 units/mL • **Hypotension/shock**: 20 units/100 mL NS = 0.2 units/mL
	• **VF/VT without pulse**: usual dose 40 units ivp single dose, 1 time only. If no response with vasopressin 5-10 min after single iv dose, it is acceptable to continue EPINEPHrine ever 3-5 min. • **Hypotension/shock drip rate**: 0.04 units/min=12 mL/hr	

HYPERLIPIDEMIA

Barnes-Jewish Hospital Pharmacy and Therapeutics Committee, June 2013

TABLE 1 **LDL-C GOALS AND TREATMENT RECOMMENDATIONS**

Risk category	LDL-C goal	Initiate TLC	Consider drug therapy
High Risk: CHD [1] or CHD risk equivalent [2] 10 yr risk > 20%	< 100 mg/dL Optional goal: < 70 mg/dL [6]	≥ 100 mg/dL [8]	≥ 100 mg/dL [3] < 100 mg/dL; consider options[9]
Moderate-high risk: 2+ risk factors [3] 10 yr risk 10-20% [4]	< 130 mg/dL [7]	≥ 130 mg/dL [8]	≥ 130 mg/dL 100-129 mg/dL; consider options [10]
Moderate risk: 2+ risk factors [3] 10 yr risk < 10% [4]	< 130 mg/dL	≥ 130 mg/dL	≥ 160 mg/dL
Low risk: 0-1 risk factor [5]	< 160 mg/dL	≥ 160 mg/dL	≥ 190 mg/dL 160-189 mg/dL: LDL-lowering drug optional

1 CHD: history of MI, unstable angina, stable angina, coronary artery procedures (angioplasty, bypass); evidence of significant myocardial ischemia.

2 CHD risk equivalents: noncoronary atherosclerosis (PVD, AAA, carotid artery disease [TIA, stroke of carotid origin, >50% obstruction of carotid artery]); DM, and 2+ risk factors with 10-yr risk > 20%.

3 Risk factors: smoking; HTN (BP ≥ 140/90 or on anti-HTN drug); HDL < 40; family history (CHD in male first degree relative < 55 yo or female first degree female relative < 65 yo); age ≥ 45 yo men or ≥ 55 yo women.

4 Electronic 10-year risk calculator available at: http://hp2010.nhlbihin.net/atpiii/calculator.asp?usertype=prof

5 Almost all people with risk factor 0-1 have a 10 yr risk < 10%, and 10 yr risk assessment in this group not necessary.

6 Very high risk favors optional LDL goal < 70 mg/dL and in patients with high triglycerides, non-HDL < 100 mg/dL.

7 Optional LDL goal < 100 mg/dL.

8 Any person with moderate to high risk with lifestyle-related risk factors (obesity, physician inactivity, elevated TG, low HDL, metabolic syndrome) is candidate for therapeutic lifestyle changes (TLC) regardless of LDL level.

9 When drug therapy initiated, intensity of therapy should achieve at least 30-40% reduction in LDL.

10 If baseline LDL < 100 mg/dL, drug therapy is optional. If a high risk person has high TG or low HDL, combining a fibrate or nicotinic acid with LDL lowering drug can be considered.

11 For moderate high risk, when LDL 100-129 mg/dL, at baseline or on TLC, drug therapy to achieve LDL < 100 is optional.

12 Lowering LDL is the primary goal for most individuals, but if TG are >500 consider starting a fibric acid derivative to lower TG. If fibrates are not tolerated, niacin or fish oil can be considered as alternatives.

TABLE 2	AVERAGE % CHANGE IN LIPID LEVELS			
Drug	Daily Dose	% LDL-C Change	% TG Change	% HDL-C Change
HMG CoA reductase inhibitors				
Fluvastatin	20 mg 40 mg 80 mg	-22 -25 -36	-12 -14 -18	+3 +4 +6
Lovastatin	10 mg 20 mg 40 mg 80 mg	-21 -24 -32 -40	-10 -10 -15 -19	+5 +7 +7 +9.5
Pravastatin	10 mg 20 mg 40 mg 80 mg	-22 -32 -34 -37	-15 -11 -24 -19	+7 +2 +12 +3
Simvastatin	10 mg 20 mg 40 mg	-30 -38 -41	-15 -19 -28	+12 +8 +13
Atorvastatin	10 mg 20 mg 40 mg 80 mg	-39 -43 -50 -60	-19 -26 -29 -37	+6 +9 +6 +5
Rosuvastatin	5 mg 10 mg 20 mg 40 mg	-45 -52 -55 -63	-35 -10 -23 -28	+13 +14 +8 +10
Pitavastatin (non-formulary)	1 mg 2 mg 4 mg	-32 -36 -43	-15 -19 -18	+8 +7 +5
Bile acid sequestrants				
Cholestyramine	4-24 gram	-15 to -30	0 to +20	+3 to +5
Colestipol	7-30 gram	-15 to -30	0 to +20	+3 to +5
Colesevelam	3.7 gram 4.3 gram	-15 -18	+10 +9	+3 +3
Fibric acid derivatives				
Fenofibrate	48-200 mg	-5 to -20	-20 to -50	+10 to +35
Other				
Niacin	1.5-6 g	-5 to -25	-20 to -50	+15 to +35
Ezetimibe	10 mg	-15 to -20	-5 to -8	+1 to +4
Omega 3 acid ethyl esters	4 g	+44.5	-44.9	+9.1

Adapted from Lexi-Drugs Online: Hyperlipidemia Management, Accessed Jan 10, 2012 and NCEP Guidelines Adult Panel III

TABLE 3	COMMON INTERACTIONS WITH STATINS	
Interacting drug	Interaction	Management
Amlodipine	↑ Simvastatin	Do not exceed 20 mg/day of simvastatin
Amiodarone	↑ Lovastatin ↑ Simvastatin	Do not exceed lovastatin 40 mg/day or simvastatin 20 mg/day
Clarithromycin	↑ Lovastatin ↑ Simvastatin ↑ Pitavastatin	• Avoid use of lovastatin and simvastatin • Consider using pravastatin, rosuvastatin, or fluvastatin if clarithromycin must be used • If lovastatin or simvastatin must be used, consider azithromycin if appropriate • Use caution with pitavastatin
Cyclosporine	↑ Atorvastatin ↑ Fluvastatin ↑ Lovastatin ↑ Pitavastatin ↑ Pravastatin ↑ Rosuvastatin ↑ Simvastatin	• Simvastatin use is contraindicated • Do not exceed lovastatin 20 mg/day, atorvastatin 10 mg/day, and rosuvastatin 5 mg • Pitavastatin is contraindicated • Fluvastatin and pravastatin may be the less likely to interact with cyclosporine. Consider using a reduced dose and monitor cyclosporine levels.
Diltiazem	↑ Atorvastatin ↑ Lovastatin ↑ Simvastatin	• Do not exceed simvastatin 10 mg/day • Use low doses of lovastatin and atorvastatin • Fluvastatin, pravastatin and rosuvastatin may be less likely to interact with diltiazem.
Erythromycin	↑ Lovastatin ↑ Simvastatin ↑ Pitavastatin	• Avoid use of lovastatin and simvastatin • Consider using a reduced dose of atorvastatin • Consider using pravastatin, rosuvastatin, or fluvastatin if erythromycin must be used • Do not exceed 1 mg/day of pitavastatin • If lovastatin or simvastatin must be used, consider azithromycin if appropriate.
Fluconazole	↑ Atorvastatin ↑ Fluvastatin ↑ Lovastatin ↑ Pravastatin ↑ Rosuvastatin ↑ Simvastatin	• Use caution when prescribing fluconazole with HMG-CoA reductase inhibitors • Fluvastatin, pravastatin, and rosuvastatin may pose the least risk of drug interactions.
Itraconazole	↑ Atorvastatin ↑ Fluvastatin ↑ Lovastatin ↑ Pravastatin ↑ Rosuvastatin ↑ Simvastatin	• Avoid use of lovastatin and simvastatin • Do not exceed atorvastatin 20 mg/day • Fluvastatin, pravastatin, and rosuvastatin may pose the least risk of drug interactions.
Ketoconazole	↑ Atorvastatin ↑ Fluvastatin ↑ Lovastatin ↑ Pravastatin ↑ Rosuvastatin ↑ Simvastatin	• Avoid use of lovastatin and simvastatin • Do not exceed atorvastatin 20 mg/day • Fluvastatin, pravastatin, and rosuvastatin may pose the least risk of drug interactions.

TABLE 3	COMMON INTERACTIONS WITH STATINS	
Interacting drug	Interaction	Management
Non-nucleoside reverse transcriptase inhibitors • Efavirenz • Etravirine	↓Atorvastatin ↓Pravastatin ↓Simvastatin	• Adjust dose based on lipid response • Do not exceed maximum recommended dose
Posaconazole	↑ Atorvastatin ↑ Lovastatin ↑ Simvastatin	• Avoid use of lovastatin and simvastatin • Consider dose reduction with atorvastatin.
Protease inhibitors	↑ Atorvastatin ↑ Fluvastatin ↑ Lovastatin ↑ Rosuvastatin ↑ Simvastatin	• Avoid use of lovastatin and simvastatin • Use lowest possible dose of atorvastatin and rosuvastatin and monitor for signs and symptoms of toxicity • Use lowest possible dose of pravastatin when using in combination with darunavir.
Verapamil	↑ Atorvastatin ↑ Lovastatin ↑ Simvastatin	• Do not exceed lovastatin 40 mg/day or simvastatin 10 mg/day • Consider dose reduction with atorvastatin • Consider using pravastatin, rosuvastatin, or fluvastatin
Voriconazole	↑ Atorvastatin ↑ Fluvastatin ↑ Lovastatin ↑ Pravastatin ↑ Rosuvastatin ↑ Simvastatin	• Consider dose reduction when using atorvastatin, simvastatin, and lovastatin • Fluvastatin, pravastatin, and rosuvastatin may pose the least risk of drug interactions.

This is list of selected serious and common drug interactions with statins. Please check references for additional information .

ICU SEDATION AND PARALYSIS

Barnes-Jewish Hospital Department of Pharmacy, June 2013

GUIDELINES FOR CONTINUOUS INFUSION SEDATIVES

1. Pain management must be addressed before initiating sedation
2. Physician should specify if continuous sedation is needed. Patients who are encephalopathic, elderly, obese, or with hepatic or renal dysfunction may be better served by intermittent sedation boluses to avoid drug accumulation and unwanted prolonged sedation
3. If continuous sedation is indicated, specify the desired level of sedation (see Richmond Agitation and Sedation Scale [RASS])
4. Achieve desired level of sedation with boluses before starting infusion
5. If patient becomes agitated, first address pain and bolus analgesia. If incomplete resolution, re-bolus sedation, then make small increments in drip rate.
6. Titrate to minimum effective dose every shift
7. Reassess need for continuous sedation daily

RICHMOND AGITATION AND SEDATION SCALE (RASS)

+4	Overtly combative, violent, immediate danger to staff
+3	Pulls or removes tubes or catheters; aggressive
+2	Frequent non-purposeful movement, fights ventilator
+1	Anxious but movements not aggressive or vigorous
0	Alert and calm
–1	Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice greater than or equal to 10 seconds
–2	Briefly awakens with less than 10 seconds eye contact to voice
–3	Movement or eye opening to voice (No eye contact)
–4	No response to voice, movement or eye opening to physical stimulation
–5	No response to voice or physical stimulation

THERAPEUTIC PARALYSIS

Indication for continued neuromuscular blockade: Poor oxygenation, patient-ventilator interaction which persists despite adequate sedation, therapeutic hypothermia.

Guidelines for therapeutic paralysis

1. Adequate sedation and analgesia must be achieved before starting paralytic agent
2. Assess TOF 15 minutes after boluses or change in continuous infusion rate
3. Once satisfactory level of paralysis achieved, monitor TOF every 4 hours (usual goal is 1 out 4 twitches)
4. Paralysis should be stopped daily (4 out of 4 twitches) to ensure adequate sedation and continued need for paralysis
5. Discontinue paralysis as soon as clinically possible
6. Concurrent use of corticosteroids or aminoglycosides should be avoided due to increased risk of myopathy
7. Provide prophylactic eye care (eye moisture chamber or eye lubrication) and VTE prophylaxis.

DRUGS FOR NEUROMUSCULAR BLOCKADE

Barnes-Jewish Hospital Department of Pharmacy, June 2013

Generic name Cost index	Bolus dosing	Continuous infusion
Pancuronium $	• Dose: 0.05-0.1 mg/kg Onset (single dose): 2-4 min • Duration (single dose): 90-100 min	• Dilution: 50 mg/50 mL • Maintenance: 1-2 mcg/kg/min • Drip increment: 0.25 mcg/kg/min
	• May cause mild tachycardia • Paralytic effects prolonged in renal and hepatic failure	
Vecuronium $	• Dose: 0.05-0.1 mg/kg Onset (single dose): 2-4 min • Duration (single dose): 35-45 min	• Dilution: 50 mg/100 mL • Maintenance: 0.5-1.5 mcg/kg/min • Drip increment: 0.25 mcg/kg/min
	• Paralytic effects prolonged in renal and hepatic failure	
Atracurium $	• Dose: 0.3-0.5 mg/kg Onset (single dose): 2-3 min • Duration (single dose): 25-35 min	• Dilution: 500 mg/100 mL • Maintenance: 5-25 mcg/kg/min • Drip increment: 5 mcg/kg/min
	• Reserved for patients with renal or hepatic dysfunction in whom train of four cannot be obtained • May cause histamine release • Dose may escalate over time	
Rocuronium $	• Dose: 0.6-1 mg/kg Onset (single dose): 1-2 min • Duration (single dose): 30 min	• Dilution: 200 mg/200 mL • Maintenance: 8-12 mcg/kg/min • Drip increment: 0.8-1.2 mcg/kg/min
	• Paralytic effects prolonged in renal and hepatic failure	
Cisatracurium (nonformulary) $$$	• Dose: 0.1-0.2 mg/kg Onset (single dose): 2-3 min • Duration (single dose): 45-60 min	• Dilution: 200 mg/100 mL • Maintenance: 2-10 mcg/kg/min • Drip increment: 2 mcg/kg/min
	• Reserved for patients with renal or hepatic dysfunction in whom train of four cannot be obtained and histamine release would not be tolerated	

Cost Index:$-$$ Low Cost; $$$ Moderate Cost;>$$$ High Cost

ASSESSING NEUROMUSCULAR BLOCKADE

Assessment	Train of Four	Action
Adequate	1-2 twitches	Continue current dose and every 4 hour monitoring
Supratherapeutic	0 twitches	Discontinue neuromuscular blockage until minimum of 1 twitch, resume at ½ of infusion rate if indicated
Subtherapeutic	3-4 twitches	If patient is decompensating, repeat bolus and increase infusion rate by 25%

DRUGS FOR ICU SEDATION

Barnes-Jewish Hospital Department of Pharmacy, June 2013

Generic name (Tradename) Cost index	Bolus dosing	Continuous infusion
Fentanyl (Sublimaze) $	• Dose: 25-100 mcg max 300 mcg in 15 min • Onset (single dose): 1-2 min peak 2-5 min • Duration (single dose): 30-60 min	• Dilution: 2500 mg/50 mL • Maintenance: 50-200 mcg/hr • Drip increment: 50 mcg/hr
	• Possible bradycardia with bolus doses • Prolonged effect in renal and hepatic failure	
Morphine (Various) $	• Dose: 10-15 mg • Onset (single dose): 5-10 min peak 20 min • Duration (single dose): 3-4 hr	• Dilution: 100 mg/100 mL • Maintenance: 1-50 mg/hr • Drip increment: 2-5 mg/hr
	• Possible hypotension due to histamine release • Prolonged effect in renal and hepatic failure	
Lorazepam (Ativan) $	• Dose: 2-4 mg • Onset (single dose): 20-40 min • Duration (single dose): 3-6 hr	• Dilution: 40 mg/40 mL requires an in-line 5 micron filter • Maintenance: 0.5-4 mg/hr • Drip increment: 0.25 mg/hr
	• Prolonged effect in renal and hepatic failure • Associated with acute tubular necrosis, lactic acidosis and hyperosmolar states with prolonged infusion	

Cost Index:$-$$ Low Cost; $$$ Moderate Cost;>$$$ High Cost

Generic name (Tradename) Cost index	Bolus dosing	Continuous infusion
Midazolam (Versed) $	• Dose: 1-5 mg max 15 mg in 15 min • Onset (single dose): 1-4 min • Duration (single dose): 30-60 min	• Dilution: 50 mg/50 mL • Maintenance: 1-8 mg/hr • Drip increment: 1 mg/hr
	• Possible hypotension with bolus • Prolonged effect in renal and hepatic failure	
Propofol (Diprivan) $	• Bolus dosing not recommended • Onset (single dose): 1-2 min • Duration (single dose): 30 min	• Dilution: 1000 mg/100 mL • Maintenance: 25-50 mcg/kg/min • Drip increment: 10 mcg/kg/min
	• 10% lipid = 1.1 kcal/mL • Possible hypotension, bradycardia, hypertriglyceridemia, pancreatitis and propofol-related infusion syndrome (PRIS)	
Dexmedetomidine (Precedex) $$$$	• Bolus dosing not recommended • Onset (single dose): 10 min • Duration (single dose): 30 min	• Dilutions: 400mg/100 mL, 200 mg/50 mL • Maintenance: 0.2-1.5 mcg/kg/hr • Drip increment: 0.1 mcg/kg/hr
	• Common adverse effects include hypotension and bradycardia • Sedative and analgesic properties	
Ketamine (Ketalar) $	• Dose: 25-50 mg • Onset (single dose): 30 sec • Duration (single dose): 5-10 min	• Dilution: 5 mg/mL • Maintenance: 1-3 mg/kg/hr • Drip increment: 0.25-0.5 mg/kg/hr
	• Sedative and analgesic properties • Low dose benzodiazepine may prevent hallucinations and increased BP, HR • Transient rash may occur, but resolves spontaneously • May concentrate up to 10 mg/mL	

Cost Index:$-$$ Low Cost; $$$ Moderate Cost; >$$$ High Cost

INSULIN, SUBCUTANEOUS
USE IN HOSPITALIZED PATIENTS

Barnes-Jewish Hospital Department of Pharmacy, June 2013

MANAGEMENT OF "NON-CRITICALLY ILL" INPATIENTS WITH DIABETES OR HYPERGLYCEMIA

TARGET GLUCOSE LEVELS

Pre-meal	< 140 mg/dL
Random or post-meal	< 180 mg/dL
Safe low glucose target	90-100 mg/dL
Reevaluate and modify the insulin regimen	When < 90 mg/dL

GENERAL PRINCIPLES FOR HOSPITALIZED PATIENTS

1. Check an A1C level if one is not documented in the last 3 months to help guide therapy.
2. Discontinue oral anti-diabetic agents for most patients. Insulin is the preferred agent to control blood sugars.
3. Adherence to therapy and incidence of hypoglycemia should be assessed prior to initiating insulin therapy. **As a general rule, decrease home insulin doses by 20% to minimize hypoglycemia during hospitalization.** Further dose reductions may be indicated if the patient is non-adherent, if new organ dysfunction is present, or if hypoglycemia is experienced at home.
4. If a patient's blood sugars are poorly controlled and a patient's home dose is greater than 1 unit/kg per day, a Diabetes Consult is recommended.
5. The Standard Subcutaneous Insulin Order Set offers a comprehensive checklist for blood glucose monitoring, ordering insulin, and treatment for hypoglycemia.
6. **A physiologic basal/bolus insulin regimen is recommended as the optimal approach for insulin therapy**. Some patients may require only scheduled meal time rapid-acting insulin while others require only basal insulin; a few patients who require limited daily insulin (< 8 units/day) may require only correction insulin. **Note: correction insulin is not a substitute for a physiologic basal/bolus insulin regimen but is useful as a correction factor for patients receiving scheduled (basal/bolus) insulin.**
7. Insulin glargine (Lantus) is the BJH preferred insulin for coverage of basal insulin needs and insulin lispro (Humalog) is the preferred pre-meal/correction insulin. If insulin NPH is used for basal insulin coverage, the daily dose can be divided over two or three administration times.
8. **Patients on basal-HEAVY regimens (i.e., >0.5 Units/Kg/day of basal insulin (>0.3 Units/Kg/day of basal insulin in patients with ESRD) with no or minimal meal-time rapid acting insulin)** are at increased risk of hypoglycemia especially when eating poorly or npo. Use the weight-based dosing estimate to develop a safe and effective insulin regimen.
9. **Blood glucose trends should be assessed daily** and the insulin regimen adjusted accordingly.
10. Hospitalization offers an opportunity to optimize non-glycemic pharmacotherapy in patients with diabetes (i.e., use of aspirin, ACEI or ARB, HMG-CoA inhibitors, etc.)

COMPARISON OF INSULIN PRODUCTS

BJH formulary insulin product	Onset	Peak	Duration
Insulin glargine (Lantus)	3-4 hrs	None	11-24 hrs*
Insulin detemir (Levemir)	3-4 hrs	Relatively flat	6-23 hrs*
Insulin NPH (Humulin N)	1-3 hrs	4-8 hrs	12-14 hrs
Insulin lispro (Humalog)	5-10 min	1-2 hrs	4-6 hrs
Insulin regular (Humulin R)	30-60 min	2-3 hrs	6-8 hrs

* greater duration of action with increases in dose

PRODUCT DISTINCTIONS

1. Insulin glargine, insulin NPH, and insulin lispro are the only insulins included in the Standard Subcutaneous Insulin Order Set.
2. A formulary insulin product regimen must be used is for patients on mixed insulins (70/30, etc) at home.
3. Insulin Regular is used primarily when intravenous insulin is indicated.

DOSING DEFINITIONS

Basal insulin	Insulin provided for continuous (basal) bodily insulin requirements whether patient is eating or npo. Basal insulin is required for all type 1 diabetics and patients status post total pancreatectomy.
Pre-meal/bolus insulin	Insulin provided to reduce blood glucose elevations associated with meals.
Correction insulin	Insulin provided in preset doses in addition to scheduled basal/meal time insulin only when blood glucose levels exceed predetermined thresholds at predetermined intervals. This term is preferred over the general use of "sliding scale insulin", which has historically referred to a similar dosing regimen without a background of scheduled basal/meal time insulin.

INSULIN DOSING CONSIDERATIONS

Insulin requirements can vary greatly among patients from 0.1 unit/kg to >1 unit/kg per day. Assess patient's level of glucose control, diabetic history, home medication adherence, and concomitant disease states (renal disease, liver disease, etc) in developing an insulin treatment plan. Use conservative dosing initially and titrate dose based on patient's response.

INITIAL BASAL/BOLUS INSULIN DOSING

1. The total daily dose (TDD) of insulin (generally 50% basal & 50% pre-meal/bolus) can be estimated using patient's actual body weight in kilograms times select multipliers based on a patient's clinical features listed below:

Clinical features of patient	Dosing multiplier
Pre-meal/ bolus ONLY (no basal) for patients on low-dose oral anti- hyperglycemic agents (i.e., metformin, pioglitazone) and reasonable blood glucose (BG) control at home	0.1-0.15 units/kg
Insulin sensitive or naive, lean or malnourished, elderly, acute kidney injury, stage 4 or 5 chronic kidney disease (CKD), pancreatectomy	0.2-0.3 units/kg

Clinical features of patient	Dosing multiplier
Patients with features of insulin sensitivity	0.4 units/kg
Indicators of insulin resistance	≥ 0.5 units/kg

2. **NOTE: Clinical judgment of the individual patient is essential in developing appropriate insulin dosing. Use the weight-based suggestions only as a guide.**

3. Example: A 50 year old 100 kg ESRD patient (A1C 9.7%) is admitted with a BG level of 230 mg/dL. Patient's prescribed insulin regimen: 30 units of Lantus qAM/ 10 units of Novolog tid with meals. Given the patient's ESRD, high insulin dose (0.6 units/ kg per day), and high A1C (which may be a marker of non-adherence to his home therapy), we would be concerned about hypoglycemia with this regimen in the hospital. Estimate his total daily dose of 30 units (100 kg X 0.3 units/kg). Recommend starting patient on insulin glargine 15 units at qAM (50% of TDD) and insulin lispro 5 units with each meal (50% TDD) with a low-dose correction insulin.

CONVERTING FROM HOME INSULIN MIX 70/30 REGIMENS

70/30 mixed insulin products are not on the BJH formulary and conversion to a physiologic basal/bolus regimen is indicated. It is reasonable to start patients on 80% of their total daily home regimen as a precaution to avoid hypoglycemia in the hospital.

Example: Patient admitted on Humulin 70/30 insulin at 35 units q breakfast & 25 units q supper. Patient's total daily insulin dose is 60 units. Use 48 units as the total daily hospital dose (80% of home dose). The basal insulin dose would be one-half the daily dose (insulin glargine 24 units qday or insulin NPH 12 units qAM and qbedtime) and the insulin lispro dose would be one-half the daily dose divided over three meals (8 units with each meal). If the patient is prescribed NPH bid (9 am; 9 pm), please select a 15 g carbohydrate snack at bedtime on the standard subcutaneous insulin order set. Upon discharge the patient's home insulin regimen can be re-initiated if appropriate.

PRUDENT DIABETIC DIET

The 1800 calorie "prudent diabetic diet" is recommended for diabetic patients. This diet is designed to provide four carbohydrate (CHO) portions per meal (~60 grams of CHO total per each meal) which allows for the same insulin lispro dose to be given with each meal during hospitalization.

ASSESS NUTRITIONAL STATUS

Nutritional situation	Necessary insulin components	Preferred regimen
NPO (or clear liquids)	• Basal insulin: 40-50% of total daily dose (TDD) • Nutritional insulin: None. • Do not hold basal insulin in Type 1 patients.	Basal insulin: Insulin glargine given once daily
Eating meals	• Basal insulin: 40-50% of TDD • Nutritional insulin: 50-60% of TDD, divided equally before each meal)	• Insulin glargine given once daily • Insulin lispro, given with the first bite of each meal

Nutritional situation	Necessary insulin components	Preferred regimen
Getting bolus tube feeds	• Basal insulin: 40-50% of TDD • Nutritional insulin: 50-60% of the TDD, divided equally before each bolus feed	• Insulin glargine given once daily. • Insulin lispro given at the initiation of each bolus
Continuous tube feeds	• Basal insulin: 40% (conservative) of TDD • Nutritional insulin: 60% of the TDD (for continuous tube feeds NPH is often used instead of a rapid acting insulin).	• No regimen clearly superior. Insulin should be given to cover basal and nutritional needs. • An insulin glargine and insulin NPH regimen is commonly employed.
Parenteral nutrition	Insulin is usually given parenterally, with the nutrition	

PATIENTS ON HIGH DOSE STEROIDS

Patients with diabetes on high dose steroids may require an insulin adjustment. Dosages of prednisone in the range of 40 mg-100 mg may increase insulin requirements ~0.5 to 3 fold. These factors should be considered when dosing insulin. A Diabetes Consult is suggested to assist in optimizing therapy in these patients.

ACUTE STABILIZATION OF HYPERKALEMIA IN NON-ICU PATIENTS

An audit at BJH demonstrated that 8.7% of patients receiving ivp regular insulin with dextrose for hyperkalemia developed hypoglycemia. Two-thirds of the hypoglycemic events involved use of insulin regular 10 units ivp with 25 g (50 mL) of dextrose 50%. An acute hyperkalemia order set for non-ICU patients is now available in Compass. To minimize hypoglycemia with 10 units of insulin regular ivp, use of 50 g (100 mL) of dextrose 50% is recommended.

EXTERNAL CONTINUOUS SQ INSULIN INFUSION PUMP THERAPY

Adult patients admitted to the hospital using an external insulin pump to manage their diabetes may continue to use their pump provided:

1. The patient is alert, oriented x3, and competent to manage the pump
2. Patient does not have contraindications to use including: an altered state of consciousness/or risk for mental status changes secondary to drug therapy, risk for suicide, patient lacks any of the necessary pump supplies, pump is not working properly, or the patient has DKA.
3. Patients admitted with an insulin pump must have an Diabetes Consult (fellow pager: 424-6259). An exception exists for OB-GYN patients; notify OB-GYN resident)
4. Patients admitted with an insulin pump must be interviewed using BJH form #8-3343-2322 and the form must be completed by the RN/LPN or MD.
5. All insulin pump orders must be entered through the Compass “Insulin Pump Orders, Subcutaneous” order set.
6. The nurse will obtain and record blood glucose per MD orders using the hospital glucose meter. The patient may monitor their own blood glucose with his/her meter but those results will not be documented in the medical record. The insulin pump log is to be completed by the nurse q8h and placed in the patients chart.
7. An alternative method of insulin delivery must be used when the pump is disconnected for more than one hour (see insulin pump order set).

8. The patient will be responsible for changing the infusion set and filling the reservoir with insulin as needed.

U-500 INSULIN USE IN THE HOSPITAL

Patients admitted to the hospital receiving regular U-500 insulin at home require special attention. The infrequent use of this product along with confusion regarding this product's concentration and administration instructions can lead to errors. U-500 insulin exhibits an onset of action of 1-3 hours and a duration of action of 12-14 hours. Despite the 5-fold concentration difference between regular U-100 insulin (100 units/mL) and U-500 insulin (500 units/mL), converting doses between the two products are variable among patients with conversion factors ranging from 1.5 to 3:1.

1. Prescribers must consult the Diabetes Service before pharmacy will process an order for U-500 for a hospitalized patient. When possible the order will be converted to a U-100 insulin regimen.

2. Orders for U-500 must be entered through the "Insulin Regular U-500, concentrated" order set which will specify the insulin concentration, the dose in units of insulin, volume in mLs, and route of administration. U-500 will be prepared by the pharmacy using a tuberculin syringe with a warning message: "Warning: concentrated insulin for subcutaneous injection".

   a. Example order: 250 units of insulin regular (U-500 -500 units/mL) Administer 0.5 mL (250 units) subcutaneously at 0700 and 1800 for diabetes.

3. The Diabetes Fellow can be reached at pager: 424-6259

Primer developed by Eli Deal, PharmD, BCPS
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IV INFUSION GUIDE

Barnes-Jewish Hospital Department of Pharmacy, June 2013

Drug (tradename) Cost index *** • Dilution (concentration)	Loading dose	Initial maintenance dose
Abciximab (ReoPro) $$$$$ • **Load**: 2 mg/mL solution given undiluted • **Infusion**: 7.5 mg/250 mL NS	0.25 mg/kg over 1 min	• 0.125 mcg/kg/min for 12 hrs • Usual maximum dose for 80 kg patient: 10 mcg/min
	• Half-life: ~ 30 min • Potent antiplatelet agent with long duration (4 days), may be reversed with platelet infusion	
Amiodarone (Cordarone) $ • **Load**: 150 mg/100 mL D5W* (1.5 mg/mL) • **Maintenance**: 450 mg/250 mL D5W* (1.8 mg/mL) or 360 mg/200 mL D5W* (1.8 mg/mL)	150 mg over 10 min	• 1 mg/min x 6 hrs • Then 0.5 mg/min
	• Half-life: 40-55 days • Antiarrhythmic with negative inotropic and vasodilating properties • May decrease BP and HR	
Argatroban $$$$$$ • 250 mg/250 mL NS (1 mg/mL)	—	• Initial dose: 0.5-1 mcg/kg/min • Usual maximum dose: 10 mcg/kg/min • Hepatic impairment initial dose: 0.5 mcg/kg/min
	• Half-life, normal liver function: 39-51 min • Half-life, impaired liver function: ~181 min • No dose adjustment required for renal impairment, but dose should be adjusted for hepatic impairment • Check PTT 2 hrs after initiation and any dose change • Target PTT ~45-90 secs • INR may be falsely elevated	
Bivalirudin (Angiomax) $$$ • **HIT:** 100 mg/100 mL NS (1 mg/mL) • **ACS**/**Cath Lab**: 250 mg/50 mL NS (5 mg/mL)	• **HIT**: no loading dose • **ACS**: 0.1 mg/kg bolus • **Cath Lab**: ✓ 0.75 mg/kg bolus immediately prior to procedure ✓ 0.5 mg/kg bolus if already receiving bivalirudin infusion	• **HIT**: 0.04-0.08 mg/kg/hr ✓ Renal impairment: 0.04-0.06 mg/kg/hr ✓ Renal replacement therapy (limited data): 0.02-0.04 mg/kg/hr) • **ACS**: 0.25/kg/hr • **Cath Lab**: 1.75 mg/kg/hr
	• Half-life: 25 min (NL renal function); 57 min (CrCl < 30 mL/min); 3.5 hrs (dialysis dependent) • Dose should be reduced for renal impairment • Check PTT 2 hrs after initiation and dose change • Target PTT ~45-70 secs • No PTT monitoring required for ACS dosing	

* Only dilution/diluent dispensed ** Variable dosage range; titrate to desired effect
*** Cost Index:$-$$ Low Cost; $$$ Moderate Cost;>$$$ High Cost

Drug (tradename) Cost index *** • Dilution (concentration)	Loading dose	Initial maintenance dose
Diltiazem (Cardizem) $ • 125 mg/125 mL NS (1 mg/mL)	• 0.25 mg/kg • Followed by 0.35 mg/kg if needed	• 5-10 mg/hr • Usual maximum dose: 15 mg/hr
	• Half-life iv bolus: 3 hrs • Half-life continuous infusions:4-5 hrs • May decrease BP • IV to po conversion calculation=(iv rate x 3 +3)x10 Example: iv rate 5 mg/hr = 180 mg po per day of appropriate oral formulation	
DOBUTamine (Dobutrex) $ • 1000 mg/250 mL NS (4000 mcg/mL)	—	• 2 mcg/kg/min • Usual maximum dose: 20 mcg/kg/min
	• Half-life: 2 min • Selective inotropic (β1) effect: may increase HR, arrhythmias	
DOPamine (Intropin) $ • 400 mg/250 mL D5W (1600 mcg/mL)	—	• Dopa: 1-3 mcg/kg/min • β: 3-10 mcg/kg/min • α: 10-20 mcg/kg/min
	• Half-life: 2 min • Clinical response is dose and patient dependent • May cause arrhythmias and increase HR	
EPINEPHrine $ • 2 mg/100 mL NS (20 mcg/mL)	—	• 1-4 mcg/min ** OR • β: ≤ 0.1 mcg/kg/min • α: > 0.1 mcg/kg/min
	• Half-life: N/A • Mixed α and β effects • Potent α1, mainly β1 at doses < 0.1 mcg/kg/min • Use central line • May increase HR and BP	
Eptifibatide (Integrilin) $$$$ • 75 mg/100 mL premixed bottle (0.75 mg/mL) • **IV bolus**: 2 mg/mL 10 mL vial	• 180 mcg/kg iv bolus • Repeat in 10 min for coronary intervention	Weight (kg) / CrCl (mL/min): ≥ 50 / < 50 ≤ 125: 2 mcg/kg/min / 1 mcg/kg/min > 125: 15 mg/hr / 7.5 mg/hr
	• Half-life: 2.5 hrs • Potent antiplatelet agent with 4 hr duration • Contraindicated in patients requiring dialysis	

* Only dilution/diluent dispensed ** Variable dosage range; titrate to desired effect
*** Cost Index:$-$$ Low Cost; $$$ Moderate Cost;>$$$ High Cost

Drug (tradename) Cost index *** • Dilution (concentration)	Loading dose	Initial maintenance dose
Esmolol (Brevibloc)) • **Central line** $: 2 g/100 mL NS (20 mg/mL) • **Peripheral line** $$: 2.5 g/250 mL D5W (10 mg/mL)	500 mcg/kg over 1 min (optional)	• 50 mcg/kg/min • Usual maximum dose 300 mcg/kg/min
	• Half-life: 9 min • Selective β1 blocker • Not eliminated by hepatic or renal routes	
Isoproterenol (Isuprel) $ • 1 mg/100 mL NS (10 mcg/mL)	—	2-10 mcg/min
	• Half-life: 2.5-5 min • Stimulates β1 and β2 receptors resulting in relaxation of bronchial, GI, and uterine smooth muscle; increased heart rate and contractility; vasodilatation of peripheral vasculature	
Labetalol (Trandate) $ • 500 mg/500 mL NS (1 mg/mL)	20-40 mg iv repeat prn at 20 min intervals	• 0.5-2 mg/min • Usual maximum dose: 6-8 mg/min
	• Half-life: ~5.5 hrs • α and β blockade • May cause bronchospasm	
Lidocaine $ • 2 g/250 mL D5W * (8 mg/mL)	• 1 mg/kg • May repeat x2	1-4 mg/min
	• Initial half life: 7-30 min • Terminal half-life: 1.5-2 hrs. May be longer in patients with heart failure, liver/renal dysfunction or shock • Decrease dose in patients with hepatic failure, acute MI, heart failure or shock • Therapeutic range 1.5-5 mcg/mL • If transitioning to mexiletine, turn lidocaine off with first dose of mexiletine	
Milrinone (Primacor) $ • 20 mg/100 mL D5W (0.2 mg/mL or 200 mcg/mL)		• 0.25-0.75 mcg/kg/min • Renal dysfunction (CrCl < 50 mL/min): 0.1-0.3 mcg/kg/min
	• Half-life normal renal function: 2.5 hrs • Half-life CVVH: 20 hrs • Inotrope with vasodilating properties • Can decrease BP and cause tachycardia	

* Only dilution/diluent dispensed ** Variable dosage range; titrate to desired effect
*** Cost Index:$-$$ Low Cost; $$$ Moderate Cost;>$$$ High Cost

Drug (tradename) Cost index *** • Dilution (concentration)	Loading dose	Initial maintenance dose
Nesiritide (Natrecor) $$$$$$ • 1.5 mg/250 NS (6 mcg/mL)	2 mcg/kg	• 0.01 mcg/kg/min • Maximum dose: 0.03 mcg/kg/min
	• Initial half-life: 2 min • Terminal half-life: 18 min • Vasodilating properties, may decrease BP	
NiCARdipine (Cardene) $ • **Central line**: 25 mg/50 mL NS (0.5 mg/mL) • **Peripheral line**: 25 mg/250 mL NS (0.1 mg/mL)	—	• 5 mg/hr or 0.2-1.5 mcg/kg/min • Usual maximum dose: 15 mg/hr
	• Half-life: 2-4 hrs	
Nitroglycerin (Tridil) $ • 50 mg/250 ML D5W (200 mcg/mL)	—	• Initial dose angina: 10-20 mcg/min • Initial dose for hypertension 25-50 mcg/min
	• Half-life: 1-4 min • Use cautiously in right ventricular infarct	
Nitroprusside (Nipride) $ • 50 mg/250 mL D5W * (200 mcg/mL)	—	• 0.25-0.5 mcg/kg/min • Usual maximum dose: 10 mcg/kg/min
	• Half life parent drug: < 10 min • Half-life thiocyanate: 2.7-7 days • Signs of toxicity include metabolic acidosis, tremors, seizures, and coma • Thiocyanate may accumulate in renal failure	
Norepinephrine (Levophed) $ • 8 mg/250 mL D5W * (32 mcg/mL)	—	2-10 mcg/min **
	• Half-life: N/A • Potent α effects, mainly β1 effects at lower doses • Use central line	
Octreotide (Sandostatin) $ • 500 mcg/100 mL NS * (5 mcg/mL)	50 mcg bolus	50 mcg/hr
	• Half-life normal organ function: ~ 2 hrs • Half-life liver/renal dysfunction: 3-4 hrs	

* Only dilution/diluent dispensed ** Variable dosage range; titrate to desired effect
*** Cost Index:$-$$ Low Cost; $$$ Moderate Cost;>$$$ High Cost

Drug (tradename) Cost index *** • Dilution (concentration)	Loading dose	Initial maintenance dose
Phenylephrine (Neo-Synephrine) $ • 25 mg/250 mL NS (100 mcg/mL)	—	10-100 mcg/min **
	• Initial half-life: ~ 5 min • Terminal half-life: 2-3 hrs • Pure α effects. May cause reflex decrease HR and decrease cardiac output • Use central line	
Procainamide (Pronestyl) $ • 2 g/250 mL D5W (8 mg/mL)	17 mg/kg at 20 mg/min	1-4 mg/min
	• Half-life procainamide: 2-5 hrs • Half-life NAPA: 6-8 hrs • Monitor QTc, serum procainamide (4-8 mg/L) and NAPA (10-20 mg/mL) levels • NAPA may accumulate in renal failure	
Prostaglandin E1 (Alprostadil) $ • 1000 mcg/100 mL NS (10 mcg/mL)	—	0.01 mcg/kg/min **
	• Half-life: 5-10 min • Pulmonary selectivity lost at higher doses	
Theophylline $ • 800 mg/500 mL D5W (1.6 mg/mL)	5-6 mg/kg over 30 min	0.2-0.9 mg/kg/hr
	• Half-life: variable depending on age, organ function and smoking history • Monitor serum levels (5-20 mg/L)	
Tirofiban (Aggrastat) $$$$$ • 12.5 mg/250 mL NS (50 mcg/mL)	• **Urgent PCI**: 25 mcg/kg over 3 min • **Medical management of ACS**: 0.4 mcg/kg/min x 30 min	• **Urgent PCI**: 0.15 mcg/kg/min up to 18 hrs • **Medical management of ACS**: 0.1 mcg/kg/min up to 72 hrs
	• Half-life: 2 hrs • Potent antiplatelet agent with 4 hr duration • Decrease dose by 50% if CrCl < 30 mL/min • Contraindicated in patients requiring dialysis	
Vasopressin (Pitressin) $ • **Hypotension/shock**: 20 units/100 mL NS (0.2 units/mL) • **GI bleed**: 100 units/100 mL NS (1 unit/mL)	—	• **Hypotension/shock**: 0.04 units/min infusion do not titrate • **GI bleed**: 0.4 units/min
	• Half-life: 10-20 min • Octreotide may be safer alternative for GI bleed	

* Only dilution/diluent dispensed ** Variable dosage range; titrate to desired effect
*** Cost Index:$-$$ Low Cost; $$$ Moderate Cost;>$$$ High Cost

MALIGNANT HYPERTHERMIA

Barnes-Jewish Hospital Departments of Perioperative Services and Pharmacy, June 2013

DESCRIPTION

Malignant hyperthermia (MH) is a rare, life-threatening, pharmacogenetic disorder that occurs in MH susceptible patients following administration of anesthetic agents commonly used in the intraoperative setting and during rapid sequence intubations. Once triggered, a rapidly progressive hypermetabolic reaction involving sustained muscle contraction occurs with catastrophic consequences.

The primary defect in MH susceptible patients resides in the skeletal muscle at the level of calcium transfer in the muscle cell. Triggering agents cause an uncontrolled release of calcium from the sarcoplasmic reticulum resulting in an increase in intracellular calcium ion concentration. This leads to prolonged and sustained muscle fiber contraction.

The reported incidence of MH is 1 in 50,000 to 1 in 150,000 anesthetic procedures. MH is more common in children and young adults.

TABLE 1	**TRIGGERING AGENTS**
Volatile inhalation anesthetics	• Halothane (Fluothane) • Isoflurane (Forane) • Enflurane (Ethrane) • Sevoflurane (Ultane) • Desflurane (Suprane)
Depolarizing neuromuscular blocker	• Succinylcholine (Anectine)

TABLE 2	**SIGNS AND SYMPTOMS**
Early signs	• Rising end-tidal carbon dioxide ($ETCO_2$) • Tachycardia • Masseter muscle spasm • Muscle rigidity • Tachypnea • Electrolyte imbalances (hyperkalemia, hyperphosphatemia, hypocalcemia) • Flushing • Respiratory acidosis
Late signs	• Temperature rise to 44-45° C (may rise as quickly as 1° C every 5 min) • Respiratory and metabolic acidosis • Ventricular dysrhythmias • Rhabdomyolysis • Myoglobinuria\myoglobinemia • Acute renal failure • Mottled skin and cyanosis • Coagulopathy

MH CART LOCATION AND REMOTE ANESTHESIA CASES

1. There are five MH Carts containing pharmacologic and medical supplies needed to treat MH. An MH Cart is located in the following OR departments: PODS 1,2,3, 4, and Labor and Delivery. Due to its close proximity, POD 5 uses the MH Cart located at POD 1.
   POD 1 Gynecology, Colorectal, General Surgery, Urology
   POD 2 Orthopedics, General Surgery, Trauma, Plastics
   POD 3 Hepatobiliary, Transplant, Vascular, Cardiothoracic
   POD 4 CAM outpatient surgery
   POD 5 Neurosurgery, ENT
2. Remote anesthesia cases are those that occur outside of PODS 1-5. To locate the nearest MH Cart to a remote anesthesia area, use Tables 3 and 4.
3. Due to its off-campus location, the **In Vitro Fertilization (IVF) Clinic** at 4444 Forest Park Parkway has a drug box containing only pharmacologic agents. The drug box is located in the procedure room.

TABLE 3 — **NEAREST MH CART BY SOUTH REMOTE AREA**

Remote anesthesia area	POD 1	POD 3	Comments
15th Floor ECT	✓		• **POD 1**: an MH Cart is located at 2EP, down the hall from the POD 1 nursing desk and OR Pharmacy • **POD 3**: the MH Cart is located at 3SWT by Room 308
8th Floor X-Ray	✓		
5th Floor MRI	✓		
3rd Floor X-Ray	✓		
2nd Floor X-Ray	✓		
Digestive Diseases Center (DDC)	✓		
Cardiac Procedure Center (CPC)		✓	

TABLE 4 — **NEAREST MH CART BY NORTH REMOTE AREA**

Remote anesthesia area	POD 4	Drug Box	Comments
10th Floor CAM GI	✓		• **POD 4**: the MH Cart is located at the North CAM OR behind Room H. • **IVF**: the MH drug box is located in the IVF Procedure Room
3rd Floor CAM MRI	✓		
North Gamma Knife	✓		
North Radiation Oncology	✓		
In Vitro Fertilization Clinic (IVF) at 4444 Forest Park Parkway		✓	

DANTROLENE PREPARATION

1. Usual dose: dantrolene 2.5 mg/kg ivp through a large bore iv q5min until symptoms subside followed by 1 mg/kg q6h for 24 hrs post-MH crisis
   a. Reconstitute each 20 mg vial with 60 ml sterile water for injection
2. Max cumulative dose is 10 mg/kg, however, if the patient remains hemodynamically unstable, proceed with 2.5 mg/kg ivp q5min.
3. Each 20 mg vial of dantrolene contains 3 grams of mannitol

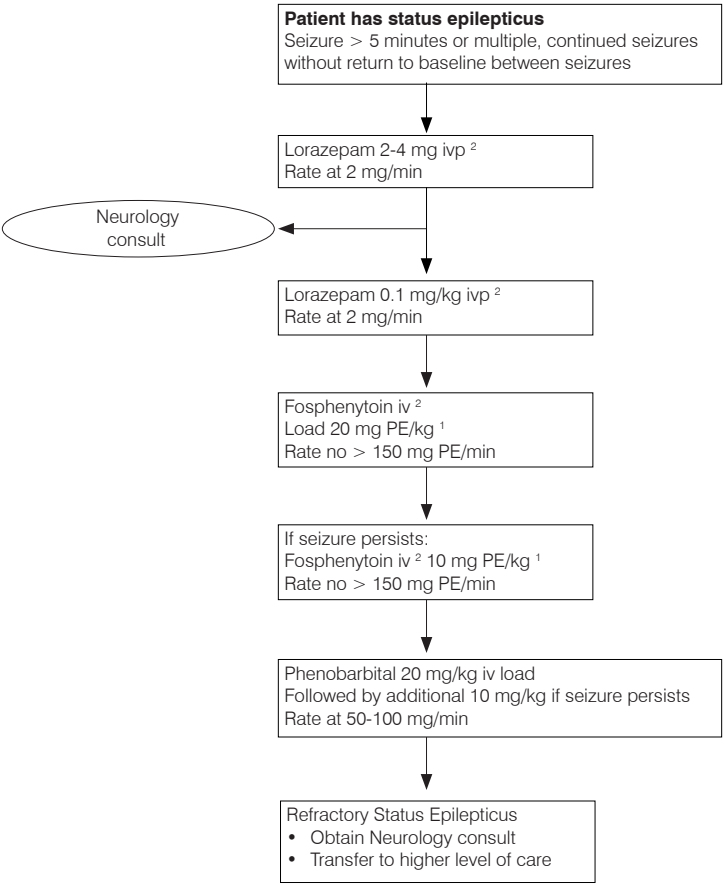
MALIGNANT HYPERTHERMIA CHECKLIST

1. **Diagnosis**. The anesthesiology attending leads the event and delegates tasks
   a. Announce diagnosis of MH crisis
   b. Discontinue volatile anesthetic gases
   c. Delegate retrieval of MH Cart and Code Cart
   d. Delegate retrieval of cooling supplies (ice, cold iv and irrigation fluids) and insulin from Pharmacy
   e. Connect Vapor-Clean filters between the anesthesia machine and breathing circuit
   f. Increase FiO_2 to 100%
   g. Increase minute ventilation to ≥ 10 L/min or 2-3x patient's minute ventilation. Monitor $ETCO_2$
   h. Initiate non-triggering anesthetics
   i. Complete/halt surgical procedure if possible
2. **Pharmacological treatment**
   a. Dantrolene 2.5 mg/kg ivp q5min
      Reconstitute each 20 mg vial with 60 ml sterile water for injection
   b. Sodium bicarbonate ivp for suspected metabolic acidosis
   c. Hyperkalemia treatment regimen for elevated K^+
   d. Antiarrhythmics for treatment of dysrhythmias
   e. Furosemide ivp to maintain UOP of 2 mL/kg/hr
3. **Labs**
   a. ABG, venous blood gas
   b. CMP, coagulation studies
   c. Serum CK, serum/urine myoglobin
4. **Cooling**
   a. Insert esophageal temp probe/axillary probe.
   b. Cool patient with ice and cold fluids if temperature >38.5° C
   c. Lavage open body cavities, stomach, bladder, and/or rectum w/ cold fluids
   d. Apply ice packs to key areas (e.g., axilla, groin, etc.)
   e. Infuse cold iv NS to maintain UOP of 2 mL/kg/hr
   f. Stop cooling measures when temperature falls <38° C
5. **Post-acute phase care**
   a. Provide handoff to ICU. Order post-op dantrolene and repeat labs.
   b. Notify Anesthesia and nursing leadership of event
   c. Enter SES and MetaVision report
   d. Call MH Hotline at 1-800-644-9737 to report event

TABLE 5	**PHARMACOLOGICAL TREATMENT**
Skeletal muscle rigidity	Dantrolene 2.5 mg/kg ivp q5min until symptoms subside
Metabolic acidosis	Sodium bicarbonate 1-2 mEq/kg ivp. Repeat prn.
Hyperkalemia	• Calcium chloride 1 g ivp • Sodium bicarbonate 1-2 mEq/kg ivp • Insulin regular 10 units ivp with 50-100 mL dextrose 50%
Arrhythmias	• Lidocaine 50-100 mg (1-1.5 mg/kg) ivp over 1-2 min ✓ May repeat q5-10 min ✓ Max 3 mg/kg) • Amiodarone 150-300 mg ivp ✓ May repeat 150 mg IVP dose x 1 in 3-5 min • **Avoid calcium channel blockers**
Post-phase treatment	Dantrolene 1 mg/kg iv q6h for 24 hrs

STATUS EPILEPTICUS IN ADULTS

Washington University, Department of Neurology, June 2013



1 **PE= phenytoin equivalents**. Fosphenytoin should always be prescribed as "mg PE"

2 **In emergent situations**, lorazepam and fosphenytoin may be given im if patient is without iv access

NOTE: These are suggested guidelines. Individual patient conditions may necessitate deviating from these guidelines.

Phenytoin Correction for Albumin or Renal Dysfunction

Adjusted concentration = measured total concentration ÷ [(0.2 x albumin) + 0.1]
If CrCl is ≤10 mL/minute: Adjusted concentration = measured total concentration ÷ [(0.1 x albumin) + 0.1].

TAKING CARE OF ACTIVELY DYING PATIENTS

Barnes-Jewish Hospital Analgesia Subcommittee, June 2013

COMFORT CARE

Patients and the families of patients at the end of life may decide to focus exclusively on comfort and to stop mechanical or artificial support. This is sometimes referred to as comfort care. Comfort care is an active treatment plan with conscientious monitoring and therapy aimed at relieving discomfort or pain. It is **not** an attempt to hasten death.

A comfort care patient who is uncomfortable or having a symptom crisis represents a medical emergency.

DEFINITIONS

Comfort care is not the same as hospice, nor is it the same as palliative care.

Palliative care is interdisciplinary care with the goal of optimizing symptom control and quality of life for patients and families facing life-limiting illness. It may be provided at any point after the diagnosis of life-limiting illness, regardless of the need for other therapies.

Hospice refers to organizations (e.g., BJC Hospice) that provide palliative care to patients and families who have an incurable disease with a prognosis of 6 months or less. Most of these organizations work with patients at home or in extended care facilities (ECFs). Most (although not all) patients and families enrolled in hospice programs have decided that they do not want to come back to the hospital.

The goal of comfort care is to provide comfort and dignity for both the patient who is dying and his/her family. Bothersome physical symptoms, along with emotional, spiritual, psychological, and social concerns, should be addressed for the patient and family in a culturally sensitive manner. The medical record should reflect that goals of care have been discussed with patient and/or the appropriate surrogate/family member, and that a decision has been made to focus exclusively on comfort. Comfort care patients should have a code status of DNR/DNI.

TAKING CARE OF A COMFORT CARE PATIENT

1. Make sure discussions surrounding goals of care and code status are documented in the medical record (both electronic and written)
2. Affirm your commitment to provide the best possible care of the patient to the patient, family and friends
3. Communicate clearly with nursing colleagues regarding comfort as the goal of care
4. Provide a quiet, calm environment. Request a private room if possible
5. Discontinue all monitoring, testing, procedures, and medications not essential to patient comfort, including but not limited to, telemetry, continuous pulse oximetry, lab draws and finger sticks. Make sure all alarms are off.
6. Vital signs are not necessary, but the patient should be monitored closely for pain (at least q4h)
7. Obtain a Spiritual Care Consult, if appropriate
8. Even if the patient appears comfortable on your initial exam, PRN medication orders for the symptoms listed above, especially dyspnea, pain, and anxiety, should be provided
9. Provide treatments for (see examples below)
   a. Pain
   b. Dyspnea
   c. Anxiety
   d. Delirium
   e. Terminal congestion/ excess secretions
   f. Fever

EXAMPLES OF MEDICATION ORDERS (OPIOID-NAIVE PATIENT)

- Morphine 5-10 mg po/sl q2h prn pain or dyspnea
- Morphine 2-4 mg iv/sc q1h prn pain or dyspnea
- Lorazepam 1-2 mg iv/po q4h prn anxiety
- Haloperidol 1-2 mg iv q4h prn agitation
- Scopolamine 0.4 mg iv/sc q4h prn excess secretions
  Note: may exacerbate delirium. Do not use patch. Onset of patch is too long to be effective in actively dying patients.
- Acetaminophen 1 g po/pr q8h prn fever

PALLIATIVE CARE CONSULT

For assistance establishing goals of care and managing symptoms
Call 747-4GOC (747-4462) and place and order in Compass

THERAPEUTIC HYPOTHERMIA FOR CARDIAC ARREST

Barnes-Jewish Hospital Code Committee, June 2013

INDICATIONS

Prevention of neurological complications after cardiac arrest after return of spontaneous circulation in patients who remain comatose; has also been studied after traumatic brain injury and stroke

RATIONALE

- Reduces cerebral metabolic rate and oxygen demand
- Preserves the integrity of the blood-brain barrier
- Decreases neurological excitotoxicity by decreasing glutamate release

CLINICAL OUTCOMES

Therapeutic hypothermia has been shown to reduce mortality by ~14% and improve the rates of favorable neurologic outcomes by 16-23%

TABLE 1	AMERICAN HEART ASSOCIATION RECOMMENDATIONS
Class I	• Ventricular fibrillation or pulseless ventricular tachycardia • Unconscious adult patients with return of spontaneous circulation after out-of-hospital cardiac arrest should be cooled to between 32° C to 34° C for 12 to 24 hours when the initial rhythm was ventricular fibrillation
Class IIb	• Pulseless electrical activity or asystole • Similar therapy may be beneficial for patients with out-of-hospital non-VF arrest (PEA or asystole) or for in-hospital arrest of any origin

OVERVIEW OF PROTOCOL

TABLE 2	TWO METHODS OF COOLING
Internal cooling	A catheter is placed in the patient's femoral vein that runs cool fluid (typically normal saline) through the catheter. The catheter acts as a cooling device and does not administer the cool fluid to the patient. Instead, the fluid is re-circulated back to the pump where it is re-cooled.
External cooling	Cooling is achieved through several mechanisms. For patients who can tolerate fluid resuscitation, 2 L of cooled normal saline (4° C) are administered over 30 minutes. In addition, external body wraps attached to a cooling device as well as ice packs are applied to the patient to achieve the desired temperature

1. Regardless of the mechanism of cooling, there is a cooling phase where the patient is gradually cooled to 33° C, typically over 4 hours.
2. The patient's core temperature should remain at 33° C for 18 hours during the maintenance phase.
3. Finally, after 18 hours the patient is gradually re-warmed to normal body temperature over about 5 hours. Vasodilation can occur during the re-warming phase, sometimes necessitating iv boluses.

TABLE 3	PHYSIOLOGICAL EFFECTS OF HYPOTHERMIA [1,7]
Organ system	Effects
Endocrine Metabolic	• Hyperglycemia due to decreased insulin release and decreased insulin sensitivity • Increased concentrations or decreased metabolism/ clearance of some medications, such as fentanyl, propofol, phenytoin, rocuronium, and vecuronium • Acidosis
Cardiovascular	• Initially tachycardia, followed by bradycardia • Other dysrhythmias, such as atrial fibrillation, asystole, VF or VT can occur at temperatures below 30° C • Decreased efficacy of electrical cardioversion administered during hypothermia • QTc interval may be prolonged and should be monitored during therapy
Hematologic	• Coagulopathies • Decreased platelet function
Renal function	Renal blood flow may be decreased but urine output typically increases
Electrolyte abnormalities	• Hypokalemia • Hypomagnesemia • Hypocalcemia
Musculoskeletal	Shivering can be treated with: • Neuromuscular blockers (vecuronium, pancuronium, etc) • Dexmedetomidine • Meperidine

PHARMACY ASPECTS OF PROTOCOL

See order sets for specifics. Pharmacological interventions are focused around the adverse effects that can be seen with hypothermia as well as post-cardiac arrest care.

1. Sedation as per the ICU Sedation Orders
   a. Although propofol and fentanyl clearance can be effected by hypothermia, these agents can still be used since nurses will be monitoring level of sedation closely and titrating infusion rates as needed
2. Neuromuscular blockade / paralysis for shivering – typically vecuronium 0.05-0.1 mg/kg iv push q1h prn. Other neuromuscular blocking agents can also be used.
3. Electrolyte repletion prior to initiation of hypothermia .
4. Insulin drip – although not part of our formalized order set, an insulin drip may be needed for hyperglycemia. This should be titrated down and closely monitored once the re-warming phase has started .
5. Acetaminophen to treat rapidly rising temperatures during the re-warming phase, as needed
6. Vasopressors and inotropes as indicated. MAP goal is typically 80 mm Hg

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APPROPRIATE TIMING OF DRUG LEVELS

1. **Peak concentration**
   a. Timing of the specimen depends on the drug formulation being given (iv vs. po)
   b. Generally for oral drugs, peak concentrations are best drawn at the end of absorption, which reflects the maximal amount of drug reaching the blood stream
   c. The time to peak for an oral drug will be affected by the type of oral formulation (rapid vs. sustained release) being administered and the rate of absorption from the GI tract. GI absorption is often affected by patient-specific factors, e.g., malabsorption syndromes, poor GI motility, poor GI perfusion because of hypotension or some other cause.
   d. See table below for drug-specific recommendations. Not all drugs require peak concentration monitoring.
2. **Trough concentration**
   a. For practicality and ease of coordination with the phlebotomist drawing the level, trough concentrations are best drawn immediately prior to a dose
3. **Random drug concentration**
   a. May be drawn at anytime, without regard to when the last dose was given. However, as with any drug level, appropriately documenting the time at which the level is drawn is always important so that the result can be properly interpreted.

Drug	Usual therapeutic range	Half-life (normal renal function)
Aminoglycosides	See Aminoglycoside Dosing monograph	
Amitriptyline	80-200 ng/mL	Half life: 9-27 hrs
	• Plasma levels do not correlate with clinical response • Trough levels recommended • Draw trough level immediately prior to the next dose	
Chloramphenicol	10-25 mcg/mL	Half life: 4 hrs
	• At the 6th dose, obtain peak level 1 hr after end of infusion • Supratherapeutic peaks are associated with bone marrow suppression. • Obtain subsequent levels weekly and follow hepatic function closely • Do not exceed usual maximum dose of 4 g per day	
Carbamazepine	4-12 mcg/mL	Half life: 15-40 hrs
	• Draw trough level immediately prior to the next dose • Absorption is complete by 4 hrs, therefore a specimen drawn 4 or more hrs after last dose is acceptable • Therapeutic or toxic effects of anticonvulsant drugs may occur at different concentrations in different patients, and the correlation between dose and clinical effect must be evaluated individually	

Drug	Usual therapeutic range	Half-life (normal renal function)
Digoxin	Disease specific ranges • CHF: 0.5-1 ng/mL • AFIB: 0.8-2 ng/mL	Half-life: 20-60 hrs
	• Draw specimen no earlier than 60 min prior to dose. Absorption is complete by 8 hrs; therefore, a specimen drawn 8 or more hrs after the last dose is acceptable. 12-24 hrs is preferred. • Spironolactone may interfere with digoxin assay. It is recommended that a digoxin level be measured before spironolactone administration in patients receiving concomitant therapy. • Total serum digoxin concentration may be spuriously high immediately after the administration of Digibind. However, this is almost entirely bound to the FAB fragment and does not reflect the amount of free digoxin available to react with receptors in the body. • Periodically monitor serum potassium, magnesium, and calcium	
Enoxaparin	See Therapeutic Enoxaparin monograph	
Flecainide	0.2-1 mcg/mL	Half life: 12-27 hrs
	• Monitoring of flecainide concentrations is not routinely recommended • May consider monitoring periodic troughs	
Flucytosine	30-80 mcg/mL	Half-life: 2-5 hrs
	• Peak levels should ideally be drawn 3-5 days after initiating therapy. Obtain peak level 2 hrs after giving dose. • Risk of toxicity is increased with peak levels > 100 mcg/mL • Monitor weekly levels. Consider more frequent monitoring in setting of changing renal function	

Drug	Usual therapeutic range	Half-life (normal renal function)
Fosphenytoin/ Phenytoin	• **Total phenytoin** 10-20 mcg/mL • **Free phenytoin** 1-2 mcg/mL	Half-life: 20-40 hrs
	• **Intravenous loading dose** ✓ Phenytoin iv - initial level can be drawn 1 hr after loading dose ✓ Fosphenytoin iv - initial level can be drawn 2 hrs after loading dose • **Oral loading dose** ✓ Phenytoin extended capsules - initial level can be drawn 18-24 hrs after loading dose ✓ Phenytoin Infatabs - initial level can be drawn 8 hrs after loading dose ✓ Oral phenytoin loading doses should not be greater than 400 mg per dose and at least 2 hrs apart to facilitate absorption • **Maintenance levels:** draw levels 2-4 days after loading dose to verify therapeutic level • Slow absorption of extended capsules and prolonged half-life minimize fluctuations between peak and trough concentrations, timing of sampling not crucial	
Heparin	See Heparin Nomogram monograph	
Itraconazole	• >1 mcg/mL • If **both** itraconazole and its bioactive metabolite (hydroxy-itraconazole) are reported, **the sum** of these should be > 1 mcg/mL	Half life: 21 hrs
	• Obtain level (anytime during dosing interval) 4-7 days after the initiation of therapy in all patients to document adequate absorption • The upper therapeutic range is not known, although toxicity has been noted at levels > 10 mcg/mL • Consider subsequent monitoring in patients with hepatic impairment, inadequate response, GI dysfunction, interacting medications or severe disease • The oral solution is preferred, since the oral capsules are erratically and poorly absorbed	
Lidocaine	1.5-5 mcg/mL	Half-life: 1.5-2 hrs
	• Lidocaine concentrations may be drawn at any time during a continuous infusion	

Drug	Usual therapeutic range	Half-life (normal renal function)
Lithium	0.6-1.3 mmol/L	Half-life: 14-30 hrs
	• For optimal therapeutic drug monitoring, specimen should be drawn 8 hrs or more after the last lithium dose was administered	
Mexiletine	0.8-2 mcg/mL	Half-life: 10-12 hrs
	• Monitoring of mexiletine concentrations is not routinely recommended • Draw trough level after patient has been receiving mexiletine for at least 3 days and just before administration of the next dose	
Nortriptyline	70-170 ng/mL	Half-life: 28-31 hrs
	• Plasma levels do not correlate with clinical response • Trough levels recommended. Draw specimen immediately before next scheduled dose (minimum 12 hrs after last dose). • Therapeutic ranges are for specimens drawn at trough (i.e., immediately before next scheduled dose)	
Phenobarbital	10-40 mcg/mL	Half-life: 50-140 hrs
	• Draw trough level immediately prior to the next dose • Absorption is complete by 4 hrs, therefore a specimen drawn 4 or more hrs after last dose is acceptable	
Posaconazole	• **Treatment** > 1 mcg/mL • **Prophylaxis** > 0.7 mcg/mL	• Half-life: 35 hrs • But due to saturable absorption, must be administered 2-4 times daily
	• Obtain level (anytime during dosing interval) 5-7 days after the initiation of therapy in all patients to document adequate absorption • Consider subsequent monitoring in patients with inadequate response, GI dysfunction or clinical decline • The upper therapeutic range is not defined • The following strategies **must** be utilized to ensure adequate absorption: ✓ Administer with a high fat meal, nutritional supplement, or acidic beverage ✓ Avoid acid suppressive therapy • Higher levels can be achieved with 200 mg po qid as compared to 400 mg po bid	

Drug	Usual therapeutic range	Half-life (normal renal function)
Procainamide	Procainamide **or** N-acetylprocainamide 4-8 mcg/mL	Half-life: 2-6 hrs
	Procainamide **and** N-acetylprocainamide (total of both) ≤30 mcg/mL	
	• **Intravenous**: draw levels 6-12 hrs after continuous iv infusion has started • **Oral**: oral formulations no longer available in the USA	
Theophylline	5-15 mcg/mL	Half-life: 6-10 hrs
	• **Oral**: check peak at steady state at least 48-72 hrs on the same dose • **Intravenous** ✓ Check level 30 min after end of iv loading dose ✓ Check level 6 hrs after starting continuous infusion and then every 24 hrs	
Trimethoprim/ sulfamethoxazole (Bactrim, Septra)	• **Trimethoprim** ✓ Trough: 2-8 mcg/mL ✓ Peak: 5-15 mcg/mL	Half-life: 6-17 hrs
	• **Sulfamethoxazole** ✓ Trough: 75-120 mcg/mL ✓ Peak: 100-150 mcg/mL	Half life: 9 hrs
	• Peak trimethoprim and/or sulfamethoxazole level(s) should be obtained 1 hr after the end of an iv dose or 2 hrs after an oral dose • For nocardiosis, a sulfamethoxazole level is recommended since it is the sulfonamide component that is active against this organism	
Valproic acid	50-100 mcg/mL	Half-life: 8-15 hrs
	• Draw trough level immediately prior to the next dose • Since absorption is complete by 4 hrs, a specimen drawn 4 hrs or more after last dose is acceptable	
Vancomycin iv	See Vancomycin Dosing and Monitoring monograph	

Drug	Usual therapeutic range	Half-life (normal renal function)
VoriCONAZOLE	> 1-2 mcg/mL but < 5.5 mcg/mL	Half-life variable depending on dose
	• Consider monitoring drug levels in patients ✓ With inadequate response to therapy, severe fungal infection, or signs of voriCONAZOLE toxicity ✓ In which a change of dosage form has been made ✓ On medications known to interact with voriCONAZOLE (CYP3A4 substrates, inducers or inhibitors) • Trough levels should be drawn at least 5-7 days after the initiation of therapy • Trough levels > 5.5 mcg/mL have been associated with an increased incidence of hepatotoxicity, neurotoxicity and visual adverse effects. Patient-specific factors such as severity of disease and risk of toxicity should be considered when assessing trough levels.	

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TOOL BOOK FOR ELECTRONIC DEVICES

Barnes-Jewish Hospital Department of Pharmacy, June 2013

THREE OPTIONS FOR VIEWING THE TOOL BOOK ELECTRONICALLY

Choose one of three ways to view the Tool Book in an electronic format. Because of poor legibility, the editors advise against reading the Tool Book on any handheld device with a small screen size (eg, smart phones). The electronic file formats listed below are all optimized for larger screens found on electronic tablet devices. Because the number, variety, screen resolutions, operating systems and modes of navigation of tablets are so highly variable, the editors cannot guarantee that Options 3 will work seamlessly on every tablet. These methods have been tested primarily on the Apple iPad. Please contact the editors to provide feedback on the Tool Book, its usefulness, navigation and readability on any device.

Please note that because of the large number and complexity of various devices, the editors cannot provide personalized assistance with installing the Tool Book on any device.

OPTION 1: TOOL BOOK IN COMPASS

1. Requirements: a desktop computer or terminal connected to the BJH LAN
2. Log onto Compass using your username and password
3. On the top menu bar, click on the blue "T" book icon. This will launch the terminal's web browser and open a window to the Pharmacy intranet site.
4. Click on "toolbook.pdf" to launch the PDF file
5. Once the PDF opens, click on the bookmark icon (3rd down in the left column) to open the Tool Book's bookmarks.
6. Please note that the Pharmacy intranet site was moved to a new server in 2012. Please update your bookmarks. If the instructions above do not work, see option 2 below.

OPTION 2: DOWNLOAD THE PDF TO A PC

1. Requirements
   a. A personal computer connected to the internet; a modern web browser installed
   b. Adobe Acrobat Reader or Acrobat Professional installed on your PC. Most modern browsers (Internet Explorer v7 or higher, Safari, Firefox, Chrome, etc.) already have PDF viewing capabilities, therefore you may not need to install a PDF reader. However, if Acrobat Reader is not already installed on your computer, it is available for free from:

      http://get.adobe.com/reader/

2. Launch your web browser and go to the Tool Book URL:

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3. Once at the website, look for instructions on how to download the PDF file
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The editors highly recommend using the iPad's native iBook application to read the Tool Book since it is easy to use and takes advantage of the Tool Book's electronic table of contents, index, and hyperlinks. Lastly, the iBook Search function is highly useful. Other PDF readers found at the iTunes Store have generally been less functional.

1. Requirements
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   b. A PC connected to the internet and with iTunes installed
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3. Connect your iPad to your PC using its dedicated USB cable and launch iTunes
4. Drag the PDF file onto the "Library" frame located on the left side of the iTunes window
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WHAT ABOUT AN iPAD APP OR READING ON ANDROID TABLETS?

In 2012, Barnes-Jewish Hospital Information Systems announced support for connecting iPads and Android tablets to the hospital's WiFi network and Compass. Details regarding device connectivity are still being finalized.

The editors are pursuing the creation of an iPad app or other electronic format that can be read on Android and Apple iOS devices. Given the large variety of devices, their constantly changing functionality, and the limited time the editors have to create such applications, users are directed to the Tool Book website for updates on the status of these applications.

FOR MORE INFORMATION

We appreciate your feedback on the Tool Book, its content and companion website and electronic file options. Contact:

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NATIONAL LEADERS IN MEDICINE

CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING

Barnes-Jewish Hospital Oncology Subcommittee, June 2013

Chemotherapy-induced nausea and vomiting (CINV) can significantly affect a patient with cancer's quality of life. Inadequate prevention or treatment of nausea and vomiting can lead to metabolic abnormalities, decline in functional status, nutrient depletion, anorexia, and potentially limit the amount of therapy the patient can receive to treat their cancer. Prevention is the key for CINV.

RISK FACTORS FOR CINV

- Female gender
- Younger age
- Non-drinker of alcohol
- Prior nausea with chemotherapy
- Prior history of motion sickness
- Emetogenic potential of chemotherapy regimen
- Anxious personality

TABLE 1 **CATEGORIES OF CINV**

Type of CINV	Definition	Neurotransmitter responsible
Acute onset	Occurs within the first 24 hours after chemotherapy usually peaking about 5-6 hours after chemotherapy	Serotonin Some substance P
Delayed onset	Develops more than 24 hours after chemotherapy, reaches its peak intensity 48-72 hours after chemotherapy but can last 6-7 days	DOPamine Substance P
Anticipatory	Occurs before the patient receives the next dose of chemotherapy	Conditioned response

TABLE 2 **EMETOGENICITY OF CHEMOTHERAPY**

Emetic risk category (rate of occurrence)	Treatment recommendations	Examples
High emetic risk (>90%) *	• 5-HT3 antagonist Day 1 • Dexamethasone Day 1-4 • Fosaprepitant Day 1	Cisplatin Cyclophosphamide $\geq$ 1500 mg/m^2 Dacarbazine
Moderate emetic risk (> 30-90%)	• 5-HT3 antagonist Day 1 • Dexamethasone Day 1-3 • $\pm$ Fosaprepitant Day 1	Oxaliplatin Carboplatin Cytarabine > 1 g/m^2 Doxorubicin Cyclophosphamide

Emetic risk category (rate of occurrence)	Treatment recommendations	Examples
Low emetic risk (10-30%)	• Dexamethasone Day 1	Paclitaxel Docetaxel Etoposide Pemetrexed Methotrexate Gemcitabine
Minimal Emetic Risk (<10%)	• No antiemetic needed	Bevacizumab Fludarabine Rituximab Vincristine

* Fosaprepitant and aprepitant are not standard of care at BJH for stem cell transplant.

SEROTONIN ANTAGONISTS
- Primary agent used for prevention of acute CINV
- At equivalent doses, serotonin antagonists have equivalent safety and efficacy and can be used interchangeably
- May cause constipation and headache

TABLE 3	**EQUIVALENT DOSES**	
Serotonin antagonist	Intravenous	Oral
Ondansetron [1]	8 mg (max 16 mg)	24 mg
Dolasetron	—	100 mg
Granisetron	1 mg	2 mg
Palonosetron [2]	0.25 mg	n/a

1 Preferred formulary agent at BJH
2 NCCN preferred serotonin antagonist

CORTICOSTEROIDS
- Dexamethasone has been most widely studied for CINV prevention and treatment
- Acute CINV prevention: dexamethasone 10-20 mg ivpb or 12 mg po
- Delayed CINV prevention: dexamethasone 8 mg po daily days 2-4
- When used with fosaprepitant or aprepitant, decrease dose of dexamethasone by 50% due to drug interaction

NEUROKININ 1 RECEPTOR ANTAGONISTS
- Reduction in Substance P is helpful for prevention of both acute and delayed CINV
- Recommended for all highly emetic chemotherapy regimens and optional for moderately emetic chemotherapy regimens
- Preferred formulary dosing regimen
  ✔ Fosaprepitant 150 mg iv on day 1

TREATMENT OF CINV
- Prevention is the key. Treatment of CINV involves utilization of drugs with different mechanisms of action.
- Typically start with one class of drug prn. If nausea and vomiting persists, schedule the drug, then add another prn agent from a different class.
- Think about the underlying neurotransmitter(s) when choosing a treatment option.

TABLE 4	PHARMACOTHERAPY OF CINV		
Class	Drug	Dose	Considerations
Phenothiazines Mechanism: dopamine antagonism (D1 and D2), anticholinergic	Prochlorperazine	• 5-10 mg iv or po q6h (max 40 mg/day) • 25 mg pr bid suppository	• May cause EPS at high doses • Do not use in patients with Parkinson's receiving dopamine agonists
	Promethazine	• 12.5-25 mg po q4h • 12.5-25 mg pr q4h suppository	• IV not available at BJH • More EPS and sedation than prochlorperazine
Benzodiazepines Mechanism: Increase GABA	Lorazepam	• 0.5-1 mg q6h po, iv or sublingual	• Good for anticipatory CINV • Sedation, hypotension
Benzamides Mechanism: D2 and 5-HT3 antagonism, stimulates GI cholinergic release	Metoclopramide	• 5-10 mg q6h iv or po • 50% dose reduction needed for CrCl < 40 mL/min	• Do not use in obstructed patients • Give 30 min prior to meals and at bedtime • Good for patients with constipation • May cause EPS
	Trimethobenzamide	• 300 mg po 3-4 times daily • 200 mg im 3-4 times daily	• Use caution in patients with renal insufficiency • May cause EPS
Antipsychotics Mechanism: D1-4 antagonism, histamine and 5-HT3 antagonism	Olanzapine	• 2.5-5 mg po bid	• May cause hyperglycemia • Use caution in elderly patients with dementia
	Haloperidol	• 0.5-2 mg iv or po q6h	• Concern for QTc prolongation • EPS
	Droperidol	• 0.625-1.25 mg iv q6h	• Concern for QTc prolongation • EPS

Class	Drug	Dose	Considerations
Anticholinergics Mechanism: M1 antagonist	Scopolamine	• 1 patch q72h topically	• Problems with dry mouth, sedation, urinary retention
Cannabinoids Mechanism: CB1 receptors within CNS	Dronabinol	• 5-10 mg po q6h	• Use caution with elderly patients • May work best for patients with previous marijuana use • Good for patients with nausea and cachexia
	Nabilone	• 1-2 mg po bid	
Serotonin antagonists	See Table 3		

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2. Antiemetics. NCCN Clinical Practice Guidelines in Oncology. V 1.2013 http://www.nccn.org

EXTRAVASATION

Barnes-Jewish Hospital Oncology Subcommittee, June 2013

MANAGEMENT OF EXTRAVASATION

1. Determine the presence of an extravasation
2. Stop infusion immediately
3. Call physician for orders for appropriate therapy
4. Leaving the catheter in place, withdraw/aspirate as much of the drug as possible
5. Administer antidotes (Tables 1-3) and/or remove the iv device
6. After administering antidote or removing the iv device
   a. Elevate the affected area for 48 hours to minimize swelling
   b. Delineate the infiltrated area on the patient's skin with a felt marker
   c. If possible, photograph the site
   d. Complete SES report
   e. Avoid pressure or friction. Do not rub area.
   f. Observe for signs of increased erythema, pain, or skin necrosis and report findings to physician

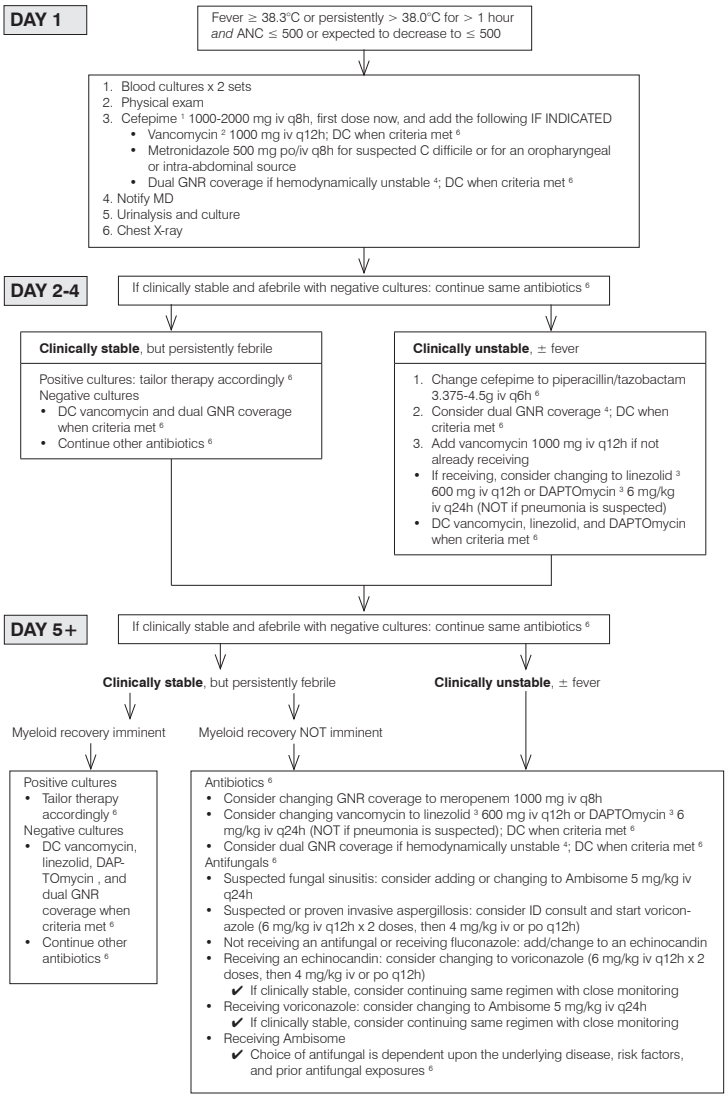
TABLE 1	**VESICANTS**	
Drugs	Doxorubicin Daunorubicin Epirubicin Idarubicin	Dactinomycin Mitomycin-C Paclitaxel Paclitaxel (albumin-bound) Streptozocin
Step 1	• Apply cold compresses and alert the pharmacy that dexrazoxane is needed • Remove cold compress 15 minutes before administering dexrazoxane • Avoid cold compress immediately after administration of dexrazoxane in order to allow sufficient blood flow to the area of extravasation	• Apply cold compresses for 15 minutes every 6 hours for 48 hours
Step 2	• Administer **dexrazoxane** 1000 mg/m^2 iv infusion via a different site over 1-2 hours, within the first 6 hours after extravasation • Give 1000 mg/m^2 on day 2 and 500 mg/m^2 on day 3 • **Max** BSA = 2 m^2 • Renal dose adjustment required	—

TABLE 2	VESICANTS	
Drugs	• Cisplatin (conc ≥ 0.5 mg/mL or more than 20 mL) • Mechlorethamine	Vincristine Vinblastine Vinorelbine Vindesine
Step 1	• Administer **sodium thiosulfate** subcutaneously into extravasation site. Mix 4 mL 10% solution with 6 mL sterile water to prepare a 1/6 Mol solution. • Give as follows: ✓ Max volume 5 mL ✓ Cisplatin: use 2 mL for each 100 mg extravasated ✓ Mechlorethamine: use 2 mL for each 1 mg extravasated	• Administer **hyaluronidase** 150 units subcutaneously or intradermally (as 5-10 injections of 0.1- 0.2 mL) using a 25 gauge needle or smaller • Cleanse area with povidone-iodine • Change needle after each hyaluronidase injection
Step 2	• Apply cold compresses for 15 minutes every 6 hours for 48 hours	• Apply warm compresses for 15 minutes every 6 hours for 48 hours

TABLE 3	IRRITANTS	
Drugs	Arsenic trioxide Bendamustine Bleomycin Busulfan Carboplatin (> 10 mg/mL) Carmustine Cisplatin (< 0.5 mg/mL or ≤ 20 mL) Dacarbazine Daunorubicin (liposomal) Docetaxel Doxorubicin (liposomal) Floxuridine Fluorouracil Gemcitabine Ifosfamide Irinotecan Melphalan Mitoxantrone Thiotepa	Etoposide [1] Teniposide [1] Oxaliplatin [2]
Step 1	Cold compresses • Apply cold compresses for 15 minutes every 6 hours for 48 hours	Warm compresses 1 Apply warm compresses for 15 minutes every 6 hours for 48 hours 2 Apply warm compress for 1 hour, then cooling as needed for comfort

FEBRILE NEUTROPENIA, STEM CELL TRANSPLANT PATHWAY

Stem Cell Transplant Unit, June 2013



1. PCN-allergy: vancomycin 1000 mg iv q12h with one of the following
   a. Aztreonam 2000 mg iv q8h (preferred)
   b. Ciprofloxacin 400 mg iv q12h; do NOT use if the patient received fluoroquinolone prophylaxis
2. Indications for empirical vancomycin
   a. Gram-positive coverage in a PCN-allergic patient receiving aztreonam or ciprofloxacin
      i. In these patients, continue vancomycin until ANC ≥ 500 x 48h, patient is afebrile x 48h, and cultures are negative x 72 hrs
   b. Known colonization with MRSA or cephalosporin-resistant streptococci
   c. Clinical evidence of
      i. Catheter tunnel infection
      ii. Skin and soft tissue infection
      iii. Hemodynamic instability, or other evidence of severe sepsis
3. Indications for empirical linezolid or DAPTOmycin
   a. Clinical deterioration while on vancomycin
   b. Do NOT use DAPTOmycin if lung involvement is suspected
4. If patient is hemodynamically unstable consider dual GNR coverage
   a. Add gentamicin (5 mg/kg iv q24h) or ciprofloxacin (400 mg iv q12h) if gentamicin contraindicated
   b. Do NOT use ciprofloxacin if the patient received fluoroquinolone prophylaxis
5. In bloodstream infections, remove the line in the following situations
   a. Cultures positive for Pseudomonas, Stenotrophomonas, Acinetobacter, VRE, S aureus, C jeikeium, or candida spp.
      i. Consider removing for other organisms
   b. Catheter tunnel infections
   c. High grade bacteremias
6. Recommendations for duration of therapy
   a. Vancomycin: DC after 72 hrs if patient is stable and cultures are negative for coagulase-negative staphylococci, MRSA, cephalosporin-resistant streptococci, and C. jeikeium, and no evidence of skin and soft tissue infection
   b. Linezolid and DAPTOmycin: DC after 72 hrs if patient is stable and cultures are negative for coagulase-negative staphylococci, MRSA, cephalosporin-resistant streptococci, C jeikeium, and VRE, and no evidence of skin and soft tissue infection
   c. Dual GNR coverage: DC after 72 hrs if patient is stable and cultures are negative for GNRs
   d. No documented infection in a clinically stable patient
      i. Discontinue antibiotics and antifungals when ANC ≥ 500 x 48h, patient is afebrile x 48h, and cultures are negative x 72 hrs
   e. Clinically or microbiologically documented infection
      i. Continue antibiotics and antifungals as warranted by the infection and at least until ANC ≥ 500 for 48h
      ii. If cultures are positive, narrow spectrum to targeted therapy once ANC ≥ 500
      iii. Consider an oral regimen when ANC ≥ 500 and mucositis has resolved

REFERENCES

On file at the BJH Drug Information Center, Department of Pharmacy, 216 S Kingshighway, St Louis, MO 63110-1026; 314-454-8399

HYPERCALCEMIA OF MALIGNANCY

Barnes-Jewish Hospital Oncology Subcommittee, June 2013

Hypercalcemia is the most common paraneoplastic syndrome, frequently occurring in advanced cancer patients. Management depends on **symptoms** and **degree of hypercalcemia.**

TABLE 1	SYMPTOMS OF HYPERCALEMIA OF MALIGNANCY
Mild	• Constipation • Fatigue • Polyuria/polydipsia • Nausea
Moderate/Severe	• Lethargy • Confusion • Stupor • Coma • Arrhythmias • Elevated serum creatinine

CORRECTED CALCIUM

Measured calcium + [0.8 x (4 – albumin)] = corrected calcium [Ca^{++}]

INTERVENTIONS

All offending medications should be discontinued or evaluated for risk/benefit (calcium supplements, vitamin D, calcitriol, thiazide diuretics, lithium).

TABLE 2	INTERVENTIONS
Asymptomatic and corrected calcium <12 mg/dL	Normal saline iv 2-4 L/day [1,2]
Asymptomatic/mildly symptomatic and corrected calcium >12 mg/dL	Normal saline iv 2-4 L/day [1,2] + Pamidronate 90 mg ivpb once [3,4]
Moderately/severely symptomatic	Normal saline iv 2-4 L/day [1,2] + Pamidronate 90 mg ivpb once [3,4] + Calcitonin 4 units/kg sq q12h for ≤ 48 hours using actual body weight and no dose cap

1. Exercise caution in patients with CHF or concern for volume overload
2. Loop diuretics are not recommended because they further contribute to dehydration and may induce rebound hypercalcemia
3. Pamidronate is the preferred bisphosphonate at BJH for hypercalcemia of malignancy. It is recommended that a minimum of 7 days elapse before re-treatment to allow complete dose response
4. Pamidronate is normally infused over 4 hours. In patients with underlying renal dysfunction, consideration should be made in extending the infusion duration (up to 24 hours)

REFERENCES

On file at the BJH Drug Information Center

OPIOID ANALGESICS FOR CANCER PAIN

Barnes-Jewish Hospital Analgesia and Oncology Subcommittees, June 2013

TABLE 1	WORLD HEALTH ORGANIZATION GUIDELINES
Step 1	• Nonopioid analgesic ie NSAIDS or APAP ± adjuvant • If pain progresses, advance to Step 2
Step 2	• Opioid formulated for mild to moderate pain ± Non-opioid analgesic ± adjuvant • If pain progresses advance to Step 3
Step 3	• Opioid formulated moderate to severe pain ± Non-opioid analgesic ±adjuvant • Initiate dose according to dose equivalency chart

ADDITIONAL RECOMMENDATIONS

1. Patients with constant pain may need basal (scheduled) opioid, as well as prn opioids for breakthrough pain.
2. Long-acting preparations may improve compliance and reduce side effects in patients with chronic pain.
3. Use immediate release preparations for breakthrough pain at 5-15% of the total daily dose of opioids and at a frequency based on the analgesic half-life.
4. If pain is uncontrolled; reassess, if necessary, admit the patient for parenteral opioids to determine daily opioid requirements.
5. Meperidine and codeine are not recommended for pain management.
6. Non-opioid analgesics and adjuvants should be considered to address the inflammatory or neuropathic component of cancer pain, and to reduce side effects related to opioids.
7. Avoid IM dosing; subcutaneous administration is equally efficacious and less painful.

EQUIPOTENT ANALGESIC DOSES OF OPIOIDS

Equipotent analgesic doses are approximate, and clinical conversions should be done carefully.

Recommendations

1. Calculate the total opioid use over the previous 24 hr period
2. Convert to oral morphine equivalent; then convert to a new opioid. This can be done by setting up an equation with:

$$\frac{\text{dose used of current drug}}{\text{equivalent dose of current drug}^*} = \frac{\text{desired drug new dose}}{\text{equivalent dose new drug}^*}$$

* obtain these numbers from equianalgesic chart below

3. Give 50% of the calculated new opioid to account for incomplete cross-tolerance between opioids
4. Divide the calculated 24-hr dosage by the number of doses to be given per day.
5. Add adequate prn dose at 5-15% of the total daily dose of new opioid for breakthrough pain
6. Schedule the prn dose frequency based on the analgesic half-life. Most oral opioids have time to peak serum concentration of ~ 1 hour; therefore, prn doses can be given as frequent as every 2 hrs.
7. For conversion to long-acting formulations, calculate the 24-hr dosage for the new opioid, as above, and divide by the number of doses to be given per 24-hrs. For morphine, i.e., MS Contin is given every 8 -12 hrs and Oxycontin is given every 12 hrs.

TABLE 2	EQUIPOTENT ANALGESIC DOSES			
Drug (Tradename)	SQ/IV Dose (mg)	PO Dose (mg)	Duration (hrs)	Half-life (hrs)
Short half-life opioids				
Morphine (various)	10	30	4	2-3.5
Oxycodone (various)	—	20	4	3
Hydromorphone (Dilaudid)	1.5	7.5	4	2-3
Hydrocodone (various)	—	30	4	3-4
Fentanyl	0.1	—	1-2	1.5-6
Long half-life opioids				
Methadone (various)	*	*	*	*

Note: iv/sq includes iv pca opioids

* Methadone is a older synthetic opioid with unique characteristics. The pharmacokinetics of methadone are highly variable and depend on factors such as individual patient hepatic and renal function, opioid tolerance and dose, and duration of dosing. When converting another opioid to oral methadone, it is recommended to use as a starting dose **10% of the 24-hr intravenous morphine** equivalent dose. The total daily methadone dose should then be administered in divided doses every 8-12 hrs. Immediate release opioids should be provided as needed for break-through pain.

(equivalent 24-hr dose of iv morphine) x 0.10 = total daily dose of oral methadone
Divide by 2 if dosing q12h OR divide by 3 if dosing q8h.

Please note that this formula will result in a lower starting dose of methadone than most published opioid conversion tables.
Because the analgesic half-life of methadone is shorter than its elimination half-life, toxicity due to drug accumulation can occur. Higher doses may be associated with prolonged QTc. Use caution in patients with risk factors for QTc prolongation such as cardiac risk factors and concomitant administration of other QTc prolonging medications. In general, steady state may be achieved in 5-7 days; therefore, dose adjustments may be made once-a-week. Achievement of stable dosing regimen may take 2-4 weeks, and in most cases will require the cooperation of both the patient and the patient's primary care provider.

Before converting to oral methadone, please discuss this treatment with the provider who will continue care after discharge.

F Formulary medication at BJH
NF Nonformulary medication at BJH

TABLE 3	CONTENT OF COMBINATION TABLETS	
Tradename	Opioid	Non-Opioid
Tylenol #3 (F)	Codeine 30 mg	Acetaminophen 300 mg
Norco 5 mg (F)	Hydrocodone 5 mg	Acetaminophen 325 mg
Percocet (Roxicet, F)	Oxycodone 5 mg	Acetaminophen 325 mg
Tylenol #4 (NF)	Codeine 60 mg	Acetaminophen 300 mg
Percocet, Tylox others (NF)	Oxycodone 2.5 mg-10 mg	Acetaminophen 325-650 mg
Lortab, Norco, Vicodin, others (NF)	Hydrocodone 2.5 mg -10 mg	Acetaminophen 300-500 mg

The P&T Committee approved the automatic substitution of hydrocodone/APAP 325 mg products for hydrocodone/APAP 500 mg products. All new orders for hydrocodone/APAP 500 mg, such as Vicodin, will be switched to an equivalent hydrocodone dose with APAP 325 mg.

TRANSDERMAL FENTANYL DOSING GUIDELINES

Transdermal fentanyl is difficult to titrate and should be reserved for patients:

- with relatively stable pain
- with oral administration issues
- not likely to require more than 400 mcg/hr in the near future

For a opioid naive patient, (ie someone with less than 2 weeks on opioid analgesics), use an equivalency ratio of 100:1 (oral morphine in milligrams per 24 hrs: fentanyl transdermal patch in micrograms per 24 hrs. This ratio translates to:

TABLE 4	TRANSDERMAL FENTANYL EQUIVALENTS	
IV/SC morphine per 24 hrs (includes iv PCA)	PO morphine per 24 hrs	Transdermal fentanyl
10 mg	30 mg	12.5 mcg/hr
20 mg	60 mg	25 mcg/hr
40 mg	120 mg	50 mcg/hr
60 mg	180 mg	75 mcg/hr
80 mg	240 mg	100 mcg/hr
100 mg	300 mg	125 mcg/hr
120 mg	360 mg	150 mcg/hr
140 mg	420 mg	175 mcg/hr
160 mg	480 mg	200 mcg/hr
180 mg	540 mg	225 mcg/hr
200 mg	600 mg	250 mcg/hr
220 mg	660 mg	275 mcg/hr
240 mg	720 mg	300 mcg/hr

1. Do not titrate the patch dose more frequently than every 3 days
2. Increase the patch dose based on the additional amount of breakthrough opioid required
3. If the patient is on a PCA, when converting to a fentanyl patch, place the patch and 8-16 hrs later, stop the previous continuous opioid analgesic. Concurrently, schedule immediate release opioids for breakthrough dosing as needed.
4. When discontinuing the fentanyl patch, remove the patch, then 1-2 hrs later start the new extended release oral opioid. Concurrently, schedule immediate release opioids for breakthrough dosing as needed.
5. Reassess dosing frequently including pain level and use of breakthrough medications.

TABLE 5	**MANAGEMENT OF OPIOID SIDE EFFECTS**
Respiratory Depression	Opioid naive patients in pain rarely experience respiratory depression. If this adverse side effect occurs and comfort care orders are not in effect, naloxone should be diluted and titrated carefully to effect. Naloxone reversal may cause patient to experience extreme pain. Sedation may be a marker for respiratory depression.
Sedation	Sedation may occur with opioid administration, and is most commonly seen with initiation and up-titration. Patients who are unable to sleep because of pain may require additional sleep as their pain management improves.
Nausea	Nausea may occur with opioid initiation and titration. Some physicians provide anti-emetics when initiating treatment with opioids. Late onset nausea may be related to inadequate treatment of constipation.
Pruritus	Some opioids trigger histamine release, and patients may complain of intense itching with administration. Unless other indicators of an allergy occur concurrently, this side effect is not a true allergy. Antihistamines alleviate pruritus and are usually only needed a day or so. If pruritus persists, consider switching opioids.
Constipation	All patients experience some degree of constipation, and patients do not develop tolerance to this side effect. Both education and a bowel regimen are required. Opioids decrease gastric motility, dry out stool, and diminish the rectal stretch reflex; therefore, consider the most likely mechanism of constipation in your patient. A stool softener alone is not adequate. Combinations of stool softener and laxatives should be titrated according to need. Need is based on consistency and frequency of stool. • Docusate and osmotic agents soften stool • There are various classes of laxatives though the most common starting oral laxative is senna • Enema or suppository laxatives may be helpful if oral laxatives are not effective • Avoid fiber laxatives • Consider switching opioids, if constipation persists despite bowel regimen • Codeine and morphine are the most constipating • For refractory opioid-induced constipation, administration of oral naloxone may be considered. Methylnaltrexone s.q. is indicated for the treatment of opiate agonist-induced constipation in patients with advanced illness who are receiving palliative care when response to laxative therapy has been insufficient. Prior to administration of methylnaltrexone it is important to rule out bowel obstruction.

FOR CONSULTS Palliative Care Service Inpatient consults, call 747-4GOC (4462)
Pain Management Inpatient Consults, 424-PAIN (7246)
Pain Management Outpatient Consults, 747-9438

PASERO OPIOID SEDATION SCALE (POSS)

Barnes-Jewish Hospital Analgesia Subcommittee, June 2013

PURPOSE

At BJH, for inpatients receiving opioids for pain control, the Pasero Opioid Sedation Scale (POSS) is used to assess the level of sedation in a patient. Caregivers should respond to increasing levels of sedation in order to prevent an adverse drug event. The level of sedation and pain using the POSS is documented in Compass under the patient's Flowsheets tab → Vital Signs → Pain.

	PASERO OPIOID SEDATION SCALE	
Level	Description	Action to take
S	Sleep, easy to arouse	None
1	Awake and alert	None
2	Slightly drowsy, easily aroused	None
3	Frequently drowsy, arousable, drifts off to sleep during conversation	• **UNACCEPTABLE** level of sedation • Monitor respiratory status and sedation level closely until sedation level is stable at less than 3 and respiratory status is satisfactory • Contact physician to consider: ✓ Decreasing opioid dose by 25-50% ✓ Or administering a non-sedating, analgesia, such as acetaminophen or NSAID, if not contraindicated • See comfort care orders if appropriate
4	Somnolent, minimal or no response to verbal or physical stimulation	• **UNACCEPTABLE** level of sedation • **Discontinue opioid** • Monitor respiratory status and sedation level closely until sedation level is stable at less than 3 and respiratory status is satisfactory • Contact physician to consider administering naloxone • If physician unavailable, call Acute Care Team (ACT) • See comfort care orders if appropriate

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3. Nisbet, AT, et al. Pain Manag Nurs. 2009;10(3):154-164.

SPINAL CORD COMPRESSION

Barnes-Jewish Hospital Oncology Subcommittee, June 2013

Spinal cord compression (SCC) is a true oncologic emergency which can lead to irreversible neurologic deficits if not treated immediately. SCC is most commonly associated with lymphoma, breast, prostate, and lung cancer. Pain is the most common presenting symptom, but the presence of more severe symptoms such as sphincter dysfunction or paraparesis should trigger a diagnostic work-up.

URGENT TREATMENT

Treatment must begin promptly when SCC is suspected

- Dexamethasone 10 mg ivp x1, followed by dexamethasone 4 mg ivp q6h
- Order a whole spine MRI (CT myelography is an alternative)
- Consult Radiation Oncology and either Neurosurgery or Spine Orthopedic Service

REFERENCES

1. DeVita V, et al. Cancer: Principles and Practice of Oncology. Philadelphia: Lippincott Williams & Wilkins. 2008:2441-5.

TUMOR LYSIS SYNDROME

Barnes-Jewish Hospital Oncology Subcommittee, June 2013

Tumor lysis syndrome (TLS) results from the rapid death of predominantly malignant cells. This rapid lysis of cells in turn releases intercellular contents into the systemic circulation more rapidly than the body can eliminate. The end result is a metabolic derangement characterized by the development of hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia, which can ultimately lead to acute oliguric renal failure.

TABLE 1	LABORATORY VS. CLINICAL DEFINITIONS
Laboratory TLS [1]	Clinical TLS [2]
Uric acid ≥ 8 mg/dL	Renal insufficiency
Potassium ≥ 6 mg/dL	Cardiac arrhythmias
Phosphorus ≥ 4.5 mg/dL	Seizures
Calcium ≤ 7 mg/dL	Sudden death

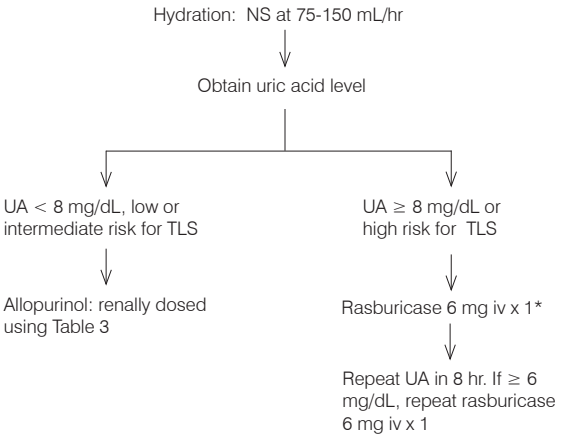
1 Two or more metabolic changes occurring 3 days before or 7 days after cytotoxic therapy. Changes are either 25% changes from baseline or abnormal values.
2 Laboratory TLS AND one or more clinical complications

TABLE 2	RISK FACTORS FOR TUMOR LYSIS SYNDROME		
Cancer Type	Low Risk	Intermediate Risk	High Risk
NHL	Indolent NHL	DLBCL	Burkitt's, lympho-blastic, B-ALL
ALL	—	WBC 50-100 K	WBC ≥ 100 K
AML	—	WBC 50-100 K	WBC ≥ 50 K, monoblastic
CLL	WBC ≤ 10 K	WBC 10-100 K, fludarabine treat-ment	—
Other hemato-logic malignancies (including CML and multiple myeloma) and solid tumors (SCLC, germ cell)	Remainder of patients	Rapid prolifera-tion with expected rapid response to therapy	—

MANAGEMENT

1. Consider discontinuing any medications known to impair uric acid excretion. These medications include:
   a. Hydrochlorothiazide
   b. Chlorthalidone
   c. Metolazone
   d Niacin

2. Using the following algorithm, initiate hydration, allopurinol and/or rasburicase



* If a dose other than 6 mg is chosen and clinically indicated, round to the nearest 1.5 mg.

TABLE 3 **RENAL DOSING OF ALLOPURINOL FOR TLS**

CrCl (mL/min)	Allopurinol Dose
> 20	300 mg po q24h
10-20	200 mg po q24h
< 10, IHD, CVVHDF, SLEDD	100 mg po q24h

MONITORING

1. Tumor lysis labs should be monitored every 8-12 hours for moderate/high risk patients or patients with elevated uric acid (BMP, phosphate, uric acid, and LDH) unless otherwise clinically indicated
2. Collect samples in a red top 8% PCA tube. This tube does NOT need to be pre-chilled, nor immersed in ice prior to transporting to lab.
3. Rasburicase should not be used in patients with prior hypersensitivity reaction to rasburicase or in patients with a history of G6PD deficiency
4. Rasburicase should not be used in patients with elevated uric acid and renal failure who are not at risk of tumor lysis syndrome

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PEDS

PEDIATRIC DOSING

Section Editors: Miranda Nelson, PharmD
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PEDIATRIC ANTIMICROBIAL DOSING

St. Louis Children's Hospital, Department of Pharmacy and
Division of Infectious Diseases, June 2013

TABLE 1 **FOR PEDIATRIC PATIENTS WITH NORMAL RENAL FUNCTION**

Drug	Pediatric Dose	Maximal Dose
Acyclovir	250-500 mg/m^2/dose every 8 hours (dose depends on specific disease)	—
Ampicillin	25-50 mg/kg/dose every 6 hours	2 gram/dose
Ampicillin/ sulbactam	25-50 mg ampicillin/kg/dose every 6 hours	2 gram/dose
Cefazolin	25 mg/kg/dose every 8 hours	2 gram/dose
Cefepime	50 mg/kg/dose every 8 hours	2 gram/dose
Cefotaxime	50 mg/kg/dose every 8 hours. Meningitis: 50 mg/kg/dose every 6 hours	2 gram/dose
Ceftazidime	50 mg/kg/dose every 8 hours	2 gram/dose
Ceftriaxone	50-75 mg/kg/dose every 24 hours Meningitis: 50 mg/kg/dose every 12 hours	2 gram/dose
Ciprofloxacin	10 mg/kg/dose every 12 hours. Cystic fibrosis: 10 mg/kg/dose every 8 hours	400 mg/dose
Clindamycin	10 mg/kg/dose every 6-8 hours	600 mg/dose
Gentamicin [1] Tobramycin [1]	2.5 mg/kg/dose every 8 hours Cystic fibrosis 3-3.5 mg/kg/dose every 8 hours- See next page for once daily dosing.	150 mg/dose
Meropenem	20 mg/kg/dose every 8 hours Meningitis: 40 mg/kg/dose every 8 hours	2 gram/dose
Nafcillin	50 mg/kg/dose every 6 hours (central line)	2 gram/dose
Oxacillin	50 mg/kg/dose every 6 hours (peripheral line)	2 gram/dose
Piperacillin/ tazobactam	60-75 mg piperacillin/kg/dose every 6-8 hours	3 gram/dose
Ticarcillin/ clavulanate	50-75 mg/kg/dose every 6 hours	3 gram/dose

1 Pediatric q8h gentamicin or tobramycin: check peak and trough with the 3rd dose

TABLE 2	NEONATAL DOSING
Drug	Dose
Acyclovir	20 mg/kg/dose every 8 hours
Ampicillin	100 mg/kg/dose every 12 hours (age < 7 days)
Cefazolin	25 mg/kg/dose every 12 hours (age < 7 days)
Gentamicin [1]	≥ 35 wk 5 mg/kg/day every 24 hours

1 Neonatal gentamicin: check peak and trough with the 3rd dose

TABLE 3	CLINDAMYCIN 5 MG/KG/DOSE IV	
Postmenstrual age (weeks)	Postnatal age (days)	Interval (hours)
≥ 35	0 to 7 >7	q8h q6h

Pediatric Dosing of Vancomycin	
Age	Initial Dose
< 3 mo	15 mg/kg/dose every 8 hours
3 mo - 11 mo	15 mg/kg/dose every 6 hours
1 yr - 8 yr	20 mg/kg/dose every 6 hours
9 yr - 13 yr	20 mg/kg/dose every 8 hours
≥ 14 yr	15 mg/kg/dose every 8 hours

1. Max Dose: 1500 mg/dose
2. Exclusions to this dosing: Patients with renal or cardiac insufficiency and patients receiving calcineurin inhibitors (cyclosporine/tacrolimus)
3. Check vancomycin trough level prior to 4th dose

ST. LOUIS CHILDREN'S HOSPITAL ONCE-DAILY GENTAMICIN/TOBRAMYCIN DOSING GUIDELINES

1. Exclusion criteria for once-daily dosing- use traditional dosing in these patients
   a. Altered volume of distribution: weight ≥ 20% IBW, ascites, or burns over ≥ 20% of body
   b. Unstable/compromised renal function or on dialysis
   c. Endocarditis, meningitis, tularemia, or osteomyelitis
   d. Hemodynamic instability
   e. PICU patients excluded unless patient has normal renal and cardiac function
   f. NICU patients

2. Dosing for children and adults *
   1 to < 14 years..... 7.5 mg/kg/dose IV every 24 hours
   ≥ 14 to < 18 years..... 6.5 mg/kg/dose IV every 24 hours
   ≥ 18 years..... 5 mg/kg/dose IV every 24 hours

   * Cystic fibrosis patients generally require 10-15 mg/kg/dose every 24 hours

3. Monitoring
   a. Consider checking a baseline serum creatinine at initiation of therapy
   b. Check a peak level 30 minutes after second dose completed
      Check an additional level 6-8 hours after the peak level
      Goal Peak 15 -25 mcg/ml
      Goal Trough <0.5 mcg/ml (trough will be extrapolated from the 2 levels drawn)
   c. Patients on long term therapy should have audiology examination and weekly serum creatinine along with aminoglycoside trough level every 7-10 days

Note: Goal peak reflects goal of achieving 8-10 times the MIC of gram-negative organisms. Certain species (i.e., Klebsiella oxytoca, E. cloacae and E. aerogenes, and Pseudomonas spp.) have the highest MICs.

FOR QUESTIONS
St. Louis Children's Hospital
Department of Pharmacy
314-454-2618

PEDIATRIC SEIZURE GUIDELINES

St. Louis Children's Hospital Department of Pharmacy, June 2013

COMMENTS

1. Physician order necessary to initiate medications
2. These are guidelines only, treatment may be individualized based on patient
3. Abbreviations used in these guidelines
   a. AED Antiepileptic Drug
   b. PE Phenytoin Equivalents
4. Approved by SLCH Pharmacy and Therapeutics Committee 5/2/2013
5. References on-file, Department of Pharmacy

SEIZURE ALGORITHM

0-4 minutes after start of seizure

Go to 5 minute stage if seizure duration unknown or > 5 minutes

- ✓ Assess ABC's and address any problems
- ✓ Diagnose seizure
- ✓ Maintain patient comfort & safety
- ✓ Complete survey examination, obtain a brief history, and consider finger stick glucose

↓

5 minutes after start of seizure and seizure continues

- ✓ Reassess ABC's and address any problems
- ✓ Call for additional help & assign team roles (RN, MD, PharmD)
- ✓ Establish IV/IO, consider electrolytes, glucose and AED levels. Treat accordingly.
- ✓ Administer IV **lorazepam** (0.1 mg/kg, maximal dose ~ 4 mg at 2 mg/min or less, typically over 2-4 minutes)
- ✓ Recommend max of 2 benzodiazepine doses in last 6 hours. If 2 benzodiazepine doses given in the 6 hours, may go to 11-14 minute stage.
- ✓ If no IV access, administer rectal **diazepam** (Diastat) while establishing IV
- ✓ **Diazepam, rectal (Diastat) dose**
  - 1-5 years: 0.5 mg/kg
  - 6-11 years: 0.3 mg/kg
  - >12 years: 0.2 mg/kg

  Dose options: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 17.5 mg, 20 mg

↓

6-10 minutes after start of seizure and seizure continues

- ✓ Reassess ABC's and address any problems
- ✓ If only one **lorazepam** dose given, may repeat IV **lorazepam** (0.1 mg/kg, see 5 minute stage for rate)
- ✓ May also go to 11-14 minute stage.

↓

continued on next page

11-14 minutes after start of seizure and seizure continues

✓ Reassess ABC's and address any problems

✓ Administer first dose of long-acting AED intravenously, fosphenytoin or phenobarbital

- If patient is already on phenytoin or fosphenytoin, consider lower loading dose of fosphenytoin or using phenobarbital
- **Fosphenytoin 20 mg PE/kg**. Maximum dose ~1500 mg PE at 3 mg PE/kg/min or less with a maximum rate of 150 mg PE/min, typically over 7-10 minutes.
- **Phenobarbital 20 mg/kg**. Maximum dose ~2000 mg at 1 mg/kg/min or less with a maximum rate of 30 mg/min if < 60 kg or 50 mg/min if > 60 kg, typically over 20 min
- If patient has significant respiratory depression or has hypotension, address problems and consider slowing infusion

✓ Consult Neurology

↓

15-30 minutes after start of seizure and seizure continues

✓ Reassess ABC's and address any problems

✓ If seizure continues ~20 minutes after starting first long-acting AED load, give an additional load of the first long-lasting AED used

- **Fosphenytoin 10 mg PE/kg**, maximum dose ~1500 mg PE at 3 mg PE/kg/min or less with a maximum rate of 150 mg PE/min, typically over 3-6 minutes
- **Phenobarbital 10 mg/kg** at 1 mg/kg/min or less with a maximum rate of 30 mg/min if < 60 kg or 50 mg/min if > 60 kg, typically over 10 minutes

✓ Consult Neurology

↓

> 30 minutes after start of seizure and seizure continues

✓ Reassess ABC's, address any problems, and consult Neurology

✓ If fosphenytoin used first, load with phenobarbital 20 mg/kg (see 11-14 minute stage for rate)

✓ If phenobarbital used first, give additional phenobarbital 10 mg/kg (see 15-30 minute stage for rate)

✓ If seizure stopped clinically or patient not returned to baseline or unsure if seizure has stopped, consider nonconvulsive status epilepticus. Arrange for EEG & consider PICU transfer.

↓

If juvenile myoclonic epilepsy (JME)

✓ Do NOT use fosphenytoin

✓ Use valproate sodium (Depacon) 15-30 mg/kg/dose IV (maximal dose 2000 mg) at 3 mg/kg/min after initial benzodiazepine, typically over 10-15 min

✓ Immediately consult Neurology

Lorazepam IV (Ativan)	
Dose	0.1 mg/kg/dose (max ~4 mg)
Available	2 mg/mL (1 mL vial)
Dilution	Dilute with equal amount of NS to 1 mg/mL
Administration	Not to exceed 2 mg/min. Give slowly (including flush) over 2-4 min
Rectal diazepam (Diastat)	
Dose	1-5 years = 0.5 mg/kg 6-11 years = 0.3 mg/kg > 12 years = 0.2 mg/kg (max 20 mg)
Available	2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 17.5 mg, or 20 mg syringes
Administration	1 Lock into dose ordered 2 Push up with thumb and pull to remove protective cover from syringe 3 Lubricate rectal tip with lubricating jelly 4 Turn patient on side, bend upper leg forward to expose rectum 5 Separate buttocks, gently insert syringe and push plunger slowly, hold in place for count of three 6 Take out syringe, hold buttocks together for count of three
Fosphenytoin IV (Cerebyx)	
Dose	Dose for status epilepticus 10-20 mg PE/kg (maximum ~1500 mg PE/dose)
Available	50 mg PE/mL (10 mL vial)
Dilution	Dilute with an equal amount of NS to 25 mg PE /mL
Administration	Not to exceed 3 mg PE/kg/min to a max of 150 mg PE/min Usually infused over 10 minutes
Phenobarbital IV (Luminal)	
Dose	Dose for status epilepticus 10-20 mg/kg (maximum ~2000 mg)
Available	130 mg/mL (1 mL vial)
Dilution	No need to dilute (OK to dilute in NS)
Administration	Not to exceed 1 mg/kg/min ~ maximum of 30 mg/min in children/adolescents < 60 kg, adults > 60 kg maximum of 50 mg/min. Usually infused over 20 minutes.

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SAFETY

PATIENT AND MEDICATION SAFETY DOSING AND TREATMENT

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BARNES-JEWISH Hospital BJC HealthCare | Washington University in St. Louis Physicians

NATIONAL LEADERS IN MEDICINE

DANGEROUS ABBREVIATIONS

Barnes-Jewish Hospital Pharmacy and Therapeutics Committee, June 2013

The following abbreviations and prescribing habits have been identified nationwide as frequent causes of medication errors. In order to reduce the risk of medication errors and to improve patient safety, the BJH Pharmacy and Therapeutics Committee has stated that these abbreviations should never be used for handwritten orders at the hospital. Please develop the habit now of using the safer alternative practices listed below.

DO NOT USE THESE ABBREVIATIONS		
Do not use	Common error/misinterpretation	Correction
U (unit)	Mistaken for "0" (zero), the number "4" (four) or "cc"	Write "unit"
IU (international unit)	Mistaken for IV (intravenous) or the number 10 (ten)	Write "International Units"
Q.D., QD, q.d., qd (daily) Q.O.D., QOD, q.o.d., qod (every other day)	Mistaken for each other. Period after the Q mistaken for "I" and the "O" mistaken for "I"	Write "daily" Write "every other day"
Trailing zero (X.0 mg) Lack of leading zero (.X mg)	Decimal point is missed	Write "X mg" Write "0.X mg"
MS, MSO4 and MgSO4	Confused for one another	Write "morphine sulfate". Write "magnesium sulfate"
STRONGLY DISCOURAGED ABBREVIATIONS		
Avoid the use	Common error/misinterpretation	Correction
μg (microgram)	Mistaken for "mg" causing an overdose	Use "mcg" or "microgram"
AU, AS, AD (Latin abbreviations for both ears, left and right ear)	Misinterpreted as the Latin abbreviation "OU" (both eyes); "OS" (left eye); "OD" (right eye)	Write "both ears", "left ear" or "right ear"
CC	Misread as "U" (units)	Use "mL" or "ml", or write "cubic centimeters" or "milliliters"
HS (half strength or Latin abbreviation for bedtime)	Mistaken for either half-strength or hour of sleep (at bedtime). qHS mistaken for every hour. All can result in a dosing error	Write out "half strength" or "at bedtime"
TIW (three times a week)	Misinterpreted as "three times a day" or "twice a week"	Use "three times a week" or specify days (e.g., Q MWF)

Version 10/11/11

DISCLOSURE OF ADVERSE EVENTS

Barnes-Jewish Hospital Patient Safety/Risk Management, June 2013

- Disclosure of adverse events should be done and documented when patients experience harm or intervention is necessary. The attending physician coordinates the disclosure efforts. Whenever possible, BJH and WUSM care teams should consult with each other about disclosure to patients, and may jointly provide disclosure so consistent messages are given to patients between services and institutions.

- Physicians employed by BJH should contact the attending physician when an adverse event has occurred prior to any discussion with the patient so they can help determine the best way to manage disclosure on a case-by-case basis.

- BJH patient safety and risk management staff should be notified of significant events and whether disclosure of these events has occurred. They provide support and guidance to care teams, if needed. They can be contacted at (office) 314-454-7566, (Hot line) 314-747-SAFE, or (on-call pager) 314-823-2649, as needed.

- Other BJH resources include Social Services, Pastoral Care, and the Medical Ethics Committee.

- Another available resource is the reference card, titled, WUSM Guidelines for Disclosure of Adverse Events to Patients that is given to first year residents and fellows. WUSM risk management staff can be contacted at (office) 314-362-6956 or (pager) 314-424-0411.

FALLS CAUSED BY HIGH RISK MEDICATIONS

Barnes-Jewish Hospital Department of Pharmacy, June 2013

Antiarrhythmic Agents
Digoxin (Lanoxin)
Disopyramide (Norpace)
Dronedarone (Multaq)
Flecainide (Tambocor)
Procainamide (Procanbid)
Quinidine

Anticholinergics
Antihistamines
Atropine
Belladonna and opium
Belladonna with phenobarbital
Chlorpheniramine
Cyproheptadine (Periactin)
Darifenacin (Enablex)
Dicyclomine (Bentyl)
DiphenhydrAMINE (Benadryl)
Flavoxate (Urispas)
Glycopyrrolate (Robinul)
Hyoscyamine
Hydroxyzine (Vistaril)
Oxybutynin (Ditropan XL/Oxytrol)
Scopolamine (Transderm Scop)
Solifenacin (Vesicare)
Tolterodine (Detrol)
Trospium (Sanctura)

Antidepressants
Amitriptyline (Elavil)
Clomipramine (Anafranil)
Desipramine (Norpramin)
Doxepin (Sinequan)
Fluoxetine (Prozac)
Fluvoxamine (Luvox)
Imipramine (Tofranil)
Paroxetine (Paxil)
Trimipramine (Surmontil)
Trazodone (Desyrel)

Antiemetics
Metoclopramide (Reglan)
Promethazine (Phenergan)
Prochlorperazine (Compazine)
Trimethobenzamide (Tigan)

Antiepileptics
Carbamazepine (Tegretol/Equetro)
Divalproex (Depakote)
Felbamate (Felbatol)
Gabapentin (Neurontin)
Phenobarbital
Phenytoin (Dilantin)
Valproic acid (Depakene)

Antipsychotics
Aripiprazole (Abilify)
ChlorproMAZINE
Clozapine (Clozaril)
Haloperidol (Haldol)
Iloperidone (Fanapt)
Lurasidone (Latuda)
Olanzapine (Zyprexa)
Olanzapine/Fluoxetine (Symbyax)
Quetiapine (Seroquel)
Risperidone (Risperdal)
Thioridazine (Mellaril)
Ziprasidone (Geodon)

Benzodiazepines
Alprazolam (Xanax)
Chlordiazepoxide (Librium)
Clonazepam (Klonopin)
Diazepam (Valium)
Lorazepam (Ativan)
Temazepam (Restoril)

Dopamine Agonists
Amantadine (Symmetrel)
Benztropine (Cogentin)
Bromocriptine (Parlodel)
Pergolide (Permax)
Pramipexole (Mirapex)
Ropinirole (Requip)
Trihexyphenidyl (Artane)

Miscellaneous
Chlorpropamide
Glyburide
Pregabalin (Lyrica)

Muscle Relaxants
Carisoprodol (Soma)
Cyclobenzaprine (Flexeril)
Metaxalone (Skelaxin)
Methocarbamol (Robaxin)
Orphenadrine (Norflex)
Tizanidine (Zanaflex)

Sedatives/Hypnotics
Eszopiclone (Lunesta)
Zaleplon (Sonata)
Zolpidem (Ambien/Ambien CR)

Vasodilators
HydrALAZINE (Apresoline)
Isosorbide dinitrate (Isordil)

Important Note: This not an all-inclusive list of medications that may increase the fall risk in the elderly population. There are several other medications and coinciding disease states that have been associated with an increased fall risk or an increased risk of injury if a fall occurs.

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HIGH RISK MEDICATIONS

Barnes-Jewish Hospital Pharmacy and Therapeutics Committee, June 2013

These medications are involved in a high number of medication errors or reviewable events and carry a high risk for abuse, errors or other adverse outcomes. Special restrictions, required competencies, standardized concentrations and redundant systems are some of the actions taken to decrease potential events associated with these medications. Some examples of high risk medications are listed below.

ADRENERGIC AGONISTS

e.g., DOBUTamine, DOPamine, EPINEPHrine, norepinephrine, phenylephrine

- Standard iv concentrations
- Infusions are validated by an second RN
- Restricted by physician availability, nursing competency, necessary equipment, and monitoring.
- Pyxis Screen Alert for EPINEPHrine 1 mg ampule – "Not for iv Use"

ANTICOAGULANTS

e.g., argatroban, bivalirudin

- Standard iv concentrations
- Infusions require a 2nd iv pump check by an RN

BENZODIAZEPINES

e.g., lorazepam, midazolam

- Standard iv concentrations
- For ICU sedation, level of sedation is assessed according to the Critical Care Policy: S-1 Sedation and Analgesia in the Critically Ill Adult – Guidelines for Sustained Use
- CADD cassettes compounded by iv room have color coded stickers
- Infusions require a 2nd iv pump check by an RN

CHEMOTHERAPEUTIC AGENTS

- See Organizational Policy: Medication Management-Chemotherapy/Biological Response Modifiers Administration
- Delivered in a sealed plastic bag with warning stickers

DEXTROSE, HIGH CONCENTRATION

- D10%W is highest concentration available in floor stock

ELECTROLYTES

e.g., calcium, magnesium, potassium

- Standard iv concentrations
- Concentrated electrolytes have limited or no availability in non-ICU patient care units
- Calcium gluconate vials are only available in restricted areas

HEPARIN
- Weight-based order set available in Compass
- Standard iv concentrations
- Infusions require a 2nd iv pump check by an RN
- Pyxis Screen Alert for heparin-"High Alert Double Check".

INSULIN, INTRAVENOUS DRIP DOSING
- Standard iv concentrations
- Infusions are validated by a second RN
- Pyxis Screen Alert for insulin-"High Alert Double Check".

INSULIN, SUBCUTANEOUS DOSING
- Doses are verified by 2 RN's
- Standardized insulin formulary
- Specialty insulins are dispensed patient specific
- Standardized order set in Compass
- Pyxis Screen Alert for insulin-"High Alert Double Check".

NEUROMUSCULAR BLOCKING AGENTS
e.g., atracurium, pancuronium, rocuronium, succinylcholine, vecuronium
- infusions require a 2nd iv pump check by an RN
- Restricted by physician availability, nursing competency, necessary equipment, and monitoring
- Access is limited in ORs
- Paralytic agents labeling and storage in Pyxis Medstations is enhanced to include "high alert caution" and "paralytic agent" labels. These are stored in containers with lids.

OPIATES
e.g., fentanyl, hydromorphone, meperidine, morphine
- Limited formulary available
- CADD cassettes compounded by the iv room have color coded stickers
- Infusions require a 2nd iv pump check by an RN

SODIUM CHLORIDE INJECTION > 0.9% CONCENTRATION
- 23.4% sodium chloride vials have warning stickers and use is limited to ICU
- Concentrated sodium chloride is not stocked outside the pharmacy except ICUs

THROMBOLYTICS
- Pyxis Screen Alert Reteplase – two separate injections thirty minutes apart
- Pyxis Screen Alert Tenecteplase – one-time injection weight-based

WAYS TO AVOID COMMON PRESCRIBING ERRORS

The Joint Commission has guidelines to improve patient safety, medication use and prevent medication errors. In order to be in compliance with the standards, a BJH policy on dangerous abbreviations was instituted along with the following medication safety initiatives.

When prescribing medications

1. **Indication or purpose for medication** must be included when ordering a new drug. Doing so helps prevent look-alike sound-alike errors by further identifying the medication by use. Indication is not required for dose or frequency changes.

Incorrect	Correct
Pravachol 30 mg po qd	Pravachol 30 mg po qday for cholesterol
Prevacid 30 mg po qd	Prevacid 30 mg po qday for GE reflux
Celebrex 200 mg po qd	Celebrex 200 mg po qday for pain
Celexa 20 mg po qd	Celexa 20 mg po qday for depression

2. **Range orders** for frequency (e.g., q4-6h) are not acceptable. Ideally range orders for dose should be tied to a specific parameter to confirm that the order has one meaning to everyone that reads it and the proper dose is given. If no specific parameters are ordered by a physician, nurses must assess the patient to determine the initial dose.

Incorrect	Correct
Morphine 2-4 mg iv q4-6h	Morphine 2 mg iv q6h prn pain score 1-6 Morphine 4 mg iv q6h prn pain score 7-10
Zofran 4-8 mg iv q6-8h prn emesis	Zofran 4-8 mg iv q8h prn emesis (Note: in this example, RN must assess patient since MD-specified parameter not part of the order)

3. **Avoid dangerous handwritten abbreviations**: see Dangerous Abbreviations monograph in this handbook.

4. **Use of patient's own medications** has been problematic because documentation of doses is often inaccurate or incomplete. The following guidelines were designed to promote patient safety.

   a. Use of home medications are limited to certain drugs (e.g., dietary supplements, investigational meds, birth control pills) and must be approved by the physician or pharmacist.
   b. Home medications must be kept in locked storage whether self-administered or administered by the nurse.
   c. Full medication orders noting use of home medications must be written/entered so these medications can be documented in Compass by Nursing.

5. **Immediate vs. sustained release**: always indicate sustained release vs immediate release products, eg, diltiazem vs diltiazem CD, NIFEdipine vs. NIFEdipine CC or XL.

6. **Correcting a handwritten order**: do not change an original order after it has been written (e.g., by scratching it out). Instead make clarifications by writing a new order.

7. **Weight-based orders**: avoid writing weight-based orders for drugs administered as intermittent infusions or single doses

Incorrect	Correct
Enoxaparin 1 mg/kg sq now	Enoxaparin 100 mg sq now for DVT
Gentamicin 5 mg/kg iv now	Gentamicin 350 mg iv now for sepsis

8. **Sound alike/look alike**: Be aware of sound alike or look alike drug names.
   a. Make orders clear, eg, Cartia vs Cardura vs Procardia
   b. When taking telephone/verbal orders, write down or enter the order immediately and read back what was written/entered to verify that the information was transcribed correctly.

9. **Patient labels**: never write an order without complete patient information present on the order sheet (using patient labels).

10. **Take care in selecting the correct patient** and the correct medication when entering electronic medication orders.

SOUND/LOOK ALIKE MEDICATION ERRORS

Barnes-Jewish Hospital Departments of Pharmacy and Patient Safety, June 2013

HOW SOUND/LOOK ALIKE ERRORS ARE REDUCED AT BJH

1. Electronic alerting within various computer systems
2. Warning stickers are placed on problematic drugs
3. TALLman lettering is used in storage areas, and when possible by existing software, within computer systems
4. Similarly named drugs are stored away from each other in Pyxis and within all storage areas
5. Indication is required for all new drug orders

BE AWARE OF THE FOLLOWING MEDICATIONS THAT SOUND OR LOOK SIMILAR TO OTHER MEDICATIONS

- ✓ AmLODIPine vs. AMILoride
- ✓ Celebrex vs. Celexa vs. Cerebyx
- ✓ Clonidine vs. Clonazepam
- ✓ Concentrated vs. Conventional liquid morphine
- ✓ Effexor XR vs. Effexor
- ✓ Folic acid vs. Folinic acid (leucovorin)
- ✓ HydrALAZINE vs. HydrOXYzine
- ✓ Hydromorphone injection vs. Morphine injection
- ✓ Insulin products
- ✓ Jantoven (warfarin), Janumet (sitagliptin/metformin), Januvia (sitagliptin)
- ✓ Lipid-based OR conventional DAUNOrubicin vs. DOXOrubicin
- ✓ QuiNINE sulfate vs. QuiniDINE gluconate vs. QuiniDINE sulfate
- ✓ Tdap vaccine (Adacel) vs. DTaP vaccine (Daptacel or Infanrix)
- ✓ Wellbutrin SR vs. Wellbutrin XL
- ✓ Zyprexa vs. Zyrtec

ASP

ANTIBIOTIC STEWARDSHIP PROGRAM

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INTRODUCTION

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

HISTORY AND PURPOSE

In 1985, the original Antibiotic Control Program (ACP) for Barnes Hospital was conceived as a joint effort of the Division of Infectious Diseases, the Department of Pharmacy, and the Program in Hospital Administration, at Washington University School of Medicine. The goal was to improve patient care by providing one-on-one teaching of house staff through interactions with infectious diseases fellows who were on-call by pager. Antibiotics were approved using criteria developed by the Antibiotic Utilization Review Subcommittee (AUR). A similar program was developed concurrently at the Jewish Hospital of St. Louis. Results of the positive impact of the original ACP have been published.[1-4]

Over the years, numerous modifications were enacted. Originally, only a handful of intravenous antibiotics were controlled. But the program was quickly expanded to include numerous broad spectrum intravenous antibiotics, oral antibiotics, as well as antifungals and antiviral agents. Clinical pharmacists were added to the list of antibiotic approval personnel in 1987. Then, mirroring the hospitals' merger in 1993, the ACP at each institution was merged into one unified program in 1994.

With two decades of experience, the ACP has transitioned into an "Antibiotic Stewardship Program" (ASP), as defined by the Infectious Diseases Society of America (IDSA)[5] Our ASP incorporates many components: a hospital committee to manage the program, which includes the expertise of ID physicians and ID clinical pharmacists; numerous hospital-specific guidelines and clinical pathways; formulary restrictions with preauthorization of selected antimicrobials; a robust informatics infrastructure to monitor drug usage; ID attendings/fellows and a large number of clinical pharmacists who make recommendations on antibiotic therapy as part of their routine practice; active surveillance of microbial resistance and a system of cascaded reporting of antimicrobial susceptibilities by our microbiology laboratory; an Informatics and Pharmacy-based dose-optimization program; and routine drug-use evaluations to assess the appropriateness of specific therapies.

As the title of this Tool Book section implies, these are only guidelines. We anticipate that departures from them will be necessary on occasion. In order to keep these guidelines up-to-date, we will seek input from numerous clinicians on campus and will continually incorporate new data based on local experience, local antimicrobial susceptibility patterns, clinical trials, and national treatment guidelines.

ACKNOWLEDGMENTS

The Pharmacy would like to acknowledge the founders of the original antibiotic control program: Gerald Medoff, MD, Gary Weil, MD, James L. Gray, PharmD, Candace Lawrenz, PharmD, Robert Woodward, PhD.

In addition, the Pharmacy would like to thank numerous attendings and fellows from the Infectious Diseases Division, and clinical and unit-based pharmacists, and pharmacy residents, who, over the years, have provided expert opinion as well as fielded antibiotic approvals via pager at BJH. Lastly, Pharmacy thanks BJH Administration for their continuing support of the program.

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PREVENTING ANTIMICROBIAL RESISTANCE IN HOSPITALIZED ADULTS

Centers for Disease Control, http://www.cdc.gov/drugresistance/healthcare

PREVENT INFECTION	
Step 1	**Vaccinate** • Give influenza/pneumococcal vaccine to at-risk patients before discharge • Get influenza vaccine annually
Step 2	**Get the catheters out** • Use catheters only when essential • Use the correct catheter • Use proper insertion and catheter-care protocols • Remove catheters when they are no longer essential
DIAGNOSE AND TREAT INFECTION EFFECTIVELY	
Step 3	**Target the pathogen** • Culture the patient • Target empirical therapy to likely pathogens and local antibiogram • Target definitive therapy to known pathogens and antimicrobial susceptibility test results
Step 4	**Access the experts** • Consult ID experts for patients with serious infections
USE ANTIMICROBIALS WISELY	
Step 5	**Practice antimicrobial control**
Step 6	**Use local data** • Know your antibiogram • Know your patient population
Step 7	**Treat infection, not contamination** • Use proper antisepsis for blood and other cultures • Culture the blood, not the skin or catheter hub • Use proper methods to obtain and process all cultures
Step 8	**Treat infection, not colonization** • Treat pneumonia, not the tracheal aspirate • Treat bacteremia, not the catheter tip or hub • Treat UTI, not the indwelling catheter
Step 9	**Know when to say "no" to vancomycin** • Treat infection, not contaminants or colonization • Fever in a patient with an iv catheter is not a routine indication for vancomycin
Step 10	**Stop antimicrobial treatment** • When infection is cured • When cultures are negative and infection is unlikely • When infection is not diagnosed
PREVENT TRANSMISSION	
Step 11	**Isolate the pathogen** • Use standard infection control precautions • Contain infectious body fluids (follow airborne, droplet, and contact precautions) • When in doubt, consult Infection Control
Step 12	**Break the chain of contagion** • Stay home when you are sick • Keep your hands clean • Set an example

ANTIBIOGRAM

Barnes-Jewish Hospital, Department of Clinical Microbiology, January-December 2012

PERCENT OF STRAINS SUSCEPTIBLE

GRAM POSITIVE COCCI	# STRAINS TESTED	AMPICILLIN	CEFTRIAXONE	CEFTRIAXONE (NON MENINGITIS)	CEFTRIAXONE (MENINGITIS)	CLINDAMYCIN	ERYTHROMYCIN	GENT - HIGH LEVEL	NITROFURANTOIN	OXACILLIN (CEFAZOLIN)	PENICILLIN	PENICILLIN (NON-MENINGITIS)	PENICILLIN (MENINGITIS)	TRIMETHA/SULFA	VANCOMYCIN
Staphylococcus aureus	1802		*			68	34			46				97	96
Staphylococcus epidermidis	257		*			55	28			25				47	99
Staphylococcus coag-negative	122		*			60	33			51				62	97
Staphylococcus lugdunensis	36		*			76	76			94				94	100
Enterococcus faecalis	201	100						64	98						89
Enterococcus faecium	158	9						94	19						23
Enterococcus species	684	78						74	80						71
Streptococcus anginosus group	149		99				77				99				
Streptococcus mitis group	46		91				25				72				
Streptococcus pneumoniae	77			93	75		51					84	52		
Streptococcus viridans group	33		91				44				67				

Shaded boxes indicate organism/antimicrobial combinations not tested routinely.
Data based on first isolates tested per patient (inpatients and ED patients).
* Staphylococci susceptible to oxacillin are always susceptible to ceftriaxone

GRAM NEGATIVE BACILLI	# STRAINS TESTED	AMPICILLIN	CEFAZOLIN	CEFEPIME	CEFOXITIN	CEFTRIAXONE	CIPROFLOXACIN	GENTAMICIN	LEVOFLOXACIN	MEROPENEM	PIPERACILLIN/ TAZOBACTAM	TICARCILLIN/ CLAVULANIC ACID	TRIMETHA/SULFA
Acinetobacter baumannii comp.	55			58				69		64	65		56
Citrobacter freundii complex	74	*	*	99	*	*	91	95		99	*		84
Citrobacter koseri	63	0	97	100	96	100	94	100		100	98		92
Enterobacter aerogenes	100	*	*	99	*	*	100	99		99	*		100
Enterobacter cloacae	216	*	*	99	*	*	93	98		99	*		85
Escherichia coli	1917	41	85	98	88	94	74	90		99	97		71
Klebsiella oxytoca	107	0	51	100	98	95	99	97		100	92		91
Klebsiella pneumoniae	652	0	89	96	83	91	89	95		97	92		80
Morganella morganii	32	*	*	100	*	*	63	81		100	*		56
Proteus mirabilis	280	78	86	100	98	99	69	90		100	99		73
Pseudomonas aeruginosa	691			91			79	83		81	92		
Serratia marcescens	85	*	*	99	*	*	93	99		100	*		89
Stenotrophomonas maltophilia	106								84			57	91

Shaded boxes indicate organism/antimicrobial combinations not tested routinely.
Data based on first isolates tested per patient (inpatients and ED patients).
* Because of the presence of inducible beta-lactamase, these organisms should be considered resistant to the antimicrobial indicated.

ANTIMICROBIAL COST INDEX

Barnes-Jewish Hospital, Department of Pharmacy, May 9, 2013

* Cost index is the daily acquisition cost of the drug relative to the daily cost of the least expensive agent in the class, respectively. Dosing is based on a 70 kg patient.

ANTIBACTERIALS

Drug	Usual Dose	Cost Index *
Ciprofloxacin po	500 mg q12h	1.0
Trimethoprim/sulfa. DS po	1 DS q12h	1.3
Ceftriaxone	1 g q24h	5.1
Cefazolin	1 g q8h	5.9
Metronidazole po	500 mg q8h	8.0
Moxifloxacin po	400 mg q24h	9.2
Azithromycin iv	500 mg q24h	10.4
Metronidazole iv	500 mg q8h	11.1
Clindamycin po	450 mg q6h	13.3
Clindamycin iv	900 mg q8h	13.3
Tobramycin	350 mg q24h	14.4
Gentamicin	350 mg q24h	15.6
Ciprofloxacin iv	400 mg q12h	16.4
Vancomycin iv	1 g q12h	26.0
Penicillin G iv	2 mU q4h	29.1
Moxifloxacin iv	400 mg q24h	30.8
Cefoxitin	1 g q6h	39.3
Amikacin	1 g q24h	46.1
Ampicillin iv	1 g q6h	55.5
Colistin	150 mg q12h	78.6
Piperacillin/tazobactam	3.375 g q6h	86.5
Vancomycin po	125 mg q6h	89.8
Cefepime	1 g q12h	96.5
Aztreonam	1 g q8h	120.5
Trimethoprim/sulfa. iv	350 mg q8h	148.9
Meropenem	500 mg q6h	169.4
Ertapenem	1 g q24h	249.2
Oxacillin iv	2 g q6h	255.4
Ceftaroline	600 mg q12h	286.7
Ampicillin/sulbactam	3 g q6h	368.1
Chloramphenicol iv	1 g q6h	422.2
Erythromycin iv	1 g q6h	610.9
Tigecycline	50 mg q12h	613.3
Linezolid po	600 mg q12h	723.4
Fidaxomicin	200 mg q12h	740.4
Linezolid iv	600 mg q12h	831.5
DAPTOmycin	420 mg q24h	1118.9
Quinupristin/dalfopristin	500 mg q8h	2000.9
Telavancin	750 mg q24h	Drug unavailable

Reference on file: 13-26, Department of Pharmacy

ANTIFUNGALS

Drug	Usual Dose	Cost Index *
Fluconazole po	400 mg q24h	1.0
Amphotericin B deoxycholate	40 mg q24h	27.8
Fluconazole iv	400 mg q24h	26.5
Itraconazole po	200 mg q24h	60.4
VoriCONAZOLE po	200 mg q12h	138.0
Micafungin	100 mg q24h	146.5
Anidulafungin	100 mg q24h	143.8
Posaconazole po	200 mg q6h	341.6
VoriCONAZOLE iv	280 mg q12h	244.3
Caspofungin	50 mg q24h	669.0
Amphotericin B liposomal	350 mg q24h	728.7

Reference on file: 13-48, Department of Pharmacy

ANTIVIRALS

Drug	Usual Dose	Cost Index *
Acyclovir po	400 mg 5x/day	1.0
Amantadine	100 mg q12h	2.3
Rimantadine	100 mg q12h	6.1
ValACYclovir po	1 g q12h	6.1
Acyclovir iv	350 mg q8h	11.3
Zanamivir	10 mg q12h	16.4
Oseltamivir	75 mg q12h	28.4
Ganciclovir iv	350 mg q12h	127.4
Foscarnet iv	4200 mg q8h	291.2
ValGANciclovir	900 mg q12h	317.8
Cidofovir iv	350 mg x1 dose	966.8

Reference on file: 13-68, Department of Pharmacy

OBTAINING ID APPROVAL

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

BARNES-JEWISH HOSPITAL
ID DIVISION PHONE ATTENDANT/PAGING SYSTEM
24 hrs/day 747-3535

WAYS TO OBTAIN ID APPROVAL

1. Call the ID Phone Attendant (747-3535). When prompted, select menu option 2. Depending on the time of day and day of week, you will be connected to an ID fellow or a clinical pharmacist.

2. Curbside or formal ID consult with an ID fellow or attending, select menu option 1

3. Clinical and unit-based pharmacists (UBPs) assigned to specific nursing divisions may also approve antibiotics. UBPs may only approve antibiotics on their designated nursing divisions. Pharmacists will refer the requesting physicians to an ID fellow (ID Team 2) if the request does not meet the AUR-designated approval criteria.

4. Between 10 pm and 8 am, Pharmacy will release one dose of any restricted antibiotic but further doses will require ID approval.

ID PHONE ATTENDANT MENU OPTIONS (747-3535)

1 ID consult/ID triage fellow
2 Inpatient antibiotic approval
3 Accidental needlestick/body substance exposure
4 Hospital Infection Control
5 Outpatient issues/ID clinic
6 ID attending physicians
7 Repeat menu

COMPASS NOTIFICATION OF ID APPROVAL

1. When entering an order for an antibiotic, prescribers will be alerted to the antibiotic's restriction status. For restricted, non-formulary, ID specialist, and ID consult required antibiotics, approval is required immediately. For controlled antibiotics, ID approval will be required 72 hours after the initiation of the order. Only ID consultants may complete Compass orders for drugs in the ID Consult Required category.

2. In the Orders tab, a blue or red R (review) icon will appear beside an antibiotic listed on the medication profile depending on the restriction status of that antibiotic and its expiration date. ID approval should be obtained whenever a prescriber sees a blue or red R icon beside an antibiotic's name. The R icon turns from blue to red on the expiration date for that antibiotic.

3. A blue R (review) icon appears immediately whenever a restricted, non-formulary or ID specialist antibiotic is ordered. In contrast, the blue R icon will appear 48 hours before the expiration date for a controlled antibiotic (which allows two days for an approval to be obtained).

4. Once the prescriber has obtained approval, the approval is entered into Compass by ID approval personnel or Pharmacy. ID approvals entered into Compass appear in the Orders tab under Infectious Diseases Approvals. When Pharmacy processes an antibiotic order, a new expiration date is entered that then establishes a new date on which the R icon will reappear, e.g., two weeks later.

ANTIMICROBIAL RESTRICTION CATEGORIES

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

- Antimicrobials are classified into eight restriction categories
- See Antimicrobial Restrictions By Drug Class for a list of drugs

CATEGORY	DEFINITION
UNRESTRICTED	Does not require ID approval to initiate therapy
CONTROLLED	ID approval is required after the initial 72 hours. Applies to these drugs only: • Amikacin • Ciprofloxacin iv • Tobramycin • Vancomycin iv
RESTRICTED	ID approval required to initiate therapy.
NON-FORMULARY	Not routinely stocked by Pharmacy and therefore a delay may occur while Pharmacy obtains the drug. ID approval required to initiate therapy.
ID SPECIALISTS	ID approval may be obtained only from a subset of approval personnel: ID attendings, ID fellows, designated clinical pharmacists (Casabar, Ritchie, BMT clinical pharmacists, ID pharmacy resident). Applies to these drugs only: • Amphotericin B deoxycholate (non-formulary) • Ceftaroline • Chloramphenicol, iv • DAPTOmycin • Linezolid, iv and po • Quinupristin/dalfopristin (non-formulary) • Telavancin • Tigecycline
ID CONSULT REQUIRED	A formal ID consult must be obtained in order to initiate therapy. Compass order bundles may be completed only by ID consultants. Applies to these drugs only: • Antibiotic lock therapy • Fidaxomicin
ROUTE	Routes listed below require ID approval to initiate therapy. Applies to these drugs only: • Non-intravenous uses of Amphotericin B deoxycholate • Colistin, inhaled
DOSE	Doses other than those listed below require ID approval to initiate therapy. Applies to these drugs only: • Fluconazole 150 mg x 1 dose for vulvovaginal candidiasis • Vancomycin po 125 mg q6h for C. difficile infection

ANTIMICROBIAL RESTRICTIONS BY DRUG CLASS

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

BARNES-JEWISH HOSPITAL
ID DIVISION PHONE ATTENDANT/PAGING SYSTEM
24 hrs/day 747-3535

An antimicrobial is added to the Formulary by the AUR Subcommittee only after a review of its therapeutic advantages, efficacy, side-effect profile and the clinical evidence to support its use. A more complete list of antimicrobials and their respective restriction categories can be found in the BJH Formulary, which is accessible only through the BJH LAN:

http://www.crlonline.com/crlsql/servlet/crlonline

In assigning an antimicrobial's restriction status, AUR considers many factors including but not limited to: the antimicrobial's role in empirical therapy; expertise needed to use the drug appropriately; potential for toxicity and misuse; and whether or not alternative drugs should be considered first-line when compared to the newer agent.

ANTIMICROBIAL	STATUS	COMMENTS
AMINOGLYCOSIDES		
Gentamicin	Unrestricted	
Tobramycin	Controlled, 72 hr	
Amikacin	Controlled, 72 hr	
ANTIFUNGALS		
Ampho. B, liposomal	Unrestricted	Ambisome
Ampho. B lipid complex	Non-formulary	ABLC (Abelcet)
Ampho B deoxycholate, iv	ID specialists only	
Ampho. B deoxy, non-iv	Route restricted	All non-iv routes restricted
Anidulafungin	Non-formulary	
Caspofungin	Non-formulary	
Fluconazole iv	Restricted	
Fluconazole po	Dose restricted	150 mg po x1 unrestricted for VVC
Itraconazole po	Unrestricted	iv no longer manufactured
Micafungin	Restricted	
Posaconazole	Restricted	
VoriCONAZOLE iv/po	Restricted	
ANTIVIRALS		
Acyclovir iv/po	Unrestricted	
Cidofovir	ID specialists only	
Foscarnet	ID specialists only	
Ganciclovir iv/po	IV restricted, po unrestricted	
ValGANciclovir	Unrestricted	
CARBAPENEMS		
Doripenem	Non-formulary	
Ertapenem	Restricted	
Imipenem	Non-formulary	
Meropenem	Restricted	

ANTIMICROBIAL	STATUS	COMMENTS
CEPHALOSPORINS		
Cefazolin (1st generation)	Unrestricted	
Cephalexin (1st generation)	Unrestricted	
Cefuroxime axetil (2nd generation)	Unrestricted	
Cefotetan (2nd generation)	Unrestricted	
Cefoxitin (2nd generation)	Unrestricted	
Ceftriaxone (3rd generation)	Unrestricted	
Ceftazidime (3rd generation)	Non-formulary	
Cefepime (4th generation)	Unrestricted	
Ceftaroline (Advanced generation)	ID specialists only	
All others	Non-formulary	
MACROLIDES		
Erythromycin	Unrestricted	
Clarithromycin	Unrestricted	
Azithromycin	Unrestricted	
All others	Non-formulary	
MISCELLANEOUS		
Aztreonam	Restricted	
Chloramphenicol	ID specialists only	
Clindamycin	Unrestricted	
Colistin	IV and inhalation restricted	
DAPTOmycin	ID specialists only	
Fidaxomicin	ID consult required	
Lactobacillus	Non-formulary	
Linezolid iv/po	ID specialists only	
Metronidazole	Unrestricted	
Quinine	Non-formulary	
Quinupristin/dalfopristin	ID specialists only (non-formulary)	
Telavancin	ID specialists only	
Tigecycline	ID specialists only	
Trimethoprim/sulfamethoxazole	Unrestricted	
Vancomycin iv	Controlled, 72 hrs	
Vancomycin po	Dose restricted	Unrestricted: 125 mg po q6h for CDI
PENICILLINS		
Ampicillin	Unrestricted	
Ampicillin/sulbactam	Unrestricted	
Amoxicillin	Unrestricted	
Penicillin	Unrestricted	
Oxacillin	Unrestricted	
Piperacillin/tazobactam	Restricted	
Ticarcillin/clavulanate	Non-formulary	
All others	Non-formulary	
QUINOLONES		
Ciprofloxacin	IV controlled 72 hrs, po unrestricted	
Moxifloxacin iv/po	Restricted	
All others	Non-formulary	

RESTRICTION CATEGORY	DEFINITION
Unrestricted	Use does not require ID approval
Controlled	Unrestricted use for initial 72 hrs, ID approval required thereafter
Restricted	ID approval required to initiate
Non-formulary	ID approval required to initiate, not stocked in Pharmacy
ID specialist	ID approval by ID specialists only
ID consult required	ID consult required to initiate therapy
Dose restricted	ID approval required to initiate non-standard doses
Route restricted	ID approval required to initiate certain routes

AMINOGLYCOSIDES

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Gentamicin
Controlled, 72 hrs	Amikacin, Tobramycin

APPROVAL CRITERIA FOR AMIKACIN AND TOBRAMYCIN

1. Presence of aerobic gram-negative infection documented by culture and sensitivity that is resistant to gentamicin but susceptible to amikacin or tobramycin

DOSING

Two methods may be used: traditional dosing vs. extended interval dosing. Prescribers should be very careful in selecting the dosing method used, since dosing errors can lead to significant toxicity. See Aminoglycoside Dosing monograph.

TOXICITY

1. Monitor for nephrotoxicity. Check serum creatinine (Scr) 2-3 times/week, if within normal limits. Check every other day if Scr is elevated but stable. Check daily if renal function unstable.
2. For >10% rise in Scr, adjust dose/interval; recheck Scr and drug concentrations.
3. Monitor for ototoxicity (e.g., high frequency hearing loss, disturbances in balance) and discontinue aminoglycosides or adjust dose as appropriate. Baseline audiometry is suggested in patients receiving therapy for more than 2 weeks. To obtain audiometric testing call 362-7489.
4. Duration of therapy is typically less than 14 days, unless treating osteomyelitis or endocarditis.

AMINOGLYCOSIDE DOSING

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

These recommendations were developed by a panel of experts from Pharmacy and Divisions of Infectious Diseases and Nephrology. Input was also obtained from specialists in critical care, bone marrow transplant/oncology and cystic fibrosis..

TRADITIONAL VS. EXTENDED INTERVAL DOSING

Traditional dosing is a dosing method in which "low" doses are given frequently, e.g., 1-2 mg/kg gentamicin q12h in patients with normal renal function. **Extended interval dosing (EID)** uses "high" doses given q24h or less frequently, e.g., 5 mg/kg gentamicin given q24h, q36h or q48h. EI dosing was adopted at BJH around 1997 for these reasons:

1. In vitro, aminoglycosides exhibit concentration dependant killing, i.e., high drug concentrations are more bactericidal.
2. With certain bacteria, aminoglycosides exhibit a post-antibiotic effect (PAE), i.e., the drug continues to kill bacteria despite low concentrations in the plasma.
3. Clinical trials suggest that both dosing strategies are effective in a variety of patient populations. However, EDI may be less toxic because its long dosing intervals allow for more drug to be cleared from the body, and as a result, accumulation of drug in the kidneys or vestibular apparati is diminished.
4. An EID nomogram for BJH was developed based on data collected on more than 500 BJH patients. Bailey TC, et al. Clin Infect Dis. 1997;24:786-95.

Although EID may have a lower risk for toxicity, it does not negate it. Regardless of which dosing method is used, toxicity is influenced by other factors, e.g., pre-existing renal or hepatic dysfunction, hypotension and concomitant nephrotoxins.

AVOIDING DOSING ERRORS

1. Carefully choose the dosing method based on Table 1
2. Determine if "overlooked" doses were recently administered, e.g., a loading dose given in the Emergency Department or doses administered prior to transfer to BJH.
3. Assess recent drug levels prior to initiating therapy
4. If prior drug levels are available, assess if they were drawn correctly
5. If not already performed, obtain baseline SCr, body weight and height prior to initiating therapy.

CHOOSING THE APPROPRIATE METHOD OF DOSING

The method of dosing is based on the drug's indication and presence of contraindications or use of chronic renal replacement therapy (CRRT) in Table 1.

TABLE 1	TRADITIONAL	EXTENDED INTERVAL (EI)
Typical gentamicin dose in a patient with normal renal function	1-2 mg/kg q12h Dose based on indication	5 mg/kg q24h 8 mg/kg q24h for CF patient
Indications	• Bone/joint infection • Endocarditis • Gram-positive infection • Mycobacterial infection • Septic shock • Skin/soft tissue infection • Urinary tract infection • When EID is contraindicated	• CNS infection • Cystic fibrosis • Febrile neutropenia • GNR bacteremia • Intra-abdominal infection • Open fracture infection • Pneumonia
Contraindications	PD is a relative contraindication	• Septic shock • CrCl < 30 ml/min • Scr > 1.5 mg/dL without febrile neutropenia (FN) • Scr > 1.9 mg/dL with FN • Underlying hearing loss • Pregnancy • Anasarca • > 20 % BSA burns • Liver dysfunction
IHD CVVHDF SLEDD	Use traditional dosing	EID contraindicated
PD	Consult Renal Fellow for assistance with dosing and lab monitoring	EID contraindicated

IHD intermittent hemodialysis, usually administered three times weekly
CVVHDF continuous venovenous hemodiafiltration
SLEDD slow extended daily dialysis, e.g., NxStage
PD peritoneal dialysis

CALCULATE THE CORRECT DOSING WEIGHT (DW)

Determine the patient's DW based on Table 2. Aminoglycosides distribute, in part, into fat, and thus an obese dosing weight (OBW) must be calculated for obese patients. Underweight patients also require a DW adjustment, since using ideal body weight (IBW) will over estimate the dose. To adjust for these extremes in body weight, the following relationships exist between current body weight (CBW), IBW, OBW and DW.

TABLE 2	DEFINITION	USE THIS DOSING WEIGHT (DW)
Underweight	CBW < IBW	CBW
Normal weight	CBW=100-120% IBW	IBW
Obese	CBW > 120% IBW	OBW

TABLE 3	EQUATION
IBW male	50 kg + 2.3·(height in inches - 60)
IBW female	45.5 kg + 2.3·(height in inches - 60)
OBW	IBW + 0.4·(CBW - IBW)

TRADITIONAL DOSING

1 Peritoneal dialysis is a relative contraindication. Contact Renal Fellow for assistance with dosing in this patient population.
2. Using the correct DW calculated in Tables 2 and 3, calculate a **loading dose (LD)** based on an indication listed in Table 4.

TABLE 4	**LOADING DOSE (LD)**	
Indication	Gentamicin/Tobramycin [1]	Amikacin [2]
Endocarditis Gram-positive infection Urinary tract infection	1 mg/kg	3.5 mg/kg
Bone/joint infection Mycobacterial infection Skin/soft tissue infection	1.5 mg/kg	6.5 mg/kg
Septic shock Other infections [3]	2 mg/kg	8 mg/kg

1 Round gentamicin and tobramycin to nearest 10 mg
2 Round amikacin to nearest 50 mg
3 Infections in which EID is usually indicated, but because of the presence of EID contraindications, traditional dosing should be used instead. These include: CNS infection; cystic fibrosis; febrile neutropenia; GNR bacteremia; intra-abdominal infection; pneumonia.

3. Using Table 5, calculate a **maintenance dose (MD)** based on the patient's current renal function or use of CRRT.

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TABLE 5	**MAINTENANCE DOSE (MD)**	
CrCl (mL/min)	% of LD	Interval
> 90	100%	q12h
80-90	92%	q12h
70-79	88%	q12h
60-69	84%	q12h
50-59	79%	q12h
40-49	92%	q24h
30-39	86%	q24h
CrCL < 30 CVVHDF SLEDD	100% LD x 1 only	Random level 24h after LD. No MD until drug level is assessed.
IHD	100% LD x 1 only	Random level just prior to next IHD session. No MD until drug level is assessed.
PD	Consult Renal Fellow for assistance with dosing	

For patients with a CrCl > 30 ml/min, the Sarubbi-Hull nomograms were adapted by preferentially selecting for longer dosing intervals. References: 1) Sarubbi FA, Hull JH. Ann Intern med. 1978;89(5):612-8. 2) Sarubbi FA, Hull JH. Ann Intern med. 1976;85(2):183-9.

4. **Laboratory monitoring** for traditional dosing
   a. Order twice-weekly aminoglycoside drug concentrations based on Table 6.
   b. Order a BUN, Scr at least twice weekly while on aminoglycoside therapy
   c. Baseline audiometry is recommended if aminoglycoside therapy is expected to last longer than 2 weeks. Consult Audiology 362-7489.

TABLE 6	TIMING OF BLOOD SAMPLE	FREQUENCY
Trough	Immediately prior to 3rd dose	At least twice weekly
Peak	1 hour after the start of the 3rd dose	

5. For patients with a CrCl greater than 30 ml/min, **goal concentrations** for traditional dosing are based on the indication listed in Table 7.

TABLE 7	GOAL CONCENTRATIONS FOR CrCl > 30	
	Gentamicin, tobramycin (mcg/mL)	Amikacin (mcg/mL)
Trough	< 1	< 4
Peak - based on indication below		
GPC infection Endocarditis UTI	3-5	10-15
Bone/joint Skin/structure Mycobacterial	6-8	20-25
Septic shock Other *	8-10	25-30

* Infections in which EID is usually indicated, but because of the presence of EID contraindications, traditional dosing should be used instead. These include: CNS infection; cystic fibrosis; febrile neutropenia; GNR bacteremia; intra-abdominal infection; pneumonia.

6. For traditional dosing in patients with a CrCl less than 30 ml/min or on CRRT, **goal concentrations** and timing of random levels is listed in Table 8.

TABLE 8	GOAL CONC. FOR CrCl < 30 mL/min OR ON CRRT		
Renal function or CRRT	Timing of level	Drug	Goal (mcg/mL)
CrCl < 30 ml/min CVVHDF SLEDD PD	Random level 24h after a dose	Gentamicin Tobramycin	< 1
		Amikacin	< 4
IHD	Random level just prior to next IHD session	Gentamicin Tobramycin	< 1
		Amikacin	< 4

EXTENDED INTERVAL DOSING (EID)

1. Using Table 1, confirm that there are no contraindications to EID. If EID contraindications are present, use traditional dosing instead.
2. Avoid EID if septic shock is present or the patient is on CRRT.
3. Using the correct DW from Tables 2 and 3, calculate a **loading dose (LD)** based on the type of infection listed in Table 9. If the infection is not listed below, then traditional dosing should be used.

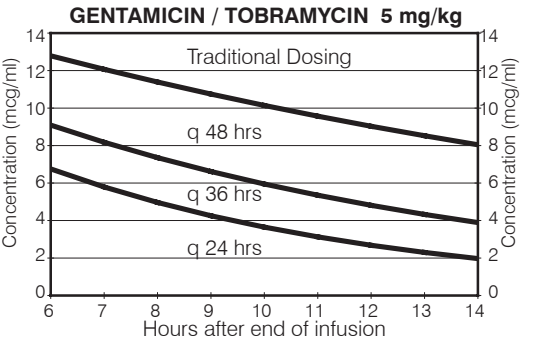
TABLE 9	Gentamicin/ Tobramycin *	Amikacin **	When to draw levels
CNS infection Febrile neutropenia GNR bacteremia Intra-abdominal infection Open fracture infection Pneumonia	5 mg/kg x 1	15 mg/kg x 1	Random level 8 hours after dose. Adjust maintenance dose based on nomograms below.
Cystic fibrosis	8 mg/kg q24h	15 mg/kg q24h	• Trough prior to next 2nd dose • Peak 30 min after 2nd dose

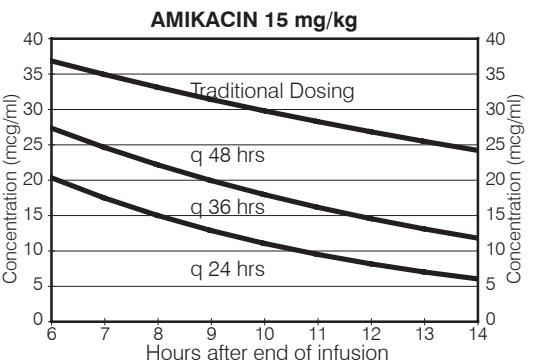
* Round gentamicin and tobramycin to nearest 50 mg

** Round amikacin to nearest 100 mg

4. **For non-CF patients, adjust the dosing interval** using the nomograms below. Bailey TC, et al. Clin Infect Dis. 1997;24:786-95.

5. If 12-14 hr level is undetectable and infection is not responding, consider traditional dosing.





6. **For CF patients,** adjust dose based on peak and trough concentrations. Do not use the nomograms above to make dosage adjustments in CF patients, since the nomograms are based on lower doses.

7. **Laboratory monitoring for EID**
   a. Order an 8 hour random aminoglycoside concentration, BUN and Scr at least twice weekly while on aminoglycoside therapy.
   c. Baseline audiometry is recommended if aminoglycoside therapy is expected to last longer than 2 weeks. Consult Audiology 362-7489.

AMINOGLYCOSIDE DOSING APPLICATION (AMI)

Given the complexity of dosing aminoglycosides, AMI (pronounced "Amy") is being developed by the expert panel. Sometime in 2013-2014, AMI will be built into the Compass dosing bundle for any of the three, formulary aminoglycosides (gentamicin, tobramycin, amikacin). At any time, prescribers have the option to override the dose suggested by AMI and may enter their own dose based on their own calculations, clinical experience or the patient's current clinical status.

AMI requires the prescriber to answer these four questions. Based on the prescriber's answers, AMI will recommend an initial dose:

1. **Current body weight (kg)?** - AMI will automatically use the patient's admission weight and height. However, prescribers are highly encouraged to enter a more recent body weight especially if the patient has recently become fluid overloaded or if there is any other reason to believe that the admission weight no longer accurately reflects the patient's current weight.
2. **On CRRT?** - Choose one option. AMI will use traditional dosing if any type of CRRT is chosen.
3. **Indication for aminoglycoside?** - Choose one option.
   a. AMI uses **traditional dosing** if one of these indications is selected:
      1. Bone/joint infection
      2. Gram-positive infection
      3. Endocarditis
      4. Septic shock
      5. Skin/skin structure infection
      6. Mycobacterial Infection
      7. Urinary tract infection
   b. AMI uses **extended interval dosing (EID)** if the prescriber chooses one of these indications, unless a contraindication to EID exists. **If the patient has septic shock**, prescribers should always choose "septic shock" regardless of the presence of any other infection.
      1. CNS infection
      2. Cystic fibrosis
      3. Febrile neutropenia
      4. GNR bacteremia
      5. Intra-abdominal infection
      6. Open fracture infection
      7. Pneumonia
4. **Contraindications for extended interval dosing?** Choose at least one option. If any choice other than "none present" is selected, AMI will use traditional dosing.

AMPHOTERICIN B

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Liposomal amphotericin B (Ambisome)
Non-formulary	Amphotericin B lipid complex (ABLC)
Route restricted	Amphotericin B deoxycholate, non-iv uses
ID specialists only	Amphotericin B deoxycholate requires ID specialist approval to initiate therapy. Only designated ID physicians or clinical pharmacists (Casabar, Ritchie, BMT clinical pharmacists, ID pharmacy resident) may approve amphotericin B deoxycholate

APPROVAL CRITERIA OF AMBISOME

1. As an alternative to an echinocandin for empirical antifungal therapy in febrile neutropenic patients on the SCTU. See Febrile Neutropenia Guidelines.
2. Candidiasis, invasive
3. Documented or suspected severe systemic mycoses in patients unsuitable for treatment with azoles or echinocandins.
4. Dosing
   a. Usual Ambisome dose: 3-5 mg/kg q24h iv
   b. The dosage for the various lipid products has not been adequately studied or compared. Dosages have ranged from 1-7.5 mg/kg/day depending on the formulation used and infection being treated.
   c. No dosing adjustments for renal, hepatic dysfunction or any form of chronic renal replacement therapy (CVVHDF, SLEDD, IHD).

NON-LIPOSOMAL PRODUCTS

1. ABLC is non-formulary and requires ID approval to initiate. It should not be confused with Ambisome, which differs in pharmacokinetics and chemical composition.
2. Because of significant toxicity and the potential for dosing errors, amphotericin B deoxycholate requires ID specialist approval. This includes non-parenteral routes, e.g., intrathecal, intravitreal, urinary bladder irrigations, etc.

AMPICILLIN/SULBACTAM

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Ampicillin/sulbactam

APPROVAL CRITERIA FOR AMPICILLIN/SULBACTAM

1. Aspiration or post-obstructive pneumonia
2. Empirical therapy of polymicrobial, non-pseudomonal infections (decubiti; sinusitis; head/neck infections; diabetic foot infections; infected human/animal bite wounds; peri-rectal abscess; intra-abdominal infection). After the first 72 hours, the regimen should be tailored based on cultures and sensitivities.
3. Documented infection with Acinetobacter susceptible to ampicillin/sulbactam. The sulbactam component, and not ampicillin, confers activity against Acinetobacter. Recommended dose is 3 g iv q6h in patients with normal renal function.

INAPPROPRIATE USES

1. Ampicillin/sulbactam should not be considered equivalent to other broad spectrum penicillin/penicillinase-inhibitor combinations (i.e., piperacillin/tazobactam).
2. Ampicillin/sulbactam lacks activity against Pseudomonas, MRSA, and AmpC GNRs.
3. Surgical prophylaxis

DOSING

1. Usual dose: 3 g iv q6h
2. Ampicillin/sulbactam doses are expressed in terms of the combination, i.e., 3 g of the combination is equivalent to 2 g of ampicillin and 1 g of sulbactam
3. Modify dosage in patients with renal dysfunction or on chronic renal replacement therapy.

Drug	Usual iv dose	CrCl (mL/min)			
		> 30	29-10	< 10, IHD	CVVHDF
Ampicillin/sulbactam	3 g	Q6	Q12	Q24	Q8

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

AZTREONAM

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Restricted	Aztreonam requires ID approval to initiate therapy

APPROPRIATE USE CRITERIA FOR AZTREONAM

1. Empirical or definitive treatment of documented or suspected serious gram-negative infections in the beta-lactam allergic patient.

INAPPROPRIATE USE

1. Gram-positive and anaerobic infection because aztreonam lacks coverage against these organisms.

DOSING

1. Usual aztreonam dose 1 g q8h
2. Consider 2 g q8h for severe, life-threatening infections and in morbid obesity
3. Modify dosage in patients with renal dysfunction or on chronic renal replacement therapy.

Drug	Usual iv dose	CrCl (mL/min)			
Aztreonam		> 30	29-10	<10, IHD	CVVHDF, SLEDD
	1 g	1 g q8h	500 mg q8h	500 mg q12h	2 g q12h
	2 g	2 g q8h	1 g q8h	1 g q12h	2 g q12h

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

CEFEPIME

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Cefepime

APPROPRIATE USE CRITERIA FOR CEFEPIME

1. Empirical or definitive treatment of serious infections due to gram-negative organisms sensitive to cefepime but resistant to other agents, including but not limited to P. aeruginosa and other AmpC-producing strains (Enterobacter, Citrobacter, Serratia).
2. Empirical treatment of febrile neutropenia, see Febrile Neutropenia Guidelines
3. As part of a combination for the treatment of intra-abdominal infections, i.e., community-acquired of high severity or healthcare-associated. See Complicated Intra-Abdominal Guidelines.
4. Prophylaxis during medicinal leech therapy: ciprofloxacin is no longer recommended because a case of ciprofloxacin-resistant Aeromonas was documented at BJH.

INAPPROPRIATE USES

1. Surgical prophylaxis
2. Infections due to resistant organisms including but not limited to oxacillin-resistant S. aureus, enterococci, and anaerobes.

TOXICITY

1. Cefepime-induced encephalopathy and status epilepticus are rare but well-described adverse effects, especially in the elderly or those with renal dysfunction.

DOSING

1. Cystitis — 1 g q12h
2. Usual dose — 1 g q8h
3. CNS and other life-threatening infections, morbid obesity — 2 g q8h
4. Modify dosage in patients with renal dysfunction or on CRRT

Cefepime	CrCl (mL/min)				
Indication	>60	30-59	10-29	<10, IHD	CVVHDF, SLEDD
Cystitis	1 g q12h	1 g q24h	500 mg-1 g q24h	500 mg q24h	1 g q12h
Usual dose	1 g q8h	1 g q12h	1 g q24h	500 mg -1 g q24h	2 g q12h
				IHD only: 2 g 3x weekly after IHD	
CNS, life-threatening infection, morbid obesity	2 g q8h	2 g q12h	2 g q24h	1 g q24h (preferred inpatient regimen)	2 g q12h
				IHD only: 2 g 3x weekly after IHD	

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

CEFOTETAN

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Cefotetan

APPROPRIATE USE CRITERIA FOR CEFOTETAN

1. Prophylaxis of selected surgical procedures as outlined in the Surgical Prophylaxis Guidelines
2. Treatment of pelvic inflammatory disease (PID) and uncomplicated, susceptible mixed bacterial infections in patients without risk factors for resistant organisms (MRSA, Pseudomonas, etc.)

TOXICITIES

1. C. difficile associated diarrhea
2. Rash, allergic reactions, eosinophilia
3. Hypoprothrombinemia, possibly related to the presence of the N-methylthiotetrazole side chain (~3% incidence)

DOSING

1. Usual cefotetan dose 1 g q12h
2. Maximal/PID dose 2 g q12h

3. Modify dosage in patients with renal dysfunction or on chronic renal replacement therapy.

Drug	Usual iv dose	CrCl (mL/min)			
		> 30	29-10	<10. IHD	CVVHDF, SLEDD
Cefotetan	1-2 g	Q12	Q24	Q48	Q12

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

CEFOXITIN

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Cefoxitin

APPROPRIATE USE CRITERIA FOR CEFOXITIN

1. Prophylaxis of selected surgical procedures, see Surgical Prophylaxis Guidelines
2. Monotherapy of mild to moderate community-acquired intra-abdominal infections (IAI), see Complicated Intra-Abdominal Infection Guidelines
3. Treatment of pelvic inflammatory disease (PID) and uncomplicated, susceptible mixed bacterial infections in patients without risk factors for resistant organisms (e.g., MRSA, Pseudomonas)
4. Unlike other cephalosporins, cefoxitin and cefotetan possess anti-anaerobic activity

DOSING

1. Usual cefoxitin dose 1 g iv q6h
2. Maximal, PID or IAI dose 2 g iv q6h
3. Modify dosage in patients with renal dysfunction or on chronic renal replacement therapy.

Drug	Usual iv dose	CrCl (mL/min)				
		> 30	29-10	<10	IHD	CVVHDF, SLEDD
Cefoxitin	1-2 g	Q6	Q8-12	Q24	2 g 3x/week after IHD	Q8-12

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

CEFTAROLINE

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

ID specialists only	Ceftaroline requires ID approval to initiate therapy. Only designated ID physicians or clinical pharmacists (Casabar, Ritchie, BMT clinical pharmacists, ID pharmacy resident) may approve ceftaroline.

APPROPRIATE USE CRITERIA FOR CEFTAROLINE

1. Alternative therapy for acute bacterial skin and soft tissue infections where MRSA is a potential pathogen
2. Alternative therapy for community acquired bacterial pneumonia (including ceftriaxone non-susceptible pneumococcus)
3. Alternative therapy for invasive MRSA or VISA (vancomycin intermediate S. aureus) infection in patients intolerant to or with strains having reduced susceptibility to other agents. Data supporting use in this setting are limited.

INAPPROPRIATE USES

1. Ceftaroline lacks clinically usefully activity against the following organisms
   a. Enterococcus, Pseudomonas, Acinetobacter and anaerobes
   b. Isolates that harbor AmpC, ESBL or KPC beta-lactamases

SUSCEPTIBILITY TESTING

1. Ceftaroline susceptibly testing will be reflexively performed for S. aureus isolates that are DAPTOmycin non-susceptible or are VISA. In all other situations, Infectious Diseases approval is required for ceftaroline susceptibility testing
2. There are no interpretive criteria for ceftaroline susceptibly testing for coagulase-negative Staphylococcus, therefore, the lab cannot perform susceptibly testing for this organism-antimicrobial combination

DOSING

1. The FDA approved dose of ceftaroline is 600 mg iv q12h
2. Dose escalation to 600 mg iv q 8 hours* may be considered for the treatment of severe infections or in obese patients (i.e. > 100 kg and BMI > 40)
3. Modify dosage in patients with renal dysfunction or on chronic renal replacement therapy.

Drug	CrCl (mL/min)				
Ceftaroline	> 50	31-50	15-30	< 15, IHD	CVVHDF, SLEDD
	600 mg iv q12h	400 mg iv q12h	300 mg iv q12h	200 mg iv q12h	400 mg iv q12h
	600 mg iv q8h *	600 mg iv q12h	400 mg iv q12h	300 mg iv q12h	600 mg iv q12h

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

CEFTRIAXONE

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Ceftriaxone
Non-formulary	Ceftazidime, all other iv 3rd generation cephalosporins

APPROPRIATE USE CRITERIA FOR CEFTRIAXONE

1. Bacterial meningitis
2. Empirical therapy of community-acquired pneumonia, see Dyspnea/CAP Treatment Guidelines
3. Documented infection due to N. gonorrhoeae
4. Mild-to-moderate, community-acquired intra-abdominal infections (IAI), see Complicated Intra-Abdominal Infection Guidelines

INAPPROPRIATE USE

1. Surgical prophylaxis
2. Infections caused by Pseudomonas, Acinetobacter, AmpC or ESBL-producing gram-negative bacteria, intra-abdominal anaerobes, MRSA, enterococci

TOXICITIES

Diarrhea, allergic reactions, eosinophilia, thrombocytosis, transaminitis, superinfections, hyperbilirubinemia, pseudolithiasis/biliary sludging

DOSING

1. Usual ceftriaxone dose	1-2 g iv q24h
2. Endocarditis, osteomyelitis, IAI	2 g iv q24h
3. Meningitis	2 g iv q12h
4. Uncomplicated gonorrhea	250 mg im or iv x 1

5. Dosage modification in patients with renal or hepatic dysfunction or on any form of renal replacement therapy (IHD, CVVHDF, SLEDD) is not necessary

CIPROFLOXACIN

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Ciprofloxacin po
Controlled 72 hrs	Ciprofloxacin iv

APPROPRIATE USE CRITERIA FOR CIPROFLOXACIN

1. Parenteral fluoroquinolones should be limited only to patients unable to take or absorb the oral formulation
2. Treatment of susceptible infections in patients with multiple drug allergies (beta-lactams, sulfonamides)
3. As an alternative to cefepime for febrile neutropenia in beta-lactam allergic patients, as outlined in the Febrile Neutropenia Guidelines.

INAPPROPRIATE USES

1. At BJH, approximately 30% of E. coli, P. mirabilis and P. aeruginosa are resistant to ciprofloxacin. As a result, the use of ciprofloxacin when these organisms are suspected may not be appropriate.
2. Allergy to quinolones
3. Pregnancy/lactation
4. Children/adolescents
5. Co-administration of oral ciprofloxacin with any oral product containing metallic di- or trivalent cations (Al, Ca, Fe, Mg), including but not limited to antacids, multivitamins, tube feeds. Administer oral ciprofloxacin either 2 hrs before or 6 hrs after these products.
6. Co-administration of oral ciprofloxacin with buffered didanosine or sucralfate. Administer oral ciprofloxacin either 2 hours before or 6 hours after these drugs.
7. Medicinal leech prophylaxis. Ciprofloxacin-resistant Aeromonas infection has been reported at BJH.
8. Fluoroquinolones have been associated with exacerbations of myasthenia gravis, and therefore should be used with caution in these patients

DOSING

1. Usual ciprofloxacin dose: 400 mg iv q12h or 500 mg po q12h
2. Severe or pseudomonal infections in, morbid obesity and CNS infections may require higher doses (400 mg iv q8h or 750 mg po q12h)
3. Modify dosage in patients with renal dysfunction or on chronic renal replacement therapy

Drug	Usual dose	CrCl (mL/min)		
	> 30	10-30	< 10, IHD	CVVHDF, SLEDD
Ciprofloxacin iv	400 mg Q12	400 mg Q24	200-400 mg Q24	400 mg Q12
Ciprofloxacin iv	400 mg Q8	400 mg Q12-24	400 mg Q24	400 mg Q12
Ciprofloxacin po	250-750 mg Q12	250-750 mg Q24	250-500 mg Q24	500-750 mg Q12

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

CLINDAMYCIN

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Clindamycin iv, po

APPROPRIATE USE CRITERIA FOR CLINDAMYCIN

1. As an alternative to a beta-lactam in susceptible gram-positive infections
2. Cellulitis

INAPPROPRIATE USE

1. Enterococcal infection

RATIONALE FOR Q8H DOSING

The half-life of clindamycin in patients with normal hepatic function is 2-3 hrs.[1,2] Comparative studies of q8h vs. q6h dosing suggest equivalent efficacy.[3,4] In addition, in vitro pharmacodynamic models suggest that rates of bacterial killing are similar with extended interval dosing.[5]

DOSING

1. Usual iv dose: 600 mg or 900 mg iv q8h
2. Usual oral dose: 450 mg po q6-8h
   a. In order to prevent GI intolerance, oral doses should not exceed 450 mg po q6h
3. Dosage adjustment for renal or hepatic dysfunction is unnecessary

REFERENCES

1. Flaherty JF, et al. Antimicrob Agents Chemother. 1988;32:1825-9.
2. McEvoy GK, et al. (eds). AHFS Drug Information, 2005. Am Soc Health System Pharmacists, Inc.
3. Yellin AE, et al. Am Surgeon. 1993, 59(4):248-55.
4. Buchwald D, et al. Rev Infect Dis. 1989;11(4):619-24.
5. Lewis RE, et al. Antimicrob Agents Chemother. 1999;43:2005-9.

COLISTIN

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Restricted	Colistin, nebulized
ID specialists only	Colistin iv requires ID approval to initiate therapy. Only designated ID physicians or clinical pharmacists (Casabar, Ritchie, BMT clinical pharmacists, ID pharmacy resident) may approve colistin.

Colistimethate (Colymycin, colistin sodium methanesulfonate, colistimethate) is a prodrug that is hydrolyzed to the active drug, colistin. Colistin, also known as polymyxin E, acts as a cationic detergent by binding to and subsequently damaging cell membranes of susceptible bacteria. The Institute for Safe Medication Practices (ISMP) recently warned that the dosing of colistin vs. colistimethate can be confused. In order to prevent this confusion, colistin dosing should be based on colistin content and ordered as "colistin" rather than "colistimethate". The maximum dose is 5 mg/kg/day (2.5 mg iv q12h for normal renal function) based on ideal body weight.

APPROPRIATE USE CRITERIA FOR COLISTIN

1. Intravenously: treatment of serious nosocomial infections due to multidrug resistant (MDR) gram-negative bacilli.
2. Nebulized: treatment of MDR gram-negative bacillary pneumonia in non-bacteremic patients.

INAPPROPRIATE USES

1. Intravenous monotherapy for MDR A. baumannii pneumonias. Treatment failures have been reported due to poor lung penetration. Addition of nebulized colistin is an alternative in this situation.
2. Colistin is not active against the following organisms: Burkholderia, Proteus, Providencia, most Serratia
3. Gram-positive or anaerobic infections

DOSING

1. Inhalation: doses vary greatly in the literature and are not supported by large, well-designed clinical trials.[1] At BJH, 150 mg q12h is used in cystic fibrosis patients.

2. Intravenous: up to 5 mg/kg/day (i.e., 2.5 mg/kg q12h). Doses should be based on ideal body weight (IBW). Round dose to nearest 10 mg.

TABLE 1	EQUATION
IBW male	50 kg + 2.3·(height in inches - 60)
IBW female	45.5 kg + 3.4·(height in inches - 60)

3. Renal dosing of the intravenous formulation has not been well studied. Recommendations in the literature vary greatly. The following table is a more practical and simplified method using creatinine clearance (CrCl), rather than urea clearance [2-8].

CrCl (mL/min)	Dose (mg/kg IBW)	Interval (h)
≥ 80	2.5	12
40-79	1.25 - 1.9	12
25-39	1.25	24
10-24	1.5	36
< 10	1.5	48
IHD	1-1.5 or	24
	2-3	3x weekly (once after each IHD session)
CVVHDF	2.5	12-24

IHD - intermittent hemodialysis
CVVHDF - continuous venovenous hemodiafiltration

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

4. To avoid confusion, Pharmacy recommends that doses be written in milligrams of colistin and NOT colistimethate. If an order for colistimethate is received by Pharmacy, colistin will be dispensed on an equivalent mg per mg basis.

5. Care should be taken when interpreting doses reported in international studies or case reports because foreign formulations of colistin vary by salt form (e.g., sulfate vs. methanesulfonate) as well as by colistin activity. In some studies, international units of colistin activity are reported.

TOXICITIES

1. Nephrotoxicity and neurotoxicity are the most common side effects
2. Neurotoxicity may manifest as circumoral or peripheral paresthesias, numbness, tingling, dizziness, vertigo, giddiness, ataxia, blurred vision or slurred speech. Severe neurotoxicity, including mental confusion, coma, psychosis and seizures, has been reported, especially in patients on high doses or with impaired renal function.

REFERENCES

1. Linden PK, et al. Clin Infect Dis. 2006;43:S89–94.
2. American Society of Health-System Pharmacists, AHFS Drug Information 2012.
3. Colistin package insert, Paddock Pharmaceuticals, version January 2012.
4. Falagas ME, et al. Clin Infect Dis. 2005;40(9):1333-41.
5. Lim LM, et al. Pharmacotherapy. 2010;30(12):1279-91.
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DAPTOMYCIN

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

ID specialists only	DAPTOmycin requires ID approval to initiate therapy. Only designated ID physicians or clinical pharmacists (Casabar, Ritchie, BMT clinical pharmacists, ID pharmacy resident) may approve DAPTOmycin

APPROPRIATE USE CRITERIA FOR DAPTOMYCIN

1. Treatment of methicillin-resistant S. aureus (MRSA) or coagulase-negative Staphylococcal infection in patients intolerant to vancomycin with an organism susceptible to DAPTOmycin
2. Treatment of vancomycin resistant enterococci (VRE)infection if the organism is susceptible to DAPTOmycin. A higher dose (8 mg/kg/day) may be considered.
3. Alternative therapy for invasive MRSA infection in patients intolerant to or with strains having reduced susceptibility to other agents. Data supporting use in this setting are limited. While DAPTOmycin may be an option in this setting, because of its cost, alternative agents should also be considered.

INAPPROPRIATE USES

1. Pneumonia and other pulmonary infections. DAPTOmycin is bound and inactivated by pulmonary surfactant.
2. Surgical prophylaxis

SUSCEPTIBILITY TESTING

The Clinical Microbiology Laboratory uses the following algorithm for reporting DAPTOmycin susceptibilities:

1. DAPTOmycin is tested on all S. aureus isolates and susceptibility is routinely reported on all MRSA and VISA isolates
2. DAPTOmycin is tested on all VRE growing from blood isolates, and susceptibility by E-test is routinely reported. However, this requires additional time (~24 hrs) for analysis prior to reporting.
3. ID approval is required to obtain DAPTOmycin susceptibilities in other circumstances

TOXICITIES

1. Muscle pain or weakness, increases in CPK, rhabdomyolysis
2. Baseline and weekly monitoring of CPK is suggested; consider more frequent CPK monitoring in patients
   a. On concomitant statin therapy
   b. Receiving high doses of DAPTOmycin (> 8 mg/kg/day)
   c. With morbid obesity and receiving > 1200 mg/day
   d. With elevated baseline CPK
3. Discontinue DAPTOmycin if CPK
   a. Asymptomatic patients: when CPK > 10x upper limit of normal (2000 IU/L)
   b. Symptomatic or sedated/non-verbal patients: when CPK > 5x upper limit of normal.
4. Eosinophilic pneumonia has been described with prolonged DAPTOmycin therapy

DOSING

1. DAPTOmycin is available in 500 mg vials. When possible, round doses to nearest 25 mg.
2. Dose adjustment is unnecessary for patients with hepatic dysfunction
3. Adjust doses based on renal function, indication and body weight.
4. Actual body weight may be used to calculate a dose even in the morbidly obese (BMI > 40). Dvorchik BH, et al. J Clin Pharmacol 2005;45:48-56.
5. For patients on IHD, the dosing table below uses the format "Mon, Wed, Fri" as a surrogate for IHD given three times weekly (Mon-Wed-Fri vs. Tue-Thu-Sat). Prescribers should note that for skin/skin structure infections and bacteremia, a higher dose should be given on the third day of dialysis. A higher dose on the third day is needed to produce DAPTOmycin concentrations, drawn 72 hrs later, similar to the previous two dialysis days, which in contrast are separated by 48 hrs. [1]

DAPTOmycin	CrCl (mL/min)			
Indication	> 30	< 30	CVVHDF, SLEDD	IHD
Skin/skin structure	4 mg/kg iv q24h	4 mg/kg iv q48h	6 mg/kg iv q48h	4 mg/kg on Mon, Wed but 6 mg/kg on Fri
Bacteremia	6 mg/kg iv q24h	6 mg/kg iv q48h	8 mg/kg iv q48h	6 mg/kg on Mon, Wed but 8 mg/kg on Fri
Enterococcal infection	8 mg/kg iv q24h	8 mg/kg iv q48h	8 mg/kg iv q48h	8 mg/kg on Mon, Wed, Fri

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

REFERENCES

1. Vilay AM, et al. Crit Care Med. 2011;39(1):19-25.
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ERTAPENEM

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Restricted	Ertapenem requires ID approval to initiate therapy

APPROPRIATE USE CRITERIA FOR ERTAPENEM

1. Treatment of polymicrobial infections resistant to other broad spectrum antibiotics but sensitive to ertapenem and when q24h dosing is required (e.g., transitioning to home iv therapy).
2. Infections due to extended spectrum beta-lactamase (ESBL)-producing Klebsiella or E. coli susceptible to carbapenems
3. Community-acquired intra-abdominal infections of mild-moderate severity. See Complicated Intra-abdominal Infection Guidelines.

INAPPROPRIATE USES

1. Although ertapenem is FDA approved for the treatment of complicated intra-abdominal infections; complicated skin/skin structure infections; complicated urinary tract infections; acute pelvic inflammatory infections; community-acquired pneumonia. However, ertapenem should not be considered a first-line therapy for any of these indications.
2. Ertapenem should not be considered equivalent to other carbapenems (doripenem, imipenem, meropenem). Ertapenem lacks activity against P. aeruginosa, Acinetobacter and enterococci.
3. Surgical prophylaxis

DOSING

1. Usual ertapenem dose: 1 g iv q24h
2. Modify dosage in patients with renal dysfunction or on chronic renal replacement therapy.

Drug	CrCl (mL/min)	
	≥ 30, CVVHDF, SLEDD	< 30, IHD
Ertapenem	1 g q24h	500 mg q24h

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

FLUCONAZOLE

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Fluconazole po 150 mg x 1 dose for vulvovaginal candidiasis
Restricted	Fluconazole iv and po at all other doses require ID approval initiate therapy

APPROPRIATE USE CRITERIA FOR FLUCONAZOLE

1. Treatment of fungemia and other systemic fungal infections caused by C. albicans, C. tropicalis, C. parapsilosis. Verify fluconazole susceptibility when treating C. glabrata. Higher doses are recommended for C. glabrata reported as susceptible or susceptible dose-dependent.
   a. Non-glabrata species: 800 mg x1, then 400 mg qday*
   b. C. glabrata: 800 mg qday*

2. Empirical treatment of confirmed or suspected systemic candidal infections in high risk patients. Loading dose: 800 mg x 1, then 400 mg qday*.

3. Treatment of UTI caused by C. albicans, C. tropicalis, C. parapsilosis, or C. glabrata in the presence of pyuria, signs and symptoms of UTI, and absence of a foreign body.
   a. Cystitis: load 400 mg x1, then 200 mg qday*
   b. Pyelonephritis: load 800 mg x1, then 400 mg qday*
   c. C. glabrata: load 800 mg x1, then 400-800 mg qday*

4. Treatment of oral or esophageal candidiasis.
   a. Oropharyngeal: load 400 mg x1, then 100-200 mg qday*
   b. Esophageal: load 800 mg x1, then 200-400 mg qday*

5. Treatment of vaginal candidiasis. Normal dose*: 150 mg po x 1

6. Antifungal prophylaxis for acute leukemics, allogeneic and matched unrelated donor transplants on SCTU per study protocols only. Autologous transplants do not receive antifungal prophylaxis. See SCTU Febrile Neutropenia Guidelines.

7. SCTU Febrile Neutropenia Guidelines: as first-line therapy of persistently febrile, neutropenic autologous BMT patients. Load: 800 mg x1, then 400 mg day*

8. Consolidation therapy of cryptococcal meningitis, typically following an initial 14-day treatment course with Ambisome ± 5-FC. Load 800 mg x1, then 400-800 mg qday*.

9. Antifungal prophylaxis for abdominal transplant.
   a. Kidney: 200 mg once weekly x 4 weeks*
   b. Liver: 200 mg once weekly for 3 months*
   c. Pancreas: 100 mg qday for 3 months*

10. Empirical therapy of healthcare-associated complicated intra-abdominal infections in non-ICU patients. See Complicated Intra-abdominal Infection Guidelines. Load: 800 mg x1, then 400 mg qday.*

* PO therapy and IV-PO transitioning should be promoted where possible; see dosage adjustments for renal dysfunction

INAPPROPRIATE USES

1. Treatment of systemic infections caused by C. krusei
2. Treatment of systemic Candidal infections in patients receiving prior sustained azole antifungal prophylaxis
3. Candiduria without pyuria or signs and symptoms of urinary tract infection
4. Candida isolated from sputum cultures. Candida pneumonia is very rare and requires a histopathological diagnosis. The recovery of these organisms in routine culture, in most cases, only represents overgrowth of organisms secondary to antimicrobial therapy.
5. Fluconazole does not have activity against molds, including Aspergillus, or azole-resistant Candida.

DOSING

1. Refer to appropriate usage criteria for dosage ranges by indication.
2. Because of excellent oral bioavailability, a dosage conversion when converting from iv to po is unnecessary
3. Modify dosage in patients with renal dysfunction

Fluconazole		CrCl (mL/min)			
Loading	Usual iv dose	≥ 50	<50	IHD	CVVHDF, SLEDD
400 mg x1	200 mg	200 mg q24h	100 mg q24h	100 mg q24h	200 mg q24h
800 mg x1	400 mg	400 mg q24h	200 mg q24h	200 mg q24h	400 mg q24h
800 mg x1	800 mg	800 mg q24h	400 mg q24h	400 mg q24h	800 mg q24h

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

GANCICLOVIR AND VALGANCICLOVIR

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Ganciclovir, po ValGANciclovir, po
Restricted	Ganciclovir, iv

APPROPRIATE USE CRITERIA FOR GANCICLOVIR AND VALGANCICLOVIR

Ganciclovir will be allowed for CMV disease (vs. infection) as defined below:

1. CMV infection: isolation from any site or histologic evidence of CMV from any tissue or cytologic specimen.

2. CMV disease - illness characterized by CMV infection, fever > 38.2 for at least 3 days, plus one of the following:

   a. Interstitial pulmonary infiltrate on chest x-ray and
      1. Positive CMV PCR of BAL or biopsy, or
      2. Positive histopathology, or
      3. Alveolar-arterial gradient >20 in presence of viremia

   b. Elevated SGPT > 2.5 times the upper limits of normal in the absence of serologic evidence for hepatitis A or B infection.

   c. Atypical lymphocytosis > 20% of total WBC.

   d. Thrombocytopenia (<100,000) on at least 3 consecutive days following withdrawal of azathioprine or mycophenolate mofetil.

EMPIRICAL USE

Some patients will satisfy the criteria for CMV disease as defined above except for virologic confirmation. In this situation, ID consultation will be obtained and ganciclovir will be approved for 72 hours (provided no contraindications are present and alternative explanations for the patient's illness have been ruled out), awaiting the results of CMV cultures. If CMV disease is not virologically confirmed, ganciclovir may be discontinued.

SOFT INDICATIONS

Two groups of patients are the most vexing in determining whether ganciclovir is indicated. The first group has evidence for CMV infection with systemic symptoms (fever, fatigue, myalgia, etc.) but no evidence of end organ involvement (pneumonitis, hepatitis, neutropenia, thrombocytopenia, etc.). The second group has evidence of organ involvement, often found unexpectedly on routine liver biopsy or bronchoscopy for other indications, but no systemic symptoms.

RELATIVE CONTRAINDICATIONS

1. Absolute neutrophil count < 500/μL
2. Platelet count < 50,000/μL

DOSING

1. Usual dose

Ganciclovir	Induction	5 mg/kg iv q12h
	Maintenance	5 mg/kg iv q24h
ValGANciclovir	Induction	900 mg po bid x 21 days
	Maintenance	900 mg po q24h

2. Modify dosage in patients with renal dysfunction or on chronic renal replacement therapy

Ganciclovir	CrCl (mL/min)					
	> 70	69-50	49-25	24-10	< 10, HD	CVVHDF, SLEDD
5 mg/kg induction	Q12	2.5 mg/kg Q12	2.5 mg/kg Q24	1.25 mg/kg Q24	1.25 mg/kg 3x/week (after each HD)	2.5 mg/kg Q12
5 mg/kg maint.	Q24	2.5 mg/kg Q24	1.25 mg/kg Q24	0.625 mg/kg Q24	0.625 mg/kg 3x/week (after each HD)	2.5 mg/kg Q24

ValGANciclovir	CrCl (mL/min)					
	> 60	59-40	39-25	< 24-11	< 10, IHD	CVVHDF, SLEDD
900 mg induct.	Q12	450 mg Q12	450 mg Q24	450 mg Q48	450 mg 3x/week (after each HD)	450 mg Q24
900 mg maint.	Q24	450 mg Q24	450 mg Q48	450 mg 2x weekly	225 mg 3x/week (after each HD)	450 mg Q48

ITRACONAZOLE

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Itraconazole po
Non-formulary	Itraconazole iv is no longer manufactured

APPROPRIATE USE CRITERIA FOR ITRACONAZOLE PO

1. Treatment of the following serious systemic mycoses:
   a. Blastomycosis, pulmonary and extrapulmonary
   b. Histoplasmosis, including cavitary pulmonary and disseminated non-meningeal histoplasmosis

PRECAUTIONS

1. The oral solution is recommended when oral therapy is required.
2. Because of poor absorption and interactions with drugs which raise stomach pH, the use of the oral capsule should be avoided.
3. Monitoring of plasma itraconazole levels is suggested in all patients. See Therapeutic Drug Monitoring monograph.
4. Liver function should be monitored in patients receiving prolonged therapy.

DOSING

1. Loading dose 200 mg po q8h x 3 days
2. Maintenance dose 200 mg po q12h

LINEZOLID

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

ID specialists only	Linezolid iv and po require ID approval to initiate therapy. Only designated ID physicians or clinical pharmacists (BMT clinical pharmacists, Casabar, Ritchie, ID pharmacy resident) may approve linezolid.

APPROPRIATE USE CRITERIA FOR LINEZOLID

Linezolid received FDA approval for a limited set of indications. Experience with the drug is limited in certain settings, unanticipated side effects may emerge, and emergence of resistance has been reported.

In general, use of the drug should be limited to situations for which there are no alternative therapies.

1. Documented vancomycin-intermediate or resistant S. aureus (VISA or VRSA) infection
2. Treatment of documented or suspected MRSA HAP/VAP as an alternative to vancomycin.
3. Documented methicillin-resistant S. aureus (MRSA) or S. epidermidis (MRSE) infection not responding to or unable to tolerate vancomycin (e.g. because of allergy, ototoxicity, neutropenia)
4. Documented vancomycin-resistant enterococcal (VRE) infection
5. Monotherapy for concomitant MRSA and VRE infection

INAPPROPRIATE USES

1. Prophylaxis
2. S. aureus endocarditis
3. Linezolid is contraindicated in patients with recent exposure or receiving concomitant serotonergic agents (including SSRIs, methylene blue, tramadol, buproprion, TCAs, fentanyl outside of the ICU setting, trazodone, mirtazapine). For patients with recent serotonergic agent exposure, allow for sufficient clearance (3-5 times half-life) before initiating linezolid.
4. Linezolid is not FDA-approved for catheter-related bloodstream or catheter-site infections and should not be routinely used in these settings

TOXICITIES

1. Thrombocytopenia, neutropenia
2. Serotonin syndrome in patients receiving serotonergic agents
3. Optic and peripheral neuritis (more common with long term treatment)
4. Lactic acidosis

DOSING

1. Usual dose: 600 mg q12h iv or po

2. Dosing adjustment in patients with renal dysfunction or on renal replacement therapy is unnecessary. Guidelines for dosing adjustments in patients with hepatic dysfunction have not yet been developed.

MEROPENEM

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Restricted	Meropenem requires ID approval to initiate therapy
Non-formulary	Doripenem, imipenem

APPROPRIATE USE CRITERIA FOR MEROPENEM

1. Culture and sensitivity proven infection due to bacteria resistant to other antibiotics but sensitive to meropenem
2. Empirical therapy in situations in which infection due to gram-negative bacteria resistant to other broad spectrum beta-lactams is likely
3. As a secondary alternative to cefepime for febrile neutropenia, as outlined in the Febrile Neutropenia Guidelines
4. As an option for the treatment of healthcare-associated intra-abdominal infections, see Complicated Intra-Abdominal Infections Guidelines

INAPPROPRIATE USES

1. Surgical prophylaxis
2. Stenotrophomonas infections
3. Severe beta-lactam allergy

PRECAUTIONS

1. Patients with severe renal insufficiency and/or history of head trauma, seizure disorders, or other central nervous system pathology should be monitored for the development of seizures, confusion, or myoclonic activity while on meropenem.
2. Consider switching from meropenem to imipenem when E. faecalis is identified and deemed a prominent pathogen. While there are no clinical data to support this practice, in vitro MICs suggest better activity with imipenem.

DOSING

1. Recommended dose: 500 mg iv q6h or 1 g iv q8h
2. Cystic fibrosis, meningitis: 2 g iv q8h
3. Modify dosage in patients with renal dysfunction as noted below
4. CVVHDF, SLEDD: 1 g iv q12h

Drug	Usual IV Dose	CrCl (mL/min)			
		≥ 50	49-25	24-10	<10, IHD
Meropenem	500 mg	500 mg iv q6h	500 mg iv q8h	500 mg iv q12h	500 mg iv q24h
	1 g	1 g iv q8h	1 g iv q12h	500 mg iv q12h	500 mg-1 g iv q24h
	2 g	2 g iv q8h	2 g iv q12h	1 g iv q12h	1-2 g iv q24h

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

METRONIDAZOLE

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Metronidazole iv and po

DOSING

1. Because of its long half-life (6-14 hours), q8h is the recommended dosing interval

2. A non-standard dosing interval, i.e., q6h, should be considered in these situations:
   a. CNS infection
   b. When higher serum levels may be desirable, e.g., anaerobic endocarditis
   c. Morbidly obese patients (BMI > 40)

3. Standard dose: 500 mg iv q8h

4. Significant hepatic insufficiency: 500 mg iv q12h

5. Dosage adjustment is unnecessary for patients with renal dysfunction or on any form of renal replacement therapy (IHD, CVVHDF, SLEDD)

6. Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026, 314-454-8399.

PRECAUTIONS

1. Metronidazole may increase the effect of warfarin
2. Disulfiram reactions are possible with ethanol-containing products

MICAFUNGIN

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Restricted	Micafungin requires ID approval to initiate therapy
Non-formulary	Anidulafungin, caspofungin

APPROPRIATE USE CRITERIA FOR MICAFUNGIN

Treatment of the following serious systemic mycoses

a. Candidiasis, invasive
b. Empirical anti-fungal therapy in febrile neutropenia, see Febrile Neutropenia Guidelines
c. Empirical anti-fungal therapy in patients with healthcare-associated intra-abdominal infections, see Complicated Intra-Abdominal Infection Guidelines
d. Aspergillosis, invasive – in patients who are intolerant of or refractory to amphotericin B or voriconazole

INAPPROPRIATE USES

1. The MICs for C. parapsilosis are high and therefore, some experts do not use micafungin to treat this organism
2. Echinocandins have poor penetration into urine, CNS and eye. Therefore, echinocandins should not be relied upon to treat infections at these sites.
3. Cryptococcosis
4. Endemic mycoses (histoplasmosis, blastomycosis, coccidioidomycosis)
5. Monotherapy for invasive mold infections other than aspergillosis (e.g., fusariosis, scedosporiosis, zygomycosis)

DRUG INTERACTIONS

Micafungin may increase plasma concentrations of sirolimus, cyclosporine and nifedipine by inhibition of CYP450. This interaction may be managed by monitoring sirolimus, cyclosporine plasma concentrations or blood pressure control with nifedipine.

DOSING

1. Usual dose: 100 mg iv q24h
2. Renal and hepatic dosage adjustments are unnecessary
3. Dosage adjustments are not necessary with any form of renal replacement therapy (IHD, CVVHDF, SLEDD)

MOXIFLOXACIN

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Restricted	Moxifloxacin iv and po require ID approval to initiate therapy

APPROPRIATE USE CRITERIA FOR MOXIFLOXACIN

1. Community-acquired pneumonia (CAP) in patients unable to tolerate cephalosporins and/or azithromycin, see Dyspnea/CAP Treatment Guidelines
2. Oral therapy should be used when possible

INAPPROPRIATE USES

1. Moxifloxacin should not be considered therapeutically equivalent to ciprofloxacin. Moxifloxacin has significantly less anti-pseudomonal activity and should not be used to treat documented or suspected pseudomonal infections.
2. Urinary tract infections, since the drug is not renally eliminated
3. Co-administration of oral moxifloxacin with any oral product containing di- or trivalent cations (Al, Fe, Mg), including but not limited to antacids, multivitamins, tube feeds. Administer oral moxifloxacin either 2 hours before or 6 hours after these products.
4. Co-administration of oral moxifloxacin with buffered didanosine or sucralfate. Administer oral moxifloxacin either 2 hours before or 6 hours after these drugs.
5. Fluoroquinolones have been associated with exacerbations of myasthenia gravis, and therefore should be used with caution in these patients

TOXICITIES

1. Prolongation of QTc intervals. Use with caution
   a. When combining moxifloxacin with drugs known to prolong QTc, including but not limited to class IA, III antiarrhythmic drugs
   b. In patients with pro-arrhythmic conditions or prolonged QTc

DOSING

1. Usual dose: 400 mg iv or po q24h
2. Dosage adjustment is unnecessary in patients with renal dysfunction or on any form of renal replacement therapy (IHD, CVVHDF, SLEDD)

PIPERACILLIN/TAZOBACTAM

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Restricted	Piperacillin/tazobactam requires ID approval to initiate therapy

APPROPRIATE USE CRITERIA FOR PIPERACILLIN/TAZOBACTAM

1. Culture and sensitivity proven infection resistant to other broad spectrum antibiotics but sensitive to piperacillin/tazobactam
2. As alternative for the treatment of complicated intra-abdominal infections, see Complicated Intra-Abdominal Infection Guidelines
3. Prophylaxis of interventional biliary procedures

INAPPROPRIATE USES

1. Treatment of serious infections caused by AmpC-producing GNRs
2. Treatment of polymicrobial infections where Pseudomonas is an unlikely pathogen

DOSING

1. Usual dose: 3.375-4.5 g iv q6h
2. Serious nosocomial infections or anti-pseudomonal coverage: 4.5 g iv q6h
3. Modify dosage in patients with renal dysfunction or receiving renal replacement therapy. Dosage modification is unnecessary with hepatic insufficiency.

Indication	CrCl (mL/min)				
	> 40	20-40	<20	IHD	CVVHDF, SLEDD
Serious nosocomial infections	4.5 g iv q6h	3.375 g iv q6h	2.25 g iv q6h	2.25 g iv q8h	3.375 g iv q6h
Other infections	3.375 g iv q6h	2.25 g iv q6h	2.25 g iv q8h	2.25 g iv q12h	3.375 g iv q6h

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

POSACONAZOLE

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Restricted	Posaconazole requires ID approval to initiate therapy

APPROPRIATE USE CRITERIA FOR POSACONAZOLE

1. Prophylaxis of Aspergillus and Candida infections in allogeneic hematopoietic stem cell transplant recipients and in patients with hematologic malignancies undergoing high-dose chemotherapy
2. Treatment of the following serious systemic mycoses
   a. Zygomycosis – in patients intolerant of or refractory to amphotericin B or when oral therapy is desired
   b. Aspergillosis, invasive – in patients who are intolerant of or refractory to amphotericin B and voriconazole

INAPPROPRIATE USE

1. Patients unable to eat or take a nutritional supplement. Posaconazole requires food for absorption.
2. Patients requiring a proton-pump inhibitor or other gastric acid suppressants
3. Patients unlikely to absorb oral medications

PRECAUTIONS

1. Bioavailability – because of poor oral absorption each dose of posaconazole should be administered with a full meal, liquid nutritional supplement, or acidic, carbonated beverage
2. Drug interactions – potential drug interactions including amiodarone, cimetidine, cycloSPORINE, midazolam, phenytoin, tacrolimus. Coadministration of the following drugs is contraindicated: astemizole, cisapride, ergot alkaloids, halofantrine, pimozide, quinidine, rifabutin, terfenadine. Drugs known to decrease posaconazole levels include proton-pump inhibitors and other gastric acid suppressants, rifampin, phenytoin, efavirenz.

DOSING

1. Serious systemic mycoses: 200 mg po q6h
2. Prophylaxis of invasive fungal infections: 200 mg po q8h
3. All doses should be administered with a full meal, nutritional supplement, or acidic carbonated beverage
4. Therapeutic drug monitoring is recommended, see Therapeutic Drug Monitoring Guidelines
5. No dosage adjustment is necessary in patients with renal dysfunction or on any form of chronic renal replacement therapy

QUININE

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Non-formulary	QuiNINE requires ID approval to initiate therapy

APPROPRIATE USE CRITERION FOR QUININE

Uncomplicated Plasmodium falciparum malaria. ID consultation is recommended in this situation.

INAPPROPRIATE USES

1. Leg cramps - quiNINE has been reported to cause prolonged QTc intervals, torsades de pointes and other fatal arrhythmias. As a result, in December, 2006, the FDA issued a stern warning for this unapproved indication. Quinine was taken off the BJH formulary in April 2007. Under P&T policy, patients may take their own quiNINE provided that the following occur:
   a. A physician order specifically states the patient may use his/her own medication
   b. A pharmacist or physician has identified and approved the drug for use
   c. Nursing will be responsible for the administration and charting of all medications, including "Patient's Own Meds"
2. All other uses

PRECAUTIONS

1. Quinine is contraindicated in patients with prolonged QTc intervals; G6PD deficiency; myasthenia gravis; optic neuritis; quiNINE hypersensitivity
2. QuiNINE should be used with caution in patients with atrial fibrillation or atrial flutter. It may also cause significant hypoglycemia, especially in pregnant women.
3. Numerous drug interactions, including but not limited to: astemizole; cimetidine; cycloSPORINE; digoxin; dofetilide; droperidol; flecainide; mefloquine; metformin; methadone; neuromuscular blockers; ranolazine; rifampin; protease inhibitors; warfarin

DOSING

1. Uncomplicated P. falciparum malaria: 648 mg po q8h for 3-7 days together with either doxycycline 100 mg po bid x 7 days or clindamycin 20 mg/kg/day in 3 divided doses for 7 days. See http://www.cdc.gov/malaria/diagnosis_treatment/treatment.html
2. Renal or hepatic dysfunction: pharmacokinetic data to guide dosing are sparse. ID consultation is recommended.

RIBAVIRIN, INHALED

Pharmacy and Therapeutics Committee, June 2013

POLICY

The Pharmacy and Therapeutics Committee, with input from the Infection Prevention Committee and the departments of Pharmacy, Environmental Health and Safety and Occupational Health, outlines protective procedures to minimize occupational exposures during inhaled ribavirin therapy.

RATIONALE

Ribavirin is carcinogenic, teratogenic and embryolethal in all animal species in which it has been tested. When nebulized, ribavirin is released into the patient's room air and presents potential risks to anyone entering the room during the nebulization.

PROCEDURES

1. The Inhaled Ribavirin Compass Order Set must be used by physicians whenever inhaled ribavirin is initiated. Additional information about ribavirin can be found in the Inhaled Ribavirin Guidelines, which may be downloaded from Phred, the Pharmacy intranet site:
   a. Access Phred from any BJC clinical desktop computer's or Compass terminal's web browser. The URL is: https://phred.carenet.org/
   b. When Phred launches, in the search field, type: inhaled ribavirin guidelines, then click on the "inhaled ribavirin guidelines" link
   c. Click on the desired PDF file
2. The Compass order set specifies the following orders:
   a. Transfer the patient to a negative pressure room
   b. Follow appropriate infection prevention isolation precautions as detailed in the BJH Isolation Policy
   c. Place the following protective equipment outside the patient's room
      1. Ribavirin Nebulization Sign
      2. N95 respirators
      3. Examination gloves
      4. Contact isolation gowns
      5. Chemical splash goggles
   d. The physician completing the order set must specify the correct dose, duration and indication for inhaled ribavirin therapy.
3. In addition, the Inhaled Ribavirin Compass Order Set communicates to Nursing, Pharmacy, Respiratory Therapy and Housekeeping additional protective procedures:
   a. Place a copy of the Inhaled Ribavirin Guidelines in front of the patient's chart
   b. Keep the patient's entry door closed during nebulization
   c. Charge nurse should modify nursing division staffing as needed to prevent pregnant/breast-feeding caregivers from entering the patient's room during the nebulization.
   d. Nursing staff should inservice visitors on ribavirin precautions
   e. No pregnant or breast-feeding women should enter the room during the nebulization
   f. Visitors should contact a nurse prior to entering the patient's room
   g. N95 respirators and examination gloves must be worn by anyone entering the room during nebulization. Examination gloves should be worn at all times if the patient is also on contact precautions.
   h. Contact isolations gowns and gloves must be worn by anyone entering the patient's room during the nebulization and at all times if the patient is also on contact precautions.
   i. Chemical splash goggles are optional, but are recommended for anyone who experiences or has known eye sensitivity to ribavirin, wears contact lenses, or those who may be exposed to gross splashing of the drug (Respiratory Therapy, Pharmacy, the patient). Goggles should be worn as needed for standard precautions.

j. Respiratory Therapy should aspirate unused ribavirin into syringes, then dispose of these syringes in the bedside chemotainer bucket
k. Daily cleaning of the room should follow standard Housekeeping policies for cleaning a Contact Precautions (CP) room. Housekeepers should not clean the room while ribavirin is being administered.
l. When the course of ribavirin therapy is finished, Housekeeping should dispose of the chemotherapy container. When the patient is discharged, routine policy for cleaning a CP room will be followed.

4. If Pharmacy receives a handwritten order to initiate ribavirin, the pharmacist will inform the physician that orders to initiate inhaled ribavirin must be written using the Inhaled Ribavirin Order Set in Compass.
5. The Inhaled Ribavirin Compass Order Set is not required to change, modify or discontinue inhaled ribavirin.
6. In order to expedite therapy, pharmacists may take telephone orders using the Inhaled Ribavirin Compass Order Set.

ADULT DOSING

Using the order set, choose from one of two dosing methods

1. Ribavirin 2 grams in 33.3 mL sterile water administered via SPAG-2 nebulizer by Respiratory Therapy over 2 hours q8 hours. [3]
2. Ribavirin 6 grams in 300 mL sterile water administered via SPAG-2 nebulizer by Respiratory Therapy over 12-16 evening and night-time hours once daily.
3. Duration of therapy is variable. Consider Infectious Diseases or Pulmonary consult.

RISKS

Refer to the Inhaled Ribavirin Guidelines (to view a copy, see Procedures, 1a-c above) for a detailed description of risks to the patient and healthcare workers.

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12. Other references on file, Drug Information Center, 314-454-8399.

TELAVANCIN

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

ID specialists only	Telavancin requires ID approval to initiate therapy. Only designated ID physicians or clinical pharmacists (Casabar, Ritchie, BMT clinical pharmacists, ID pharmacy resident) may approve telavancin.

DRUG SUPPLY

As of the Tool Book's publication date, the supply of telavancin is uncertain.

APPROPRIATE USE CRITERIA FOR TELAVANCIN

1. Alternative therapy for acute bacterial skin and soft tissue infections where MRSA is a potential pathogen
2. Alternative therapy for invasive MRSA or VISA infection in patients intolerant to or with strains having reduced susceptibility to other agents. Data supporting use in this setting are limited..

INAPPROPRIATE USES

1. Telavancin's role for non-FDA-approved indications is evolving. Though clinical trial data and extensive clinical experience are lacking, some experts have used this antibiotic for treatment of other systemic infections where other therapies have failed, are contraindicated, or are not tolerated. ID consultation is recommended.
2. VRE or VRSA infection

TOXICITIES

1. Nephrotoxicity may occur, necessitating careful monitoring of renal function. Telavancin should be used with caution in patients with renal dysfunction
2. The most common adverse effects are taste disturbances, nausea, vomiting
3. Telavancin is a derivative of vancomycin, so cross-allergenicity is a possibility
4. Telavancin may prolong the QTc interval; therefore, it should be avoided in patients with known QTc prolongation at baseline. ECGs should also be closely monitored when telavancin is combined with other medications that prolong QTc.

PREGNANCY WARNING

1. If possible, avoid during pregnancy. FDA pregnancy category C
2. Women of childbearing potential should have a serum pregnancy test prior to initiation of therapy. Telavancin is part of a Risk Evaluation Mitigation System (REMS) and all patients should receive a patient medication guide to understand the risks associated with the drug. Serum pregnancy testing and the patient medication guide are part of the Compass order set for telavancin.

DRUG-LAB INTERACTION

Telavancin interferes with commercially available assays used for measuring PT, INR, aPTT, ACT, and coagulation based factor Xa tests which may result in artificial elevations in these labs. No evidence of increased bleeding risk has been observed with telavancin. To minimize this interaction, these coagulation tests should be drawn just prior to a telavancin dose (i.e., at a telavancin trough concentration).

DOSING

1. Usual dose: 10 mg/kg iv q24 based on actual body weight
2 No dosage adjustment needed for hepatic dysfunction
3. Modify dosage in patients with renal dysfunction or on chronic renal replacement therapy

Drug	CrCl (mL/min)				
	≥ 50	49-30	< 30	CVVHDF, SLEDD	HD
Telavancin	10 mg/kg Q24	7.5 mg/kg Q24	10 mg/kg Q48	7.5 mg/kg Q24	10 mg/kg 3x/week (after each HD session)

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

TIGECYCLINE

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

ID specialists only	Tigecycline requires ID approval to initiate therapy. Only designated ID physicians or clinical pharmacists (Casabar, Ritchie, BMT clinical pharmacists ID pharmacy resident) may approve tigecycline

APPROPRIATE USE CRITERION FOR TIGECYCLINE

In patients allergic to, intolerant of, or not responding to other therapies and without bacteremia:

1. Empirical treatment of complicated skin and soft tissue infections caused by mixed organisms.
2. Empirical treatment of community-acquired intra-abdominal infection of mild to moderate severity, see Complicated Intra-Abdominal Infection Guidelines
3. As an alternative, definitive treatment of 1 and 2 above caused by multi-drug resistant organisms testing sensitive to tigecycline

INAPPROPRIATE USES

1. Due to low serum concentrations, tigecycline should not be used for bacteremias or CNS infections
2. Infections where Pseudomonas aeruginosa, Providencia sp., or Proteus sp. are suspected or confirmed pathogens
3. Surgical prophylaxis
4. Pregnant or breast-feeding women
5. Children
6. Tetracycline allergy

SUSCEPTIBILITY TESTING

Tigecycline susceptibility should be obtained to verify the appropriateness of therapy

DOSING

1. Normal hepatic function
   100 mg iv load, followed by 50 mg q 12 hours

2. Severe hepatic impairment (Child-Pugh C)
   100 mg load followed by 25 mg q 12 hours.

3. Dosage adjustment is unnecessary for renal insufficiency or any form of renal replacement therapy (IHD, CVVHDF, SLEDD)

TOXICITIES

The most common adverse events reported with tigecycline are GI related. Nausea and vomiting have both been experienced in 25-39% of patients in clinical trials. Acute pancreatitis has also been reported. Pooled analysis, conducted by the FDA, of 13 trials suggests that tigecycline may be associated with an increased risk of death. This was most apparent in patients with ventilator-associated pneumonia, an unapproved use.

VANCOMYCIN

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Unrestricted	Vancomycin 125 mg po q6h for C. difficile infection
Controlled, 72 hrs	Vancomycin iv
Dose restricted	Vancomycin po in doses other than 125 mg po q6h

APPROPRIATE USE CRITERIA FOR VANCOMYCIN IV

1. Treatment of serious infections due to beta-lactam resistant gram-positive bacteria
2. Treatment of infections due to gram-positive bacteria in patients with serious allergy to beta-lactam antimicrobials
3. Endocarditis prophylaxis in high risk patients allergic to ampicillin, amoxicillin or penicillin and undergoing dental, oral, upper respiratory tract, genitourinary or gastrointestinal procedures
4. Prophylaxis for select cardiothoracic, orthopedic, neurosurgical procedures given as a single dose for procedures lasting less than 6 hours. Patients undergoing procedures lasting more than 6 hours should receive one additional dose. See Surgical Prophylaxis Guidelines.
5. Treatment of healthcare-associated intra-abdominal infections in patients at risk for MRSA. See Complicated Intra-abdominal Infection Guidelines.

APPROPRIATE USE CRITERIA FOR ENTERAL VANCOMYCIN

1. Treatment of C. difficile infection, see C. difficile Guidelines.
   a. Vancomycin is unrestricted at a dose of 125 mg po q6h. All other doses require ID approval. See C. difficile Guidelines for indications for higher doses.
   b. Vancomycin per rectum is restricted and requires ID approval. See C. difficile Guidelines for indications for rectal vancomycin.

INAPPROPRIATE USES OF VANCOMYCIN IV AND PO

1. Prophylaxis for procedures not stated in the Surgical Prophylaxis Guidelines
2. Empirical therapy for febrile neutropenia unless there is strong evidence that the patient has a gram-positive infection (e.g., inflamed central catheter exit site). See Febrile Neutropenia Guidelines.
3. Treatment of a single positive blood culture for coagulase negative Staphylococcus, if other blood cultures drawn at the same time are negative
4. Continued empirical use for presumed infections in patients whose cultures are negative for beta-lactam resistant bacteria
5. MRSA decolonization
6. Primary treatment of C. difficile infection
7. Intravenous vancomycin is potentially nephrotoxic. Alternative therapy should be considered in patients with acute renal insufficiency.
8. Vancomycin treatment of S. aureus strains with a vancomycin MIC of 2 is controversial. ID consultation is recommended

VANCOMYCIN, EMPIRICAL DOSING

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

VANCOMYCIN THERAPEUTIC RANGE

In April, 2011, the AUR Subcommittee updated the therapeutic range for vancomycin at BJH. These new ranges became effective July 1, 2011. These changes were a result of increasing reports of vancomycin-induced nephrotoxicity at BJH and in the medical literature. The update also reflects the changing susceptibility pattern and MIC breakpoints for methicillin-resistant S. aureus (MRSA). The new therapeutic ranges are indication specific.

TABLE 1	**Trough or random vancomycin concentration**
Uncomplicated skin and soft tissue infections	10-20 mcg/mL
All other infections	15-20 mcg/mL
Critical trough or random level (Chemistry Lab to contact physician)	Any value ≥ 21 mcg/mL

EMPIRICAL DOSING OF VANCOMYCIN IV

Vancomycin pharmacokinetics exhibit great interpatient variability, and as a result, achieving vancomycin concentrations within a narrow therapeutic range is often difficult. The following recommendations should be considered general guidance for initial dosing only. Patient-specific factors **must** be considered to individualize initial dosing.

Calculating an initial dose

1. Obtain the patient's actual body weight (kg).
   a. For all patients the dose should be 15 mg/kg, up to a max single dose of 2.25 g
   b. The maximum, empirical total daily dose is 4.5 g (e.g., 2.25 g q12h)
   c. Round doses to the nearest 250 mg

2. Using the Cockroft-Gault equations in Table 2, estimate the patient's creatinine clearance (CrCl). Compass automatically calculates the CrCl based on the most recent serum creatinine (SCr) for a patient's admission.

TABLE 2	Equation
CrCl male	$\frac{(140 - \text{age}) \times (\text{ideal body weight in kg})}{72 \cdot (\text{Scr in mg/dL})}$
CrCl female	CrCl male x 0.85

3. Choose an interval based on the patient's estimated CrCl and age
   a. Because of the potential for vancomycin-induced nephrotoxicity, use iv vancomycin cautiously in patients with a CrCl < 30 mL/min who are not on dialysis. Consider alternatives in this situation.

TABLE 3	**VANCOMYCIN DOSING**	
CrCl (mL/min)	Suggested regimen [1]	Monitoring levels [2]
> 90 age ≤35yr age >35yr	• 15 mg/kg q8h • 15 mg/kg q12h	Draw a trough level prior to 4th dose
50-90	15 mg/kg q12h	Draw a trough level prior to 4th dose
30-49	15 mg/kg q24h	Draw a trough level prior to 3rd dose
<30	15 mg/kg x 1	Draw a random level 24 hours later
CVVHDF SLEDD	• 15 mg/kg q24h • In patients on SLEDD, give first dose "now" and subsequent doses after each SLEDD	Draw a trough level prior to the third dose
PD	15 mg/kg x 1	Draw a random level 24 hours later
IHD	• 10-15 mg/kg to a max of 1.5 g after each IHD • In patients on IHD, give first dose "now" and subsequent doses after each IHD	Draw a trough level just prior to the third IHD session

The above recommendations should be considered general guidance only. Patient-specific factors **must** be considered to individualize dosing.

1 Round dose to nearest 250 mg. Max single dose 2.25 g. Max total daily dose 4.5 g.
2 Vancomycin levels are recommended in patients for whom the anticipated duration of therapy is at least 3 days. Patients on prolonged therapy should have trough levels drawn twice weekly. Vancomycin peak levels are not routinely recommended.

ADJUSTING VANCOMYCIN DOSES ONCE LEVELS RETURN
See Vancomycin Dosage Adjustments monograph

DURATION OF INFUSIONS
1. At BJH, in order to prevent red man syndrome, vancomycin doses that are rounded to the nearest 250 mg are administered over the following durations for either peripheral or central intravenous lines.

TABLE 4	Duration of infusion
≤ 500 mg	30 min
750-1250 mg	60 min
1500-1750 mg	90 min
2000-2250 mg	120 min

VANCOMYCIN DOSAGE ADJUSTMENTS

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

To initiate new therapy, see Vancomycin Dosing and Monitoring monograph

ASSESSING THE APPROPRIATENESS OF DRAW TIMES

1. Before adjusting doses, verify that vancomycin levels were drawn appropriately as described in Table 1.
2. For levels drawn outside of the parameters stated in Table 1, consider contacting a pharmacist for assistance with interpreting the level.

TABLE 1	INTERPRETING VANCOMYCIN LEVELS
CrCl (mL/min)	What is considered an appropriately drawn level
> 50	Trough immediately prior to at least 4th dose
30-49	Trough immediately prior to at least 3rd dose
<30	Random level 24 hours after the dose
CVVHDF SLEDD	Trough immediately prior to the third dose
PD	Random level 24 hours after the dose
IHD	Trough immediately prior to the third IHD session
Using the lab draw times and dosing administration times in Compass, verify that the level was in fact appropriately obtained in relation to the dose as stated above.	

ADJUSTING VANCOMYCIN DOSES BASED ON A LEVEL

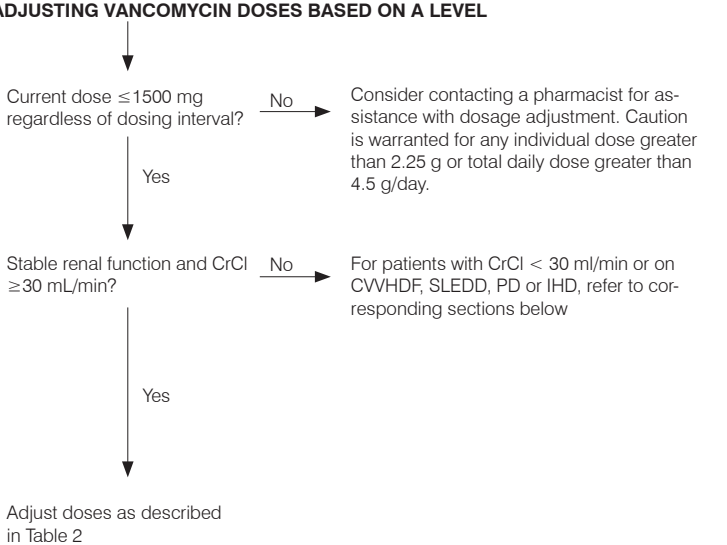

TABLE 2	ONLY FOR PATIENTS WITH INDIVIDUAL DOSES ≤ 1500 MG AND CrCl ≥ 30 ML/MIN		
Vancomycin trough level (mcg/mL)	Currently on q8h dosing	Currently on q12h dosing	Currently on q24h dosing
≤ 5	Pursue alterative therapy [1]	Change to q8h at same dose in mg	Change to q12h at same dose in mg
5.1-10	↑ dose by 250-500 mg and keep q8h	↑ dose by 250-500 mg and keep q12	↑ dose by 250-500 mg and keep q24h
10.1-15	↑ dose by 250 mg and keep q8h (OR no change in current dose for uncomplicated skin infection)	↑ dose by 250 mg and keep q12h (OR no change in current dose for uncomplicated skin infection)	↑ dose by 250 mg and keep q24h (OR no change in current dose for uncomplicated skin infection)
15.1-20	No change in current dose	No change in current dose	No change in current dose
20.1-25	• ↓ dose by 250 mg and keep q8h, OR • Change to q12h at same dose in mg	• ↓ dose by 250 mg and keep q12h, OR • Change to q24h at same dose in mg	↓ dose by 250 mg and keep q24h
> 25	Hold vancomycin [2]	Hold vancomycin [2]	Hold vancomycin [2]

1. Extreme difficulty in achieving therapeutic troughs is expected; q6h dosing is impractical. ID consultation is suggested in this situation
2. Consider vancomycin-induced nephrotoxicity as the cause of the high level. Consider alternative therapy and ID consultation if nephrotoxicity has occurred. If vancomycin is to be continued, check vancomycin levels every 24 hours until < 20 mcg/mL. When level < 20 mcg/mL, re-dose with 15 mg/kg and check another level 24 hours after this dose.

TABLE 3	FOR PATIENTS ON CVVHDF, SLEDD
Vancomycin trough level (mcg/mL)	Dosage adjustment
≤ 10	↑ dose by 250-500 mg and keep q24h
10-15	↑ dose by 250 mg and keep q24h
15.1-20	No change in current dose
20.1-25	↓ dose by 250 mg and keep q24h
> 25	Hold vancomycin [2]

1. These recommendations only apply to patients on CVVHDF or SLEDD with stable flow rates and without interruptions of chronic renal replacement therapy
2. Check vancomycin levels every 24 hours until < 20 mcg/mL. Re-dose vancomycin when level < 20 mcg/mL

INTERPRETING IHD LEVELS

1. Ideally, pre-dialysis vancomycin levels should be used to adjust doses in patients on IHD. A standard, 3 hour high-flux IHD session reduces pre-dialysis blood levels by approximately 40%. The following recommendations assume that the patient is receiving IHD three times weekly.

TABLE 4	FOR PATIENTS ON IHD
Pre-dialysis vancomycin level (mcg/mL)	Dosage adjustment
≤ 20	↑ dose by 250-500 mg
20-30	No change in current therapy
> 30	↓ dose by 250-500 mg

FOR PATIENTS WITH CrCL < 30 ML/MIN OR ON PD

1. Redose with 15 mg/kg when level is < 20 mcg/mL

ASSESSING FOR VANCOMYCIN-INDUCED NEPHROTOXICITY

1. Because of the potential for vancomycin-induced nephrotoxicity, use iv vancomycin cautiously in patients with underlying and/or acute renal insufficiency. Consider alternative therapies in this situation. ID consultation is recommended.
2. Serum creatinine and/or trough level increases should raise suspicion for the possibility of vancomycin-induced nephrotoxicity.

MONITORING RECOMMENDATIONS

1. Twice weekly BMP and vancomycin troughs while on vancomycin.
2. Goal troughs: 15-20 mcg/mL for all infections except uncomplicated skin infections (10-20 mcg/mL). Regardless of infection site, troughs should always be ≥ 10 mcg/mL

VORICONAZOLE

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

Restricted	VoriCONAZOLE, iv and po

APPROPRIATE USE CRITERIA FOR VORICONAZOLE

1. Treatment of the following serious systemic mycoses in patients who are intolerant of or refractory to other therapies:
   a. Aspergillosis, invasive (first-line therapy)
   b. Scedosporium apiospermum infection
   c. Fusarium spp. infection, including Fusarium solani
   d. Candidal infections resistant to fluconazole but sensitive to voriCONAZOLE.

INAPPROPRIATE USES

1. Fungal urinary tract infections
2. Zygomycosis

PRECAUTIONS

1. Visual disturbances (blurry vision, photophobia, chromatopsia) are common and occur in up to 46% of patients. Patients should be warned of these adverse effects and avoid driving or other hazardous tasks while taking voriCONAZOLE.
2. Because voriCONAZOLE is metabolized by CYP2C19, CYP2C9, CYP3A4, clinicians should carefully monitor for numerous, potential drug interactions. Coadministration of the following drugs is contraindicated: terfenadine, astemizole, cisapride, pimozide, quinidine, sirolimus, long-acting barbiturates, rifampin, rifabutin, carbamazepine, ergot alkaloids. Some interactions require dosage modification:
   a. Phenytoin: voriCONAZOLE maintenance dose - 5 mg/kg q12h
   b. Efavirenz: voriCONAZOLE maintenance dose - 5 mg/kg q12h AND decrease efavirenz dose to 300 mg qbedtime
3. Because the cyclodextrin vehicle may accumulate in patients with renal dysfunction, iv voriCONAZOLE is not recommended in patients with a CrCl $<$ 50 ml/min. Consider using the oral route in this situation. Cyclodextrin has been reported to cause pancreatic adenocarcinomas in rats but not other animals. The clinical significance of cyclodextrin accumulation in humans is not known. CVVHDF appears to remove cyclodextrin.

DOSING

1. Dosage adjustments are unnecessary for renal dysfunction or in any form of chronic renal replacement therapy (IHD, CVVHDF, SLEDD).
2. Consider alternative therapies in patients with severe hepatic dysfunction. If use is necessary, reduce maintenance doses by 50% in patients with severe hepatic dysfunction.
3. Monitoring drug levels is recommended. See Therapeutic Drug Monitoring monograph
4. Oral bioavailability is greater than 95%. When feasible, use oral therapy. Round all doses to nearest tablet sizes (50 mg, 200 mg) * A 40 mg/mL oral suspension is available

Loading dose	6 mg/kg iv q12h x 2 doses
Maintenance dose, iv	4 mg/kg iv q12h
Maintenance dose, po *	$\geq$ 40 kg: 200-300 mg po q12h, or 4 mg/kg po q12h *
	$<$ 40 kg: 100-150 mg po q12h, or 4 mg/kg po q12h *

IDTG

INFECTIOUS DISEASES TREATMENT GUIDELINES

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NATIONAL LEADERS IN MEDICINE

ANTIBIOTIC LOCK THERAPY

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RESTRICTION STATUS

ID consult and IV Therapy consult required	Initiation of antibiotic lock therapy requires both an ID and IV Therapy consult. Call 7-3535 to initiate an ID consult. Submit a Compass order for an IV Therapy Consult.

ROLE OF ANTIBIOTIC LOCK THERAPY (ALT)

The ideal treatment of a catheter-related blood stream infection involves the removal of the infected catheter and administration of intravenous antibiotics directed at the causative organism. In rare instances, the risks of removing an infected catheter outweigh the benefits. One method to salvage the catheter is to administer systemic antibiotics in addition to antibiotic lock therapy (ALT). ALT involves the instillation of an antibiotic solution into the catheter and allowing the solution to dwell for a period of time. The use of ALT is controversial and is supported primarily by descriptive studies and expert clinical opinions.[1] Administering ALT is complicated and numerous steps are required in order to safely give these solutions. In order to provide guidance to the prescriber, both an IV Therapy and ID consult are required to initiate ALT.

RELATIVE CONTRAINDICATIONS TO ALT

1. Patients in whom attempts to remove the infected catheter have not been exhausted. ALT should be considered a rarely used salvage regimen.
2. Patients receiving continuous, 24 hour infusions of any medications requiring a dedicated lumen or line, including but not limited to: amiodarone, argatroban, bivalirudin, diltiazem, DOBUTamine, heparin, narcotics, pressors, total parenteral nutrition (TPN). In order to be effective, ALT requires that all lumens of the catheter be locked with an ALT solution. Even if an attempt is made to "rotate" lumens used for ALT and the 24-hour drug infusion, providing ALT in this manner may render ALT ineffective, is logistically difficult to manage and highly prone to error.
3. Patients in whom ALT must be continued upon discharge from BJH. Since the course of therapy may be prolonged, prescribing ALT at home or at a long-term care facility, may be required. Prescribers should consider if the patient will be discharged to a facility that can continue ALT once it has been started at BJH. BJC Home IV Therapy can continue ALT on selected patients. However, other home infusion companies may not be equipped to handle the complexity of this treatment. Prescribers should contact the patient's case manager for assistance with these outpatient issues.
4. Prophylactic ALT, as an attempt to prevent future catheter-related infections. This guideline is for the management of a catheter infection in the setting of a retained catheter. It does not address the use of antibiotic locks as a preventive measure.
5. Patients requiring a drug other than saline or heparin to maintain catheter patency, examples include but are not limited to alteplase (TPA, Activase). The stability of these drugs in combination with vancomycin or gentamicin was not tested.
6. Patients allergic to gentamicin and/or vancomycin should not receive ALT with these antibiotics.
7. Patients with allergy or intolerance to heparin, including heparin-induced thrombocytopenia (HIT), should not receive heparin-containing solutions.

BJH ANTIBIOTIC LOCK SOLUTIONS

The Infectious Diseases Society of America and several investigators have promoted a variety of solutions for ALT. The integrity of these solutions was examined by BJH Pharmacy. A yet unpublished in vitro study at BJH identified four solutions which are chemically and physically stable at 72 hrs.[2] After a review of the literature, and based on the results of the BJH stability study, the only ALT solutions endorsed by AUR and allowed for use at BJH are listed below. No antifungal ALT solutions were tested by Pharmacy, therefore an

antifungal option is unavailable. An order bundle is available in Compass, but it can only be accessed by ID consultants.

ALT WITH OR WITHOUT HEPARIN

The use of heparin for maintaining patency of lines is highly variable across institutions and within BJH. In addition, the concentration of heparin needed to maintain the stability of ALT solutions (2500 units heparin/mL) is much higher than the concentration of heparin needed to lock a hemodialysis catheter (1000 units heparin/mL) or peripheral line (10 units heparin/mL). **In order to prevent the accidental overdose of heparin during ALT, heparin containing solutions are generally not recommended and are reserved for certain catheter types and patient populations as noted below**.

Solutions without heparin

1. Vancomycin 5 mg/mL in NS
2. Gentamicin 1 mg/mL in NS

Heparin-containing ALT solutions

1. These solutions should be limited to these catheter types. For all other patients, saline-based ALT solutions (above) are recommended.
   a. Hemodialysis catheters.
   b. Pheresis catheters
   c. Tunneled catheters
   d. Implanted ports
2. Vancomycin 2.5 mg/mL + heparin 2500 units/mL
3. Gentamicin 1 mg/mL + heparin 2500 units/mL

TABLE 1: CATHETER TYPE

Catheter type	ALT solution volume dispensed
Small bore catheters or ports	• 2 mL ALT solution in 5 mL syringe • These catheters will require less than or equal to 2 mL ALT solution to fill a lumen • Administer only the amount needed to fill the lumen. Each lumen may require a different volume.
Large bore catheters or ports	• 2 mL ALT solution in 5 mL syringe • Because of their size, these catheters may require more than 2 mL of ALT solution to fill a lumen, i.e., multiple syringes for each lumen may be needed.

TYPES OF CATHETERS AND LUMEN VOLUME

Approximately 10 different types of catheters are used routinely at BJH. The choice is determined by a patient's needs as well as physician preference. On occasion, patients may be transferred from outside facilities on catheters not typically used at BJH. The volume of ALT solution needed to fill, but not flush, a catheter depends on its lumen size and patient-specific physical characteristics (e.g., for a PICC, the distance from the patient's antecubital fossa to vena cava). Central lines, which are not tunneled, have plastic labels on each lumen which indicate the volume needed to fill each lumen. For catheters with multiple lumens, the volume needed to fill one lumen may differ from another.

In order to prevent excessive doses of antibiotics and heparin, only the amount of ALT solution needed to fill a lumen should be instilled. **Given the variety and complexity of catheter types, it is imperative that an IV Therapy consult be obtained to determine the type of catheter being used, the volume of each lumen, and whether or not a heparin-containing ALT solution should be used.**

TO INITIATE ALT

1. Obtain the required ID consult. ID consultant will:
   a. Determine if ALT is appropriate and whether or not contraindications are present
   b. If ALT is deemed appropriate, ID consultant will enter the following orders
      1. IV Therapy consult. The IV Therapy RN should review the patient's line then pass the following information on to the ID consultant and the primary care nurse.
         a. Catheter type and number of catheter lumens
         b. Volume(s) needed to fill each of the catheter's lumens. Nurses should note that these volumes may vary depending on which lumen is being filled
         c. Whether or not heparin should be in the ALT solution
      2. ALT order bundle - ID consultants can access the ALT order bundle using the search term "antibiotic lock". Choose the appropriate ALT solution based on the need for heparin and the organism being treated.
2. Only ID consultants can complete the ALT order bundle in Compass.
3. If needed, the IV Therapy consult note can be found in Compass in the patient's Documents Review tab as a Vascular Access Note. Use the Group By icon to group documents alphabetically by document name.

PHARMACY COMPOUNDING

In order to prevent accidental heparin overdosage, heparin-containing ALT solutions are recommended only for certain patient populations. For solutions containing heparin, cloudiness may be noted upon addition of heparin during compounding. Usually, this initial cloudiness clears with continued addition of heparin to its final concentration. ALT solution should not be dispensed by Pharmacy if the final compounded solution is cloudy or has other evidence of precipitation. Cloudy solutions should never be administered to a patient. ALT Kits are maintained by Pharmacy and are available in Remstar.

NUMBER OF ALT SOLUTION SYRINGES NEEDED PER DAY

The number of syringes needed per day will depend on the number of lumens that the infected catheter contains, as well as the frequency at which the catheter is accessed. RNs may request additional ALT syringes through Compass using Order Message Manager. ALT solutions will be delivered by Pharmacy to the nursing divisions and stored with other medications in refrigerated patient-specific bins.

ALT ADMINISTRATION

1. Obtain ALT solutions and ALT Kit from Pharmacy. The ALT Kit contains:
   a. ALT sign - to be placed at the head of the patient's bed by RN
   b. Written nursing instructions on how to administer ALT. These instructions should be communicated to each subsequent nurse at each shift change. If there are questions on how to administer solutions, contact an IV Therapy nurse.
   c. "Antibiotic Lock Therapy" labels. Each time the patient's line is accessed a new label should be wrapped around the patient's line. The label serves as an additional reminder that this catheter should be treated with special care.
2. ALT solutions should not be utilized/instilled if there is any evidence of precipitation or cloudiness observed in the ALT syringes.
3. **Instill only the amount of ALT solution needed to fill each lumen**. The appropriate volume of ALT solution to administer should be obtained from the initial IV Therapy consult. Some non-tunneled catheters have plastic labels on each lumen indicating the lumen-specific volume.
4. ALT solution should be allowed to dwell until the line is accessed again, for up to 48 hours (up to 72 hours in line used for hemodialysis).
5. In order to prevent the inadvertent overdosage of heparin, gentamicin or vancomycin, if a medication needs to be administered through the line, **the ALT solution should be withdrawn from all lumens and never flushed through.**
6. When access to a lumen is required
   a. Withdraw the old ALT solution from the lumen being accessed
   b. Flush this lumen with NS
   c. Administer the drug or draw blood from this lumen as needed

   d. Once completed, flush this lumen again with NS again
   e. Instill new ALT solution into this lumen
   f. Relock the remaining lumens with new ALT solution using procedures a, b, e above.
7. Fresh ALT solution may dwell until the next use of the catheter (not to exceed 48 hours, or 72 hours in dialysis patients). A daily supply of fresh ALT solutions will be dispensed to the nursing division by Pharmacy✎
8. Alternative solutions during patient transfers or procedures
   a. For patients requiring transfer to a procedural area or bedside procedures in which the line may require accessing, withdraw ALT solution from all lumens prior to patient leaving the PCU or the bedside procedure✎
   b. Flush the line with the appropriate non-antibiotic locking solution (i.e., saline alone or heparin alone), as indicated by the type of line and previous orders.

CONCOMITANT SYSTEMIC ANTIBIOTIC THERAPY

Concomitant systemic antibiotics should accompany ALT for the duration of therapy.

DURATION OF ALT

The typical duration of ALT is 14 days.

REFERENCES

1. BJH Medication Management Policy: Antibiotic Lock Therapy (available through the BJH policy website)
2. Mermel LA, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis. 2009:49:1-45.
3. Ciamacco C, et al. In vitro evaluation of physical and chemical stability of antibiotic-heparin lock solutions. Barnes-Jewish Hospital, April, 2011. Publication in progress. Data on file with Dave Ritchie, PharmD.

GUIDELINES DEVELOPED BY

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CLOSTRIDIUM DIFFICILE INFECTION

Divisions of Infectious Diseases and Gastroenterology and Section of Colorectal Surgery, Washington University Medical Center, June 2013

The recommendations that follow are based on critical review of the literature and opinions of local experts✎ The definitions below are intended to provide a clinical framework upon which to approach C. difficile infection✎ Not all strategies work for all patients and treatment should be individualized.

DEFINITIONS

1. **C. difficile infection (CDI)**
   - ✓ Patient with C. difficile toxin A or B positive stool with clinically significant diarrhea (at least three bowel movements per day or diarrhea plus abdominal pain/cramping) or ileus and other causes of diarrhea or ileus excluded.
   - ✓ Or pseudomembranes seen on endoscopy or histopathology

   Note: BJH uses an enzyme immunoassay (EIA) that detects toxins A and B. Based on the CDI prevalence at BJH, the negative predictive value of this assay is greater than equal to 95%. Automatic repeat testing after a negative test should not be performed.

2. **Successful therapy**
   - ✓ Decrease in stool output to near baseline plus resolution of all other symptoms attributed to CDI

3. **Recurrent CDI**
   - ✓ Previous successful therapy and recurrence of symptoms ≤ 60 days after completion of full course of successful therapy plus either of the following:
   1. Stool positive for C. difficile toxins A or B and other causes of diarrhea or ileus excluded
   2. Pseudomembranes seen on endoscopy or histopathology

4. **Refractory CDI**
   - ✓ Lack of improvement after 6 days of adequate therapy or worsening symptoms

TREATMENT

1. General management issues for all cases of CDI

   Supportive therapy as needed
   - ✓ Fluid, electrolyte, hemodynamic management

   Modify risk factors
   - ✓ Avoid unnecessary antibiotics, and stop offending antibiotic(s) if possible
   - ✓ Avoid unnecessary gastric acid suppression
   - ✓ Avoid anti-motility/antiperistaltic agents
   - ✓ Avoid lactose containing foods

   Initiate contact precautions
   - ✓ Gowns and gloves should be worn whenever entering the patient's room. See Isolation Precautions

   Practice good hand hygiene
   - ✓ Wash hands thoroughly or use alcohol hand hygiene products before and after all patient contact

TABLE 1	GRADING OF CDI SEVERITY
CDI severity	Any of the following
Mild	• Diarrhea and minimal symptoms
Moderate	• IV fluids needed (not hypotensive) • Abdominal pain • Mucus or blood in stool • WBC 10K - 20K without other obvious cause • Fever of 38.0 to 38.5˚ C • Endoscopic evidence of colitis
Severe	• IV fluids needed (hypotensive, if vasopressors required, then consider life-threatening) • Ileus • Peritoneal signs • WBC > 20K without other obvious cause • Fever > 38.5˚ C
Life-threatening	• Perforation • Toxic megacolon • Colonic ischemia • Colonic bleeding requiring transfusion • Hemodynamic collapse (i.e. vasopressors required) without other obvious cause

2. Treat based on the following disease categories
   a. **First episode**
      1. Mild to moderate CDI
      2. Severe CDI without ileus, or life-threatening CDI and able to take oral medications
      3. Severe CDI with ileus or life-threatening CDI and unable to take oral medications
   b. **Recurrent disease**
      1. First recurrence
      2. Second or greater recurrence
   c. **Refractory disease**

FIRST EPISODE

1.. **Mild to moderate CDI**
   a. Metronidazole 500 mg po tid x 14 days
   b. Pregnant or intolerant of metronidazole
      1. Vancomycin 125 mg po qid x 10-14 days
      2. Vancomycin per rectal enema is not indicated
   c. Fidaxomicin may be appropriate, ID consult required

3. **Severe CDI without ileus or life-threatening CDI and able to take oral medications**
   a. Vancomycin 125 mg po qid x 10-14 days*
   b. Vancomycin per rectal enema is not indicated in patients able to take oral medications
   c. Colorectal Surgery consult should be obtained
   d. Infectious Diseases and/or Gastroenterology consult should be obtained
   e. Fidaxomicin may be appropriate, ID consult required

4. **Severe CDI with ileus or life-threatening CDI and unable to take oral medications**
   a. Metronidazole 500 mg IV q8h **
   b. Plus
      1. Vancomycin 500 mg per NG tube q6h
      2. And/or vancomycin 500 mg/L 250 mL per rectal enema q6h
      3. And/or vancomycin 500 mg/L 1 L per cecal catheter 1-3 ml/min gtt or per small bowel tube 1-3 ml/min gtt.**
   c. Colorectal Surgery consult should be obtained
   d. Infectious Diseases and/or Gastroenterology consult should be obtained
   e. Switch to oral therapy as soon as possible (metronidazole or vancomycin per above)

   ** Note: Efficacy of IV metronidazole and vancomycin enemas or per cecal catheter has not been established; vancomycin per rectum may be associated with an increased risk of bloodstream infections.

RECURRENT

✓ Up to 20% of first CDI episodes recur within 60 days of resolution, and up to 65% of recurrent episodes lead to further recurrences.
✓ The management goal for recurrent CDI is to
   1. Treat the recurrent episode and
   2. Prevent further recurrences
✓ Although recurrent episodes usually resolve with standard therapy, data regarding efficacy of treatment regimens for preventing further recurrences are extremely limited, and there is no single management approach with proven superiority.
✓ For frequently recurring CDI, consultation with Infectious Diseases or Gastroenterology is recommended.

1. **First recurrence**
   a. Treat as First Episode

2. **Second or greater recurrence**
   Refer for ID consultation. Strategies that can be considered include
   a. Treat as for first or second episode. Avoid prolonged metronidazole therapy.
   b. Tapered dose vancomycin regimen [1]
   c. Pulsed dose vancomycin regimen [2]

   [1] Tapered regimens have not been standardized but small observational studies suggest that vancomycin 125 mg po qid x 7-14 days with a gradual taper over another 14-28 days may be effective.
   [2] Pulsed regimens have not been standardized but small observational studies suggest that vancomycin 125-500 mg po single doses given every 2-3 days for 14-28 days may be effective. Pulsed regimens were usually given following a standard or tapered course of antibiotic therapy.

REFRACTORY

- ✓ No data exist for treatment of refractory CDI.
- ✓ In severe cases, response may take as long as seven days. In vitro resistance to metronidazole and vancomycin is rare (even with recurrent CDI), and actual in vivo resistance is difficult to establish.
- ✓ For refractory CDI, consultation with Infectious Diseases, Gastroenterology, or Colorectal Surgery is recommended.
- ✓ If a case is truly thought to be refractory, consider switching therapy (metronidazole to vancomycin or vancomycin to fidaxomicin. ID consult required to initiate fidaxomicin).

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COMPLICATED INTRA-ABDOMINAL INFECTIONS

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

RISK STRATIFICATION

To guide antimicrobial therapy, patients with complicated intra-abdominal infections (IAI) should be placed into one of three groups using criteria from the Surgical Infection Society (SIS)/Infectious Diseases Society of America (IDSA) Guidelines.[1]

1. **Community-acquired intra-abdominal infections - two subgroups**

   a. **Presenting without severe sepsis or septic shock**
   (infections of mild to moderate severity)

   b. **Presenting with severe sepsis or septic shock**
   (infections of high severity)

   c. Patients with community-acquired IAI are those without history of
      1. Hospitalization for more than 48 hours
      2. Residence or treatment in a healthcare facility within the prior 6 months
      3. Use of antibiotics for more than 3 days during the previous 3 months

2. **Health care-associated intra-abdominal infections**
   a. Defined as any patient who does not meet the criteria for community-acquired IAI

GENERAL TREATMENT PRINCIPLES

1. When necessary, modify antimicrobial doses based the patient's current renal or hepatic function
2. Assess severity of beta-lactam allergy. Generally, patients with a history of only a rash to penicillin can be safely treated with a cephalosporin or carbapenem in the absence of a history of a reaction to one of those agents
3. All patients with health care-associated IAI should have cultures obtained, and culture and susceptibility testing should be requested for all Gram-negative aerobic isolates

COMMUNITY-ACQUIRED IAI OF MILD TO MODERATE SEVERITY

1. Without significant beta-lactam allergy
   a. Cefazolin 2 g iv q8h + metronidazole 500 mg iv q8h, or
   b. Cefoxitin 2 g iv q6h, or
   c. Ceftriaxone 2 g iv q24h + metronidazole 500 mg iv q8h, or
   d. Ertapenem 1 g iv q24h

2. With significant beta-lactam allergy
   a. Aztreonam 2 g iv q8h + clindamycin 900 mg iv q8h
   b. Ciprofloxacin 400 mg iv q12h + metronidazole 500 mg iv q8h
      1. At BJH, fluoroquinolones are discouraged because of increasing resistance of Enterobacteriaceae, particularly E. coli
      2. Prior to initiating empirical fluoroquinolone therapy, cultures should be obtained from all patients. Culture and susceptibility testing should be requested for all Gram-negative aerobic isolates.
   c. Tigecycline 100 mg iv x1, then 50 mg iv q12h
      1. Requires ID specialist approval to initiate

COMMUNITY-ACQUIRED IAI OF HIGH SEVERITY

1. Without significant beta-lactam allergy
   a. Cefepime 2 g iv q8h + metronidazole 500 mg iv q8h, or
   b. Piperacillin/tazobactam 4.5 g iv q6h

2. With significant beta-lactam allergy
   a. Aztreonam 2 g iv q8h + metronidazole 500 mg iv q8h + vancomycin 15 mg/kg q12h

HEALTHCARE-ASSOCIATED IAI

1. Without significant beta-lactam allergy, in order of preference
   a. Piperacillin/tazobactam 4.5 g iv q6h
   b. Cefepime 2 g iv q8h + metronidazole 500 mg iv q8h + vancomycin 15 mg/kg iv q12h
   c. Meropenem 1 g iv q8h

2. With significant beta-lactam allergy
   a. Aztreonam 2 g iv q8h + metronidazole 500 mg iv q8h + vancomycin 15 mg/kg q12h

SPECIAL CONSIDERATIONS IN PATIENTS WITH HEALTHCARE-ASSOCIATED IAI

1. **Empirical anti-fungal therapy**
   a. For healthcare-associated IAI consider empirical antifungal therapy if:
      1. History of recent GI surgery and presents with severe sepsis or septic shock, or
      2. History of recent treatment with several courses of broad-spectrum antimicrobial therapy, or
      3. Yeast are identified on gram-stain from intra-abdominal source, or
      4. History of recent total parenteral nutrition (TPN), or
      5. Presence of necrotizing pancreatitis
   b. Choice of antifungal therapy should be based on severity of illness
      1. Critically ill, ICU patient: micafungin 100 mg iv q24h
      2. Less critically ill patient: fluconazole 800 mg iv x1, then 400 mg iv q24h
   c. Discontinue antifungal therapy if fungi are not isolated from peritoneal cultures

2. **Empirical treatment of methicillin-resistant S. aureus (MRSA)**
   a. Consider for patients
      1. With history of previous MRSA infections
      2. Colonized with MRSA
   b. Preferred agent: vancomycin 15 mg/kg iv q12h
   c. Discontinue vancomycin if this organism has not been isolated from peritoneal cultures

3. **Empirical treatment of vancomycin-resistant enterococci (VRE)**
   a. Consider for patients
      1. Colonized with VRE
      2. At very high risk for infection with VRE, e.,g recent vancomycin therapy for more than 7 days
   b. Treatment options
      1. Linezolid 600 mg iv q12h
         a. Avoid in patients with platelet counts < 100 K or on drugs with selective serotonin reuptake inhibitor (SSRI) activity
         b. Requires ID specialist approval
      2. DAPTOmycin 6 mg/kg iv q24h
         a. Requires ID specialist approval
   c. In patients receiving meropenem, if E. faecalis has been isolated, consider switching meropenem to imipenem 500 mg iv q6h, since meropenem is less active against this organism.
   d. Discontinue drugs directed at VRE if this organism is not isolated from peritoneal cultures

OTHER CONSIDERATIONS

1. **De-escalation of therapy**: for patients with high severity community-acquired or health care-associated IAI, pathogen-specific therapy for Gram-negative and other aerobic organisms should be utilized once culture and susceptibility results are available. Generally, this will mean that antimicrobial therapy can be de-escalated to a regimen utilized for mild-to-moderate community-acquired infections, if no resistant organisms are isolated from cultures. However, alternative agents may be needed if resistant organisms are isolated. Anti-anaerobic therapy should be continued even if anaerobic organisms are not isolated.

2. **Duration of antimicrobial therapy** should not exceed 4 to 7 days. Discontinue antimicrobials in patients who are afebrile, have a normal white blood cell count, and can consume an oral or enteral diet. Continuation with oral therapy is not recommended.

3. **For patients who are still symptomatic at 7 days** (continued fever, leukocytosis, or inability to tolerate an oral/enteral diet), appropriate diagnostic studies should be undertaken to identify the source of the ongoing symptoms rather than prolonging the course of antimicrobial therapy or switching to alternative agents.

RERERENCES

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GUIDELINES DEVELOPED BY

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CONTINUOUS VENOVENOUS HEMODIAFILTRATION (CVVHDF), DOSING OF SELECTED ANTIMICROBIALS

Division of Nephrology and Department of Pharmacy, June 2013

The nomenclature and abbreviations used for the different modes of renal replacement therapy (RRT) vary widely in the literature and are often confused. For this primer, the following terms and abbreviations for the various RRT modes are used:

Continuous renal replacement therapy	CRRT
Continuous venovenous hemofiltration	CVVH
Continuous venovenous hemodialysis	CVVHD
Continuous venovenous hemodiafiltration	CVVHDF
Glomerular filtration rate	GFR
Intermittent hemodialysis	IHD
Slow continuous ultrafiltration	SCUF
Urea clearance	UrCl

CVVHDF FLUID FLOW AND LINE CONNECTIONS

Figure 1 - Simplified diagram of fluid flow during CVVHDF
Figure 2 - Prisma dialysis machine line connections

STANDARDIZED CVVHDF AT BJH

1. To minimize errors and limit confusion, when CRRT is desired, the Division of Nephrology primarily uses Prisma dialysis machines set to CVVHDF mode. Other CRRT modes are available on this machine, but generally are not utilized. The dialysis mode indicator is located at the top right corner of the machine's display.

2. CVVHDF is indicated when hemodynamic instability precludes the use of IHD. CVVHDF is utilized only in the ICU where proper hemodynamic monitoring can occur.

FIGURE 1 - SIMPLE DIAGRAM OF CVVHDF FLUID FLOW

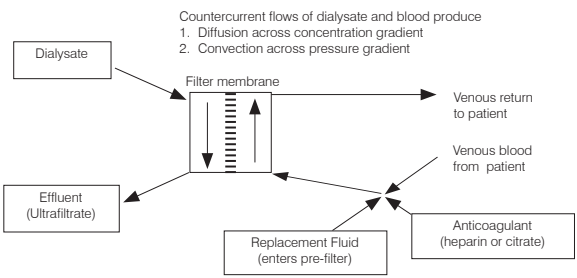
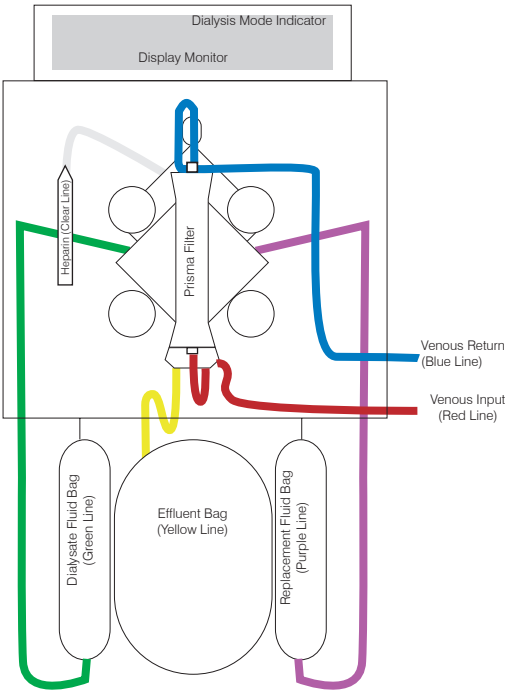


FIGURE 2 - PRISMA DIALYSIS MACHINE LINE CONNECTIONS



SOLUTE AND DRUG CLEARANCE BY CVVHDF

1. During CVVHDF, total urea clearance (UrCl) is a result of clearance of solute by diffusion plus the clearance of solute by convection. The various forms of CRRT differ only in their respective rates of dialysate, replacement fluid and blood flows. Thus, in contrast, UrCl during CVVHD occurs primarily by diffusion, while CVVH clears solutes primarily by convection.

3. Clearance of solutes by diffusion is approximately equal to the dialysate flow rate.

4. Clearance of solutes by convection is approximately equal to the patient's own endogenous urea clearance (i.e., patient's fluid removal rate) plus the replacement fluid rate.

5. For drug dosing purposes, the estimated GFR is approximately 70% of the urea clearance provided by CVVHDF.

6. **Table 1** - Clearances provided by CVVHDF
   Total UrCl = diffusion clearance + convection clearance + patient's clearance
   ≈ dialysate flow rate + [replacement fluid rate + patient's fluid removal rate]
   + patient's clearance

TABLE 1	CLEARANCES BY CVVHDF	
Total UrCl (volume per day)	Total UrCl (volume per minute)	Estimated GFR
60 L/day	42 ml/min	30 ml/min
48 L/day	33 ml/min	23 ml/min
36 L/day	25 ml/min	17 ml/min
24 L/day	16 ml/min	11 ml/min

TABLE 2	FACTORS AFFECTING DRUG CLEARANCE
Drug Factors	• Molecular size and weight • Hydrophilicity • Polarity • Protein binding • Volume of distribution
Dialysis factors	• Dialysis filter porosity • Dialysis filter surface area • Other physiochemical properties of the dialysis filter, which vary by model and manufacturer • Rate of blood flow through the dialysis filter
Patient factors	• Intrapatient variability in endogenous drug clearance, e.g., day to day variations in organ perfusion and function • Alterations in plasma pH, which results in altered plasma protein binding • Altered plasma protein concentrations due to malnutrition, uremia, etc. • Conditions known to increase the volume of distribution of drugs, e.g., anasarca, ascites, pregnancy, > 30% BSA burns.

7. **Table 3** - Dosage adjustments for selected antimicrobials during CVVHDF. Choose higher doses when the patient's total UrCl is "high" (≥ 48 L/day). Clinicians should contact the Renal Consult Service or the Renal Fellow On-Call to determine what total UrCl has been set for a particular patient. Other factors such as site/severity of infection and clinical response should be considered when selecting antibiotic doses. Doses listed are based on clinical studies of CVVHDF drug clearance when available. Otherwise, for some drugs, doses listed are based on the drug's pharmacokinetics, estimated GFR provided by CVVHDF, and extent of removal by IHD, if known.

8. For many drugs, data are lacking to guide dosage modifications during CVVHDF. Alternatively, estimated GFR during CVVHDF can be used to guide drug dosing.

TABLE 3
RECOMMENDED DOSING FOR SELECTED ANTIMICROBIALS DURING CRRT

Antimicrobial	CVVHDF/SLEDD	IHD
Acyclovir	• CNS infections, varicella zoster:10 mg/kg q12-24h • HSV infections: 5 mg/kg q12-24h	• CNS infections, varicella zoster: 5 mg/kg q24h • HSV infections: 2.5 mg/kg q24h
Ambisome	3-5 mg/kg q24h	3-5 mg/kg q24h
Amikacin	See Aminoglycoside Dosing monograph	
Ampicillin	2 g q6-8h	2 g q12h
Ampicillin/sulbactam	3 g q8h	3 g q24h
Azithromycin iv/po	250-500 mg q24h	250-500 mg q24h
Aztreonam	2 g q12h	500 mg-1 g q12h
Cefazolin	2 g q12h	• Preferred inpatient dose: 1 g q24h • Three times weekly IHD: 2 g each Mon, Wed, but 3 g each Fri
Cefepime	2 g q12h	• Preferred inpatient dose: 500 mg-1 g q24h • Three times weekly IHD: 2 g each Mon, Wed, Fri
Cefotetan	1-2 g q12h	1-2 g q48h
Cefoxitin	1-2 g q8-12h	2 g each Mon, Wed, Fri
Ceftaroline	• Usual dose: 400 mg q12h • Dose escalated: 600 mg q12h	• Usual dose: 200 mg q12h • Dose escalated: 300 mg q12h
Ceftriaxone	• Usual dose 1-2 g q24h • Meningitis 2 g q12h	• Usual dose 1-2 g q24h • Meningitis 2 g q12h
Ciprofloxacin iv	400 mg q12h	200-400 mg q24h
Clindamycin iv	600-900 mg q8h	600-900 mg q8h
Colistin	2.5 mg/kg q12h-24h	• Preferred inpatient dose: 1-1.5 mg/kg q24h • Three times weekly IHD: 2-3 mg/kg each Mon, Wed, Fri
DAPTOmycin	• Skin/skin structure: 6 mg/kg q48h • Bacteremia: 8 mg/kg q48h • Enterococcal infection: 8 mg/kg q48h	• Skin/skin structure: 4 mg/kg Mon, Wed and 6 mg/kg Fri • Bacteremia: 6 mg/kg Mon, Wed and 8 mg/kg Fri • Enterococcal infection: 8 mg/kg Mon, Wed, Fri

Antimicrobial	CVVHDF/SLEDD	IHD
Doxycycline	100 mg iv q12h	100 mg iv q12h
Ertapenem	1 g q24h	500 mg q24h
Fluconazole	See Fluconazole monograph • 400 mg x1 then, 200 mg q24h • 800 mg x1, then 400 mg q24h • 800 mg q24h	See Fluconazole monograph • 400 mg x1, then 100 mg q24h • 800 mg x1, then 200 mg q24h • 800 mg x1, 400 mg q24h
Ganciclovir	• Induction: 2.5 mg/kg q12h • Maintenance: 2.5 mg/kg q24h	• Induction: 1.25 mg/kg Mon, Wed, Fri • Maintenance: 0.625 mg/kg Mon, Wed, Fri
Gentamicin	See Aminoglycoside Dosing monograph	
Itraconazole	200 mg q8h x 3 days, then 200 mg q12h	200 mg q8h x 3 days, then 200 mg q12h
Linezolid iv	600 mg q12h	600 mg q12h
Meropenem	1 g q12h	See Meropenem monograph • 500 mg q24h • 500 mg-1 g q24h • 1-2 g q24h
Metronidazole	500 mg q8h	500 mg q8h
Micafungin	100 mg q24h	100 mg q24h
Moxifloxacin	400 mg q24h	400 mg q24h
Oxacillin	2 g q4-6h	2 g q4-6h
Piperacillin/tazo.	3.375 g q6h	• Serious nosocomial infection: 2.25 g q8h • Other infection: 2.25 g q12h
Posaconazole	200 mg po q6h	200 mg po q6h
Rifampin	• GPC synergy: 300 mg q8h • TB: 600 mg q24h	• GPC synergy: 300 mg q8h • TB: 600 mg q24h
Telavancin	7.5 mg/kg q24h	10 mg/kg each Mon, Wed, Fri
Tigecycline	100 mg x 1, then 50 mg q12h	100 mg x 1, then 50 mg q12h
Tobramycin	See Aminoglycoside Dosing monograph	
Trimethoprim/sulfa.	5-7.5 mg/kg q12h	5 mg/kg q24h
ValGANciclovir	• Induction: 450 mg q24h • Maintenance: 450 mg q48h	• Induction: 450 mg each Mon, Wed, Fri • Maintenance: 225 mg liquid each Mon, Wed, Fri
Vancomycin	See Vancomycin Dosing and Monitoring monograph	

Antimicrobial	CVVHDF/SLEDD	IHD
Voriconazole iv	• IV maintenance: 6 mg/kg q12h x 2, then 4 mg/kg q12h	• PO therapy is recommended. See Voriconazole monograph.

1 Choose higher doses when the total UrCl by CVVHDF is "high" (> 48 L/day) Severity, site of infection and clinical response should also be taken into consideration when choosing an antimicrobial dose.
2 Clinical studies or case reports documenting the extent of drug removal by CVVHDF or other modes of CRRT are lacking. Dose listed is based on the drug's pharmacokinetics; estimated GFR provided by CVVHDF (Table 1); and extent of removal by IHD, if known.
3 References on file in Drug Information Center, 314-454-8399
4 For patients on IHD, the dosing table above uses the format "Mon, Wed, Fri" as a surrogate for IHD given three times weekly (Mon-Wed-Fri vs. Tue-Thu-Sat).

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References on file
Drug Information Center
314-454-8399

DYSPNEA/COMMUNITY-ACQUIRED PNEUMONIA (CAP)

Division of Emergency Medicine Advanced Triage Protocol, June 2013

PROTOCOL STATEMENT

1. As a general rule, laboratory, x-ray, and procedures should be ordered by a physician. Under certain circumstances, particularly for the purpose providing prompt patient care, nurses may obtain certain laboratory specimens, order x-rays, and initiate interventions per Advanced Triage Protocols.
2. A physician order will be obtained for all other interventions except as noted in established Advanced Triage Protocols.
3. Purpose: To facilitate the delivery of prompt care to patients in the BJH ED

EQUIPMENT

1. Blood tubes
2. Saline lock
3. X-ray requisition
4. ECG machine
5. Pulse oximetry
6. Oxygen source
7. Order set – Dyspnea/Community Acquired Pneumonia

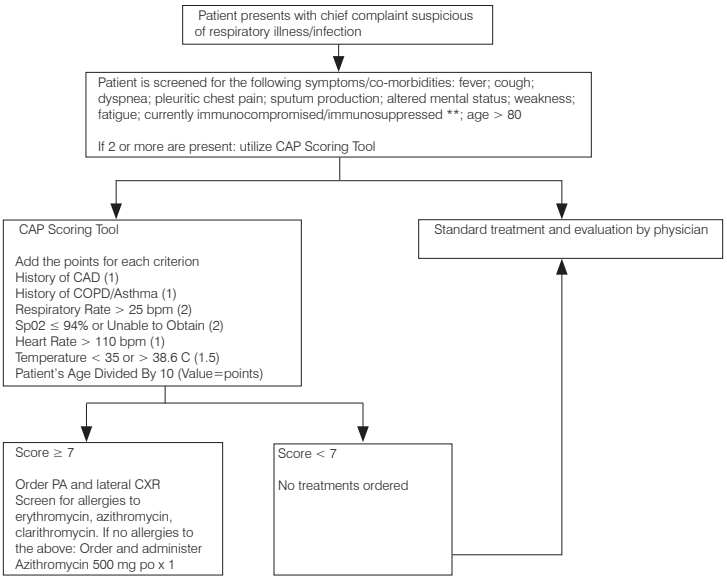
PROCEDURE

1. Assessment
   a. Assess patient condition and identify complaints of dyspnea, cough, and hypoxia.
   b. Determine if patient care will be expedited with prompt nursing interventions.
2. Plan
   a. Gather equipment
   b. Explain interventions to the patient
   c. Document initiation of Dyspnea/Community Acquired Pneumonia Protocol. Document tests ordered and interventions performed.
3. Implementation
   a. Check vital signs and pulse oximetry on room air.
   b. Apply oxygen, 2-4 liters per minute, for respiratory rate of $\geq$ 20/min. or oxygen saturation of less than 93% on room air. Titrate supplemental oxygen to achieve oxygen saturation of greater than or equal to 95%.
   c. Perform 12 lead ECG on men and women over age 35 with cardiac history, hypertension history, diabetic history or complaints of cardiac origin and present immediately to ED attending physician for interpretation. Expedite movement of patients with “high risk” ECG to the ED treatment area.
   d. If the ECG is non-diagnostic, place a saline lock and send blood for CBC, BMP, BNP, PT/PTT/INR, Troponin I, and myoglobin.
   e. For patients with history of obstructive lung disease or wheezing on lung exam, order Respiratory Therapy to evaluate and treat. Order nebulized albuterol and ipratropium.
   f. For patients with history of congestive heart failure or inspiratory crackles on lung exam or peripheral edema, order PA and lateral chest x-ray.
   g. Consider applying a face mask to patients with cough and high fever or for cough for greater than two weeks and history of weight loss.
   h. For patients presenting to triage with 2 of the following complaints: dyspnea, cough, pleuritic chest pain, sputum production, altered mental status, weakness, fatigue, are currently immunocompromised/immunosuppressed, temperature greater than 38.0 degrees Centigrade at triage or reported fever prior to arrival, or are greater than 80 years of age, utilize the CAP screening protocol to determine likelihood of pneumonia. (See attached protocol algorithm: Figure 1)

1. Patients with a CAP score of greater than or equal to 7: order a PA and lateral chest x-ray and screen the patient for allergies to the following: erythromycin, azithromycin, clarithromycin. If the patient denies allergies to those medications, administer 500 mg po azithromycin x1. If the patient reports nausea as the only allergy symptom the ED RN will document this response. The medication may be administered in cases of nausea. This will be documented in the medication administration record. If the patient is taking digoxin this will be documented but not preclude the patient from receiving azithromycin.
2. If the patient has a score less than 7, patient is not enrolled in the CAP pathway.

i. After the chest x-ray is complete, the radiology scheduler will contact the ED communication center secretary and have the assigned physician or nurse (if no physician assigned to the patient) notified that the film has been completed.
j. The physician will read the chest x-ray promptly and perform a focused assessment for risk of Community Acquired Pneumonia.
k. These patients should be placed into a treatment room at the first opportunity.
l. In patients to receive antibiotic therapy and with no contraindications, the first line antibiotic treatment should be a 3rd generation cephalosporin along with a macrolide. (This can be oral if the patient can tolerate po medications.) In patients with contraindications to first line therapy the physician will determine the appropriate antibiotic therapy. Those contraindications include:
   1. Failed first line therapy (i.e. cephalosporin/macrolide)
   2. Are allergic to first line therapy
   3. Have documented infection with highly drug resistant pneumococcus
m. For patients that have not been placed into a treatment room with in two hours of the antibiotic orders being written, the intramuscular or oral medications are preferred and should be given at that time.

FIGURE 1 CAP PATHWAY PROTOCOL



** Immunocompromised/Immunosuppressed

Chronic oral steroids or immunosuppressive medications; history of HIV/AIDS; cystic fibrosis, leukemia, lymphoma; bone marrow transplant; organ transplant; chemotherapy or radiation in the last three months

HIV : ANTIRETROVIRAL THERAPY

Infectious Diseases Clinic, Washington University, June 2013

TREATMENT INDICATED IF

- History of AIDS-defining illness
- CD4 < 500
- Pregnant woman
- Co-infection with HBV when HBV treatment is indicated
- HIV-associated nephropathy

Initial ART combinations usually consist of 3 drugs: 2 NRTIs and either 1 NNRTI or 1 PI or 1 INSTI

* Preferred agents for initial therapy

** Alternate

DHHS ART Guidelines http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf

Generic Name	Tradename	Other Names
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)		
Abacavir	Ziagen	ABC
Didanosine	Videx	DDI
Emtricitabine	Emtriva	FTC
Lamivudine	Epivir	3TC
Stavudine	Zerit	D4T
Zidovudine	Retrovir	ZDV, AZT
Nucleotide Reverse Transcriptase Inhibitors (NRTI)		
Tenofovir	Viread	TDF
Fixed Dose Combinations		
Tenofovir + Emtricitabine + Efavirenz *	Atripla	TDF + 3TC + EFV
Tenofovir + Emtricitabine *	Truvada	TDF + FTC
Abacavir + Lamivudine **	Epzicom	ABC + 3TC
Zidovudine + Lamivudine	Combivir	CBV; ZDV + 3TC
Zidovudine + Lamivudine + Abacavir	Trizivir	ZDV + 3TC + ABC
Rilpivirine + Tenofovir + Emtricitabine **	Complera	RPV + TDF + FTC
Tenofovir Emtricitabine Cobicistat Elvitegravir**	Stribild **	TDF+FTC+COBI+ELV

Generic Name	Tradename	Other Names
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)		
Efavirenz *	Sustiva	EFV
Etravirine	Intelence	ETV
Nevirapine	Viramune	NVP
Rilpivirine **	Edurant	RPV
Protease Inhibitors		
Atazanavir *	Reyataz	ATV
Darunavir *	Prezista	DRV
Fosamprenavir **	Lexiva	F-APV
Indinavir	Crixivan	IDV
Lopinavir/ritonavir **	Kaletra	LPV/r; LPV + RTV
Nelfinavir	Viracept	NFV
Ritonavir	Norvir	RTV
Saquinavir-hard gel	Invirase	SQV-HGC
Tipranavir	Aptivus	TPV
Fusion Inhibitor		
Enfuvirtide	Fuzeon	T-20, ENF
Integrase Inhibitor		
Raltegravir *	Isentress	RAL
CCR5 Antagonist		
Maraviroc	Selzentry	MCV

Zalcitabine, delavirdine, amprenavir, and saquinavir soft gel are not included in this document. These antiretrovirals are either no longer available or no longer used in clinical practice.

Generic	Usual Dose	Renal (CrCl in mL/min) or Hepatic Insufficiency	Food Restrictions
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs)			
Abacavir (Ziagen, ABC) if HLAB5701 test is negative	300 mg po bid or 600 mg qday	No	No

Generic	Usual Dose	Renal (CrCl in mL/min) or Hepatic Insufficiency	Food Restrictions
Didanosine (Videx, DDI)	≥ 60 kg: 400 mg po qday With tenofovir: 250 mg po qday < 60 kg: 250 mg po qday With tenofovir: < 200 mg po qday	≥ 60 kg: CrCl: 30-59: 200 mg po qday 10-29: 125 mg po qday < 10 or CAPD/HD: 125 mg po qday < 60 kg: CrCl: 30-59: 125 mg po qday 10-29: 125 mg po qday < 10 or CAPD/HD: 75 mg po qday use oral solution	0.5 hr before or 2 hrs after meal
Emtric-itabine (Emtriva, FTC)	200 mg po qday	CrCl: 30-49: 200 mg po q48h 15-29: 200 mg po q72h < 15 or HD: 200 mg po q96h	No
Lamivudine (Epivir, 3TC)	150 mg po bid or 300 mg po qday	CrCl: 30-49: 150 mg po qday 15-29: 150 mg po x1, then 100 mg po qday 5-14: 150 mg po x1, then 50 mg po qday < 5 or HD: 50 mg po x1, then 25 mg po qday	No
Stavudine (Zerit, D4T)	≥ 60 kg: 40 mg po bid < 60 kg: 30 mg po bid	≥ 60 kg: CrCl 26-50: 20 mg po q12h 10-25 or HD: 20 mg po qday < 60 kg: CrCl 26-50: 15 mg po q12h 10-25 or HD: 15 mg po qday	No
Tenofovir (Viread, TDF)	300 mg po qday	CrCl: 30-49: 300 mg q48h 10-29: 300 mg 2x/week (q72-96 hrs) HD: 300 mg qweek	No
Zidovudine (Retrovir, ZDV, AZT)	300 mg po bid	CrCl: < 15 or HD: 100 mg q8h or 300 mg qday	No

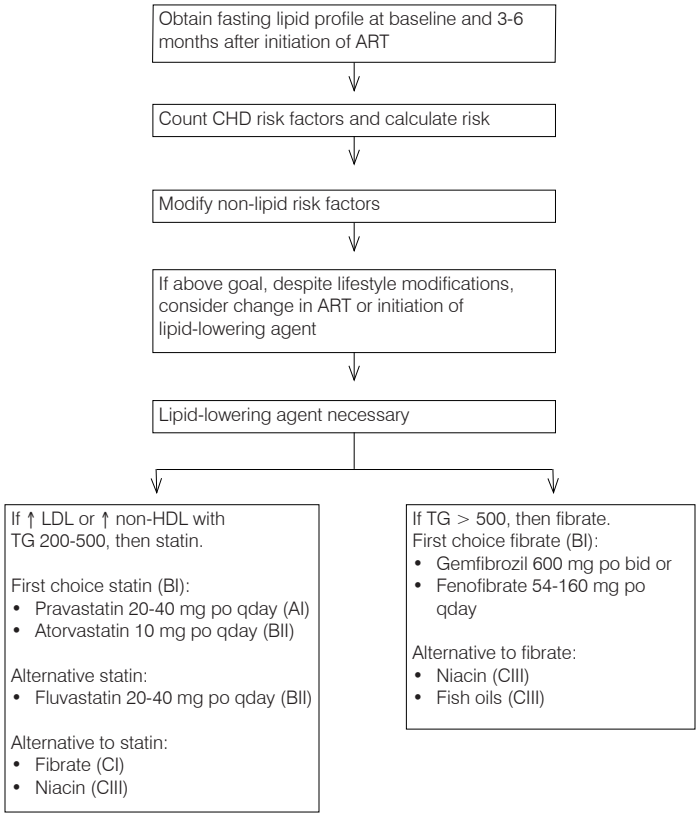
Generic	Usual Dose	Renal (CrCl in mL/min) or Hepatic Insufficiency	Food Restrictions
Fixed Dose Combinations			
Tradename	Composition Per Tablet	Dose	Comments
Combivir (CBV)	AZT 300 mg 3TC 150 mg	One tab po bid	See individual drugs for dosing adjustments and food restrictions
Trizivir	AZT 300 mg 3TC 150 mg ABC 300 mg	One tab po bid	
Truvada	TDF 300 mg FTC 200 mg	One tab po qday	
Epzicom	ABC 600 mg 3TC 300 mg	One tab po qday	
Atripla	TDF 300 mg FTC 200 mg EFV 600 mg	One tab po qday	
Complera	RPV 25 mg TDF 300 mg FTC 200 mg	One tab po qday	
Stribild	TDF 300 mg FTC 200 mg COBI 150 mg ELV 150 mg	One tab once daily • CrCl < 70: Avoid initiating Stribild • CrCL < 50: discontinue Stribild • Child Pugh A or B: no dosage adjustment • Child Pugh C: Stribild is not recommended because of lack of data	Take with food
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)			
Efavirenz (Sustiva, EFV)	600 mg po qbedtime	No recommendation, but caution if hepatic insufficiency	Empty stomach
Etravirine (Intelence, ETV)	200 mg po bid	No adjustment for renal insufficiency; no adjustment for Child-Pugh Class A or B, no recommendation for Child-Pugh Class C	Take with food
Nevirapine (Viramune, Viramune XR, NVP)	200 mg po qday x 14 days then 200 mg po bid XR: 200 mg po qday x 14 days then 400 mg po qday	Contraindicated if Child-Pugh B or C. No adjustment for renal insufficiency.	No

Generic	Usual Dose	Renal (CrCl in mL/min) or Hepatic Insufficiency	Food Restrictions
Rilpivirine (Edurant, RPV)	25 mg po qday	No adjustment for renal insufficiency; no adjustment for Child-Pugh Class A or B, no recommendation for Child-Pugh Class C	Take with food
Protease Inhibitors(PIs)			
Atazanavir (Reyataz, ATV)	Treatment naive: 400 mg po qday Boosted dose (preferred): 300 mg po qday + RTV 100 mg po qday With tenofovir or treatment experienced: 300 mg po qday + RTV 100 mg po qday	Treatment naive on HD: • 300 mg po qday + RTV 100 mg po qday Treatment experienced on HD: • Not recommended RTV boosting not recommended with hepatic impairment. Child-Pugh: 7-9: 300 mg po qday >9: Not recommended	With food
Darunavir (Prezista, DRV)	800 mg po qday + RTV 100 mg po qday If DRV mutations: 600 mg po bid + RTV 100 mg po bid	Renal dosing unnecessary Not recommended in severe hepatic impairment	With food
Fosamprenavir (Lexiva, F-APV)	Treatment naive: • 1400 mg po bid, or • 1400 mg + RTV 100-200 mg po qday, or • 700 mg + RTV 100 mg po bid Treatment experienced: • 700 mg + RTV 100 mg po bid	Renal dosing unnecessary PI-naive, Child-Pugh: 5-9: 700 mg po bid 10-15: 350 mg bid PI- naive or PI-experienced, Child Pugh: 5-6: 700 mg po bid + 100 mg RTV qday 7-8: 450 mg bid + 100 mg RTV qday 10-15: 300 mg bid + 100 mg RTV qday	No
Indinavir (Crixivan, IDV)	800 mg po q8h With ritonavir: 800 mg po bid + RTV 100 or 200 mg po bid	Renal dosing unnecessary Mild to moderate hepatic insufficiency due to cirrhosis: 600 mg po q8h	1 hour before or 2 hrs after meal; may be taken with food if taken with RTV
Lopinavir/ Ritonavir (Kaletra, LPV/r)	• 2 tabs po bid, or • 4 tabs po qday. Each tab contains 200 mg LPV and 50 mg RTV	Renal dosing unnecessary No recommendation with hepatic insufficiency, use with caution	No

Generic	Usual Dose	Renal (CrCl in mL/min) or Hepatic Insufficiency	Food Restrictions
Nelfinavir (Viramune, NFV)	1250 mg po bid	No adjustment in renal insufficiency; contraindicated if Child-Pugh B or C	Take with food
Ritonavir (Norvir, RTV)	"Boosts" other PIs See other PIs for doses		With food
Saquinavir (Invirase, SQV-HGC)	1000 mg po bid + RTV 100 mg po bid	Renal dosing unnecessary; caution with mild-moderate hepatic impairment; contraindicated with severe hepatic disease	No
Tipranavir (Aptivus, TPV)	With ritonavir: 500 mg po bid + RTV 200 mg po bid	Renal dosing unnecessary Child-Pugh A: use caution Child-Pugh B-C: contraindicated	With food
Fusion Inhibitor (FI)			
Enfuvirtide (Fuzeon, T-20)	90 mg subcutaneous bid	Renal insufficiency: No Hepatic insufficiency: No recommendations	No
Integrase Inhibitor (II)			
Raltegravir (Isentress, RAL)	400 mg po bid	No dosage adjustment in renal or hepatic insufficiency	No
CCR5 Antagonist			
Maraviroc (Selzentry, MVC)	With strong 3A4 inhibitor like PIs, except TPV/r: 150 mg po bid Others, including TPV/r: 300 mg po bid With 3A4 inducers, including EFV: 600 mg po bid	CrCl < 30 ml/min or HD • Without potent 3A4 inhibitor or inducer: 300 mg bid • With potent 3A4 inhibitor or inducer: not recommended Hepatic insufficiency: no recommendations	No

HIV : HYPERLIPIDEMIA

Infectious Diseases Clinic, Washington University, June 2013



SPECIAL CONSIDERATIONS WITH HIV

✓ Do not combine lovastatin, simvastatin with protease inhibitors

✓ Other treatment options
- Ezetimibe
- Fish oils (eicosapentaenoic acid, docosahexaenoic acid)

✓ Bile acid sequestering resins may affect absorption of ART, may increase TGs.

✓ For drug interactions between statins and ART, see
DHHS Guidelines: http://aidsinfo.nih.gov
HIV Insite: http://hivinsite.ucsf.edu/

TABLE 1	**ANTIRETROVIRAL-INDUCED HYPERLIPIDEMIA**
Drug	Manifestation
All boosted PIs	Increased LDL, TG, HDL
Stavudine, Zidovudine	Increased TG, LDL
Efavirenz	Increased TG, LDL, HDL

REFERENCES

1. DHHS Guidelines For Use of Antiretroviral Therapy
http://aidsinfo.nih.gov/

2. Guidelines For Management of Dyslipidemia in HIV
http://www.journals.uchicago.edu/doi/full/10.1086/378131

3. HIV Insite at University of San Francisco
http://hivinsite.ucsf.edu/

HIV : OI PRIMARY PROPHYLAXIS

Infectious Diseases Clinic, Washington University, June 2013

PNEUMOCYSTIS JIROVECI PNEUMONIA (PCP)

1. CD4 < 200
2. Preferred: TMP/SMX DS One tab po qday
3. Alternatives
   a. TMP/SMX SS One tab po qday
   b. TMP/SMX DS one tab po 3x/week
   c. Dapsone 100 mg po qday (if G6PD within normal limits)
   d. Atovaquone 1500 mg po qday

TOXOPLASMA GONDII (IF TOXO IgG+)

1. CD4 < 100
2. Preferred: TMP/SMX DS One tab po qday
3. Alternatives
   a. TMP/SMX SS one tab po qday or DS one tab 3 times/week
   b. Dapsone 50 mg po qday + pyrimethamine 50 mg po qweek + leucovorin 25 mg po qweek
   c. Dapsone 200 mg po + pyrimethamine 75 mg po qweek + leucovorin 25 mg po qweek
   d. Atovaquone 1500 mg po qday ± pyrimethamine 25 mg po qday + leucovorin 10 mg po qday

MYCOBACTERIUM AVIUM COMPLEX (MAC)

1. CD4 < 50
2. Preferred
   a. Azithromycin 1200 mg po qweek
   b. Clarithromycin 500 mg po bid
   c. Azithromycin 600 mg twice weekly
3. Alternative: Rifabutin 300 mg po qday

HIV : POST-EXPOSURE PROPHYLAXIS FOR SEXUAL ASSAULT (HIV nPEP*)

Divisions of Emergency Medicine and Infectious Diseases, June 2013

* nPEP is non-occupational post-exposure prophylaxis

GUIDELINES

1. **Offer nPEP only in high risk sexual assaults**, defined as any one of the following situations

   a. Perpetrator with one or more of the following risk factors
      1. IV drug abuse
      2. Obtains sex for drugs/money
      3. History of incarceration
      4. History of multiple sexual assaults
      5. Rumored or known HIV+
      6. Man who has had sex with men

   b. Assault features. One or more of the following
      1. No condom
      2. Anal/genital injury
      3. Semen contacted mucosa
      4. Multiple assaults to victim

2. **When to initiate**: if given, HIV nPEP should be started asap, but MUST be within 72 hours of exposure

3. **Obtain consent/refusal for treatment**. Discuss

   a. **Efficacy**
   Based on studies in animals, and human clinical and observational studies of PEP for occupational exposures, antiretroviral therapy started within 72 hours of exposure and continued for 28 days may reduce seroconversion in high-risk assaults. Observational studies of nPEP have been described.[1,2]

   b. **Drug supply**: a 28 day supply (Truvada, raltegravir) will be given free of charge through BJH Emergency Department. Kits available in Emergent 1 & 2 pyxis. Available to victim since cost of these medications may not be covered by insurance.

   c. **Side effects**
      1. Nausea, vomiting, diarrhea
      2. Headaches
      3. Fatigue
      4. Hepatitis
      5. Rash
      6. Instruct patient to return to ED immediately if side effects are severe

   d. **Drug interactions**
      1. Raltegravir + Truvada is considered a first line regimen because they produce significantly less GI intolerance and are less likely to interact with other medications. This is in contrast to protease inhibitor containing regimens which produce many CYP3A4 drug interactions and have high rates of GI intolerance.
      2. Protease inhibitors (boosted atazanavir, Kaletra) may decrease OC plasma concentrations by ~48%. Since protease inhibitors are part of the HIV nPEP regimen, instruct patient to use condoms in addition to OC for contraception.

3. Instruct patient - "Inform your physicians and pharmacists if you are currently on any other medications or if you start any new medications while taking HIV nPEP." This includes drugs of abuse, erectile dysfunction drugs, health food supplements (garlic, St. John's wort).
4. Drug interaction database tool online (see reference 3)

e. **Prevent HIV transmission** - instruct patient
   1. Do not donate blood, share needles
   2. Practice safe sex (e.g., abstinence, use condom)

f. **Give patient teaching sheet**. Included in the HIV nPEP dose packs.

4. **Draw baseline labs** - HIV Ab, CBC, BMP, LFTs

5. **Establish follow-up**
   a. Patient MUST obtain follow-up within 5 days with one of the following physicians
      1. Patient's private MD
      2. ID clinic (if referring here, call ID fellow 7-3535)
      3. ConnectCare
      4. SAM Clinic at SLCH if < 19 yo (454-2879)
   b. Follow-up labs
      1. CBC, BMP, LFTs at 2 weeks
      2. HIV testing at 3 and 6 months

6. **Offer medications**. Regimens below.

7. **Complete documentation**
   a. HMED order sets: sexual assault, HIV prophylaxis kit
   b. On prescription vials: write patient name, physician name, and date on attached labels
   c. Place copy of prescription label in patient's paper chart

HIV PEP MEDICATIONS

1. First line regimen
   Truvada + Raltegravir

2. Alternative regimens
   Truvada + Boosted Atazanavir
   Truvada + Kaletra
   Combivir + Boosted Atazanavir
   Combivir + Kaletra

Truvada

1. Each tablet contains: tenofovir 300 mg + emtricitabine 200 mg
2. Usual dose: one tablet po q24h
3. Take with food at same time as boosted atazanavir.
4. Primary side effects: stomach upset, rash, darkening of soles of feet/palms, headache, dizziness, vivid dreams

Raltegravir

1. Usual dose: 400 mg po q12h. Note: although Truvada is given once daily.
2. Primary side effects: nausea, headache, insomnia, fatigue
3. May be taken with or without food.

Boosted atazanavir

1. Two drug regimen containing:
   Atazanavir one, 300 mg capsule po q24h PLUS
   Ritonavir one, 100 mg capsule po q24h
2. Ritonavir is added to increase blood levels of atazanavir and allows for qday dosing
3. Take with food at same time as Truvada
4. Primary side effects: GI upset, transaminitis, rash, hyperbilirubinemia, changes in taste sensation
5. Numerous drug interactions

Combivir

1. Each tablet contains: zidovudine 300 mg + lamivudine 150 mg
2. Usual dose: one tablet po q12h
3. Can be taken with or without food
4. Primary side effects: nausea, vomiting, abdominal pain, pancytopenia, headache, myalgia, arthralgia, fatigue

Kaletra

1. Each tablet contains: lopinavir 200 mg + ritonavir 50 mg
2. Usual dose: TWO tablets po q12h
3. Take with food
4. Primary side effects: nausea, vomiting, abdominal pain, headache. Less commonly transaminitis
5. Numerous drug interactions

ANTIEMETIC THERAPY

1. Promethazine is part of the 28-day HIV nPEP dose pack
2. Usual dose: promethazine 25 mg po q6h for first few days, then q6h prn thereafter
3. Common side effects: drowsiness, rash, dry mouth, difficulty urinating, blurred vision

REFERENCES

1. CDC HIV nPEP Guidelines, January 21, 2005
   http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5402a1.htm

2. Prophylaxis following nonoccupational exposure to HIV
   University of San Francisco, http://hivinsite.ucsf.edu/
   Search term: nPEP

3. McNicholl IR, et al.
   Database of antiretroviral drug interactions,
   University of San Francisco. http://hivinsite.ucsf.edu
   Search term: drug interaction database

Guidelines developed by: Steve Liang, MD
Craig McCammon, PharmD
Ed Casabar, PharmD

HIV+ PREGNANT PATIENTS

Washington University Infectious Diseases Division, June 2013

OBSERVE STRICT CONFIDENTIALITY INCLUDING BUT NOT LIMITED TO

- No disclosure to anyone of HIV status without patient's permission
- All discussion of patient's HIV status to occur in private
- No discussions of HIV-related medications or treatments in presence of others

CONSULT

- Formal consult with Adult ID Fellow on admission
  Call 747-3535 (option 1 to page Adult ID Triage Fellow or ID Fellow On-Call)

INTERPARTUM

1. **Stat**: Zidovudine loading dose (Retrovir, AZT, ZDV) 2 mg/kg iv over one hour
   iv zidovudine can and should be started in triage
2. **Followed by**: Zidovudine 1 mg/kg/hr iv intrapartum
   Stop zidovudine when baby born
3. Continue other oral antiretroviral medications (if po permissible)
4. 3 hours of zidovudine should be administered prior to elective cesarean sections
5. **Avoid invasive procedures if possible**: fetal scalp electrode and sampling, AROM, episiotomy, IUPC, internal monitors, vacuum/forceps

DELIVERY

- Pediatrics to be called for all deliveries by HIV+ mothers
- Infants are not to be given injections (e.g., vitamin K, hepatitis B vaccine, glucose sticks) or ophthalmic erythromycin ointment (Ilotycin) until after first bath
- Universal standard precautions should be observed in all deliveries regardless of mother's HIV status

POSTPARTUM

- No breast feeding
- Document reliable oral contraception: tubal ligation, oral contraception, DepoProvera, IUD, Nuva Ring, Implanon, Ortho Evra
- Circumcision of infant may be performed after first 24 hours of life and first bath

ADULT ID FELLOW TO NOTIFY ALL OF THE FOLLOWING

- Pediatric ID pager 424-6877
- Adult pregnancy coordinator: Debbie Gase, RN, MSN
  Pager 836-1658 or Office 747-4373

FOR PREGNANT PATIENTS WITH HIV+ PARTNER

1. Rapid HIV test (OraQuick) on the mother
2. If the mother is at risk for acute infection (i.e., she has not seroconverted yet), send HIV viral load on mother
3. Intrapartum zidovudine for mother as above, regardless of OraQuick results if high suspicion for acute infection (nonspecific viral/febrile illness and/or known unprotected sex with HIV+ partner in 6 weeks prior to delivery)
4. The Adult ID Consult Team should be involved in discussion of additional prophylaxis for mother
5. STAT pediatric ID phone consult to decide infant medications (contact numbers above)

CONFIRM

- Mothers should continue their HAART through labor and delivery and afterwards unless otherwise directed by Adult ID Consult Team
- Mother/guardian should not be discharged without zidovudine and other medications prescribed for newborns in hand

HIV PROPHYLAXIS FOR EXPOSED NEWBORNS

Washington University Infectious Diseases Division, June 2013

OBSERVE STRICT CONFIDENTIALITY INCLUDING BUT NOT LIMITED TO

- No disclosure to anyone of HIV status without mother's permission
- All discussion of mother's and infant's HIV status to occur in private
- No discussions of HIV-related medications or treatments in presence of others

DELIVERY

- **Avoid invasive procedures if possible**
- Infants are not to be given injections (vitamin K, hepatitis B vaccine, glucose sticks) or ophthalmic erythromycin ointment (Ilotycin) until after first bath
- Reminder: universal standard precautions should be observed in all deliveries regardless of mother's status
- Standard resuscitation measures followed for sick infants using standard aseptic technique

MEDICATIONS

- **Stat**: House staff to start exposed newborn on zidovudine stat, by 2 hours after birth
- Discussion with Pediatric ID is not necessary before starting zidovudine

Neonatal zidovudine (ZDV, AZT) dosing for HIV prophylaxis

		Gestational age at birth		
		< 30 weeks	30-34 weeks	≥ 35 weeks
Weeks of age	0-2 weeks	2 mg/kg/dose po q12h or 1.5 mg/kg/dose iv q12h	2 mg/kg/dose po q12h or 1.5 mg/kg/dose iv q12h	4 mg/kg/dose po q12h or 1.5 mg/kg/dose iv q6h
	2-4 weeks	2 mg/kg/dose po q12h or 1.5 mg/kg/dose iv q12h	2 mg/kg/dose po q8h or 1.5 mg/kg/dose iv q8h	
	4-6 weeks	2 mg/kg/dose po q8h or 1.5 mg/kg/dose iv q8h	2 mg/kg/dose po q8h or 1.5 mg/kg/dose iv q8h	

- **Other medications**: added in **high risk** cases based on individualized assessment by Pediatric ID Consult Team

✓ **Nevirapine**: 3 dose series for infants born to mothers not on HAART and infants born to mothers with nevirapine-sensitive virus and significant viral load

Birth weight	Nevirapine dose	Dosing interval
< 1.5 kg	Call Peds ID Consult for recommendation	STAT after birth, 48 hours after first dose, and 96 hours after second dose
1.5-1.9 kg	8 mg po per dose	
≥ 2 kg	12 mg po per dose	

✓ Additional drugs: may be used for infants with resistant maternal virus

1. **Lamivudine**: 2 mg/kg/dose po q12h
2. **Didanosine**: 50 mg/m^2/dose po q12h

LABS
- House staff to obtain: CBC with differential; RPR; HIV DNA PCR; urine CMV culture

PEDIATRIC ID CONSULT
- Weekdays: notify Pediatric ID Fellow pager 790-7784 or office 454-6050
- Nights and weekend Pediatric ID Fellow pager 424-6877
- The Pediatric ID Fellow will notify Cynthia Maxey Brown, RN at pager 490-9137 or office 454-4304 ASAP after birth

DISCHARGE
- Nursery case manager or designee will obtain a 6 week supply of zidovudine and other antiretroviral medications for patient at discharge
- Prescriptions for the infant's outpatient medications should be placed with Pharmacy 24 hours prior to discharge. The nursery team will make sure this happens for infants of private pediatricians
- **All mothers and guardians and infants must be discharged with all medicines in hand**

PROTOCOL FOR NEWBORNS BORN TO MOTHERS WITH HIV+ PARTNER
1. Infants to receive zidovudine prophylaxis
2. Stat call to Pediatric ID Fellow pager 454-6877
3. Remainder of procedures is the same as above.

OBESE DOSING ADJUSTMENTS FOR SELECTED ANTIMICROBIALS

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

1. BJH is an American Society of Metabolic and Bariatric Surgery Center of Excellence (http://www.asmbs.org). The following dosage recommendations were developed by AUR in response to the increasing number of bariatric procedures performed at BJH. Data supporting these recommendations are sparse. Only antibiotics that have been studied in the obese and that are commonly used in bariatric surgery are listed. If studies were unavailable, doses were chosen based on the known pharmacokinetics of these selected antibiotics.

2. **Table 1**: recommended antibiotic dosing for patients with BMI greater than 40 kg/m2 AND body mass greater than 100 kg based on creatinine clearance (CrCl [ml/min]). Other factors such as site and severity of infection and clinical response should be considered when selecting antibiotic doses.

3. Body mass index (BMI)
   = mass in kg / height in meters^2
   = 703 x (weight in lbs / height in inches^2)

4.

NIH classifications	BMI (kg/m^2)
Underweight	18.5
Normal weight	18.5 - 24.9
Overweight	25 - 29.9
Obese	30 - 39.9
Extremely obese	≥ 40

TABLE 1	**Antibiotic dosing BMI > 40 AND body mass > 100 kg**			
Cefazolin	CrCl ≥ 35		CrCl 11-34	CrCl ≤ 10
	2 g iv q8h		2 g iv q12h	2 g iv q24h
Cefepime	CrCl ≥ 60	CrCl 30-59	CrCl 10-29	CrCl < 10
	2 g iv q8h	2 g iv q12h	2 g iv q24h	1 g iv q24h
Cefoxitin	CrCl ≥ 30		CrCl 10-29	CrCl < 10
	2 g iv q6h		2 g iv q12h	2 g iv q24h
Ciprofloxacin iv	CrCl ≥ 30		CrCl 10-29	CrCl < 10
	400 mg iv q8h		400 mg iv q12-24h	400 mg iv q24h
Piperacillin/tazo.	CrCl ≥ 40	CrCl 20-39	CrCl < 20	
	4.5 g iv q6h	3.375 g iv q6h	2.25 g iv q6h	

Other factors such as site and severity of infection should be considered when selecting antibiotic doses. References on file in the Barnes-Jewish Hospital Drug Information Center 90-52-411, 216 S. Kingshighway, St. Louis, MO 63110-1026 314-454-8399.

REFERENCES

1. Wurtz R, Itokazu G, Roldvold K✎ Antimicrobial dosing in obese patients✎ Clin Infect Dis. 1997;25:112-118.
2. Harbarth S, Nobre V, Pittet D✎ Does antibiotic selection impact patient outcome? Clin Infect Dis.2007;44:87-93.
3. Harbarth S, Garbino J, Pugin J, et al✎ Inappropriate initial antimicrobial therapy and its effect on survival in a clinical trial of immunomodulating therapy for severe sepsis✎ Am J Med✎ 2003;115:529-35.
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RENAL DOSING FOR SELECTED ANTIMICROBIALS

Barnes-Jewish Hospital Department of Pharmacy, June 2013

Drug	Usual dose	CrCl (mL/min)	Renal adjustment
Acyclovir	• CNS infections, varicella zoster 10 mg/kg q8h ideal body weight	≥ 50	10 mg/kg q8h
		25-49	10 mg/kg q12h
		10-24	10 mg/kg q24h
		< 10	5 mg/kg q24h
	• Non-CNS HSV infections 5 mg/kg ideal body weight	≥ 50	5 mg/kg q8h
		25-49	5 mg/kg q12h
		10-24	5 mg/kg q24h
		< 10	2.5 mg/kg q24h
Ambisome	3-5 mg/kg q24h	No dosage adjustment necessary	
Amikacin	See Aminoglycoside Dosing monograph		
Ampicillin	1-2 g q4-6h	≥ 50	1-2 g q4-6h
		10-50	1-2 g q6-8h
		< 10	1-2 g q12h
Ampicillin/sulbact.	3 g q6h	≥ 30	3 g q6h
		15-29	3 g q12h
		< 15	3 g q24h
Azithromycin	250-500 mg q24h	No dosage adjustment necessary	
Aztreonam	1 g q8h	≥ 30	1 g q8h
		10-30	500 mg q8h
		< 10	500 mg q12h
	2 g q8h	≥ 30	2 g q8h
		10-30	1 g q8h
		< 10	1 g q12h
Cefazolin	1-2 g q8h	≥ 35	1-2 g q8h
		11-34	1 g q12h
		≤ 10	1 g q24h

Drug	Usual dose	CrCl (mL/min)	Renal adjustment
Cefepime	1 q12h	≥ 60	1 g q12h
		30-59	1 g q24h
		10-29	500 mg-1 g q24h
		< 10	500 mg q24h
	1 g q8h	≥ 60	1 g q8h
		30-59	1 g q12h
		10-29	1 g q24h
		< 10	500 mg-1 g q24h
	2 g q8h	≥ 60	2 g q8h
		30-59	2 g q12h
		10-29	2 g q24h
		< 10	1 g q24h
Cefotetan	1-2 g q12h	≥ 30	1-2 g q12h
		10-29	1-2 g q24h
		< 10	1-2 g q48h
Cefoxitin	1-2 g q6h	≥ 30	1-2 g q6h
		10-29	1-2 g q8-12h
		< 10	1-2 g q24h
Ceftaroline	• Usual dose 600 mg q12h	≥ 50	600 mg q12h
		30-50	400 mg q12h
		15-29	300 mg q12h
		< 15	200 mg q12h
	• Dose escalated 600 mg q8h	≥ 50	600 mg q8h
		30-50	600 mg q12h
		15-29	400 mg q12h
		< 15	300 mg q12h
Ceftriaxone	• Usual dose 1-2 g q24h • Meningitis 2 g q12h	No dosage adjustment necessary	
Ciprofloxacin	• Usual dose 400 mg q12h	≥ 30	400 mg q12h
		10-29	400 mg q24h
		< 10	200-400 mg q24h
	• Dose escalated 400 mg q8h	≥ 30	400 mg q8h
		10-29	400 mg q12-24h
		< 10	400 mg q24h

Drug	Usual dose	CrCl (mL/min)	Renal adjustment
Clindamycin iv	600-900 q8h	No dosage adjustment necessary	
Colistin	2.5 mg/kg q12h	≥ 80	2.5 mg/kg q12h
		40-79	1.25-2 mg/kg q12h
		25-39	1.25 mg/kg q24h
		10-24	1.5 mg/kg q36h
		< 10	1.5 mg/kg q48h
DAPTOmycin	4 mg/kg q24h actual body weight	≥ 30	4 mg/kg q24h
		< 30	4 mg/kg q48h
	6 mg/kg q24h actual body weight	≥ 30	6 mg/kg q24h
		< 30	6 mg/kg q48h
	8 mg/kg q24h actual body weight	≥ 30	8 mg/kg q24h
		< 30	8 mg/kg q48h
Doxycycline	100 mg q12h	No dosage adjustment necessary	
Ertapenem	1 g q24h	≥ 30	1 g q24h
		< 30	500 mg q24h
Fluconazole	400 mg x 1, then 200 mg q24h	≥ 50	200 mg q24h
		< 50	100 mg q24h
	800 mg x 1, then 400 mg q24h	≥ 50	400 mg q24h
		< 50	200 mg q24h
	800 mg q24h	≥ 50	800 mg q24h
		< 50	400 mg q24h
Ganciclovir	Induction 5 mg/kg	≥ 70	5 mg/kg q12h
		50-69	2.5 mg/kg q12h
		25-49	2.5 mg/kg q24h
		10-24	1.25 mg/kg q24h
		< 10	1.25 3x/week
	Maintenance 5 mg/kg	≥ 70	5 mg/kg q24h
		50-69	2.5 mg/kg q24h
		25-49	1.25 mg/kg q24h
		10-24	0.625 mg/kg q24h
		< 10	0.625 mg/kg 3x/week
Gentamicin	See Aminoglycoside Dosing monograph		
Itraconazole	200 mg q8h x 3 days, then 200 mg q12h	No dosage adjustment necessary	
Linezolid	600 mg q12h	No dosage adjustment necessary	

Drug	Usual dose	CrCl (mL/min)	Renal adjustment
Meropenem	500 mg q6h	≥ 50	500 mg q6h
		25-49	500 mg q8h
		10-24	500 mg q12h
		< 10	500 mg q24h
	1 g q8h	≥ 50	1 g q8h
		25-49	1 g q12h
		10-24	500 mg q12h
		< 10	500 mg -1 g q24h
	2 g q8h	≥ 50	2 g q8h
		25-49	2 g q12h
		10-24	1 g q12h
		< 10	1-2 g q24h
Metronidazole	500 mg q8h	No dosage adjustment necessary	
Micafungin	100 mg q24h	No dosage adjustment necessary	
Moxifloxacin	400 mg q24h	No dosage adjustment necessary	
Oxacillin	2 g q4-6h	No dosage adjustment necessary	
Piperacillin/tazo.	4.5 g q6h	> 40	4.5 g q6h
		20-40	3.375 g q6h
		< 20	2.25 g q6h
	3.375 g q6h	> 40	3.375 g q6h
		20-40	2.25 g q6h
		< 20	2.25 g q8h
Posaconazole	200 mg q6h	No dosage adjustment necessary	
Rifampin	GPC synergy 300 mg q8h	No dosage adjustment necessary	
	TB 600 mg q24h	No dosage adjustment necessary	
Telavancin	10 mg/kg actual body weight	≥ 50	10 mg/kg q24h
		30-49	7.5 mg/kg q24h
		< 30	10 mg/kg q48h
Tigecycline	100 mg x 1, then 50 mg q12h	No dosage adjustment necessary	
Tobramycin	See Aminoglycoside Dosing monograph		

Drug	Usual dose	CrCl (mL/min)	Renal adjustment
ValGANciclovir po	Induction 900 mg q12h	> 60	900 mg q12h
		40-59	450 mg q12h
		25-39	450 mg q24h
		11-24	450 mg q48h
		≤ 10	450 mg 3x/week
	Maintenance 900 mg q24h	> 60	900 mg q24h
		40-59	450 mg q24h
		25-39	450 mg q48h
		11-24	450 mg 2x/week
		≤ 10	225 mg 3x/week liquid
Vancomycin iv	See Vancomycin Dosing and Monitoring monograph		
VoriCONAZOLE iv	Maintenance 4 mg/kg q12h	≥ 50	4 mg/kg q12h
		< 50	Oral route preferred. See VoriCONAZOLE monograph

Monograph by: Ed Casabar, PharmD
Dave Ritchie, PharmD
Bennett Bain, PharmD
References on file
Drug Information Center
314-454-8399

SEXUAL ASSAULT, ADULT : STD PROPHYLAXIS AND EMERGENCY CONTRACEPTION

Washington University Division of Emergency Medicine, June 2013

GONORRHEA

Ceftriaxone 250 mg im x 1*
PLUS Azithromycin 1 g po x 1 OR doxycycline 100 mg po q12h x 7 days

CHLAMYDIA

1. First line: azithromycin 1 g po x 1*
2. Alternatives
   a. Doxycycline 100 mg po bid x 7 days or
   b. Erythromycin 500 mg po q6h x 7 days
3. Culture mandatory ONLY in children

TRICHOMONAS VAGINALIS (TV)/BACTERIAL VAGINOSIS (BV)

1. First line: metronidazole 2 g po x 1*
   Alternative: metronidazole 500 mg po bid x 7 days
2. Wet mount
   a. Saline prep - motile trichomonads noted (TV)
   b. KOH prep - fishy odor on “whiff test”, clue cells (BV)

HEPATITIS B/C

1. Hepatitis B vaccine (Engerix-B) 20 mcg (1 ml) im x 1
   Follow-up booster at 1 and 6 months
2. Hepatitis B immune globulin 0.06 ml/kg im x 1 if assailant known to be positive.
3. Tests
   a. Hepatitis B surface Ab
   b. Hepatitis B surface Ag
   c. Hepatitis B core Ab-IgM
   d. Hepatitis C Ab
4. Vaccine should be offered if vaccination status unclear. May be of benefit up to 3 weeks post-exposure due to long incubation period of virus.

SYPHILIS

1. First line: benzathine penicillin G 2.4 million units im x 1 if known high risk exposure*
2. Alternative: doxycycline 100 mg po bid x 10-14 days
3. Obtain RPR
4. Routine empirical treatment not recommended

TETANUS

1. First line: tetanus diphtheria vaccine 0.5 ml im x 1
2. Administer vaccine if no immunization in last 5 years

HIV POST-EXPOSURE PROPHYLAXIS

1. See Tool Book HIV nPEP guidelines

EMERGENCY CONTRACEPTION

1. Levonorgestrel (Plan B One Step) 1.5 mg po x 1
2. Prepackaged in pyxis. Dose to be given in ED.

ANTIEMETIC

1. First line: promethazine 25 mg po q6h prn.
2. Give 30-50 minutes before first dose of HIV prophylaxis. Part of HIV nPEP 28-day dose pack. Available in Emergent 1,2 pyxis machines.

REFERENCES

1. http://www.cdc.gov/STD/treatment/
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SURGICAL ANTIMICROBIAL PROPHYLAXIS FOR SELECTED SURGICAL PROCEDURES

Barnes-Jewish Hospital Antibiotic Utilization Review Subcommittee, June 2013

GENERAL GUIDELINES

1. To achieve the highest plasma concentrations at the time surgery commences, infusions of prophylactic antibiotics should end just prior to (within 0-60 minutes) the first surgical incision. Vancomycin should be hung 60-120 minutes prior to incision and completed prior to the first incision.

2. A single dose generally provides adequate tissue concentrations throughout the procedure. For surgical procedures that are prolonged (longer than 3-4 hours) or where extensive blood loss occurs, an additional dose of antibiotic should be administered.

3. For patients weighing more than 80 kgs (175 lbs), the following dosage modifications are suggested.
   a. Cefazolin 2 g IV
   b. Cefotetan 2 g IV
   c. Cefoxitin 2 g IV

4. If necessary, each 1 g dose of the following antibiotics can be given by iv push over 3-5 minutes. Two gram doses should be administered over 6-10 minutes.
   a. Aztreonam
   b. Cefazolin
   c. Cefotetan
   d. Cefoxitin

5. When indicated by these guidelines, staff pharmacists may give ID approval for aztreonam for a duration of no more than 24 hours (i.e., pharmacy protocol approval).

6. Except for cardiac procedures, surgical prophylaxis should not exceed a 24-hour duration. For cardiac procedures, prophylaxis should be limited to 48 hours. At other medical centers, 24 hours of prophylaxis for cardiac procedures has been effective and no increase in infections has been seen.

PREVENTION OF SURGICAL SITE INFECTIONS IN PATIENTS UNDERGOING SELECT SURGICAL PROCEDURES

1. **Cardiac surgery**: procedures including but not limited to CABG, valve replacement; other open heart surgery; pacemaker or defibrillator implant associated with open heart surgery
   a. Vancomycin 1 g iv or 15 mg/kg iv plus cefazolin 1-2 g iv [1]
   b. May continue antibiotic for up to 48 hours after CABG or other cardiac sternotomy-requiring procedures
   c. Penicillin/cephalosporin allergic:
      Vancomycin 1 g iv or 15 mg/kg iv plus aztreonam 1 g iv [1]

2. **Thoracic (non-cardiac) surgery**
   a. Cefazolin 1-2 g iv [1]
   b. Penicillin/cephalosporin allergic:
      Vancomycin 1 g iv or 15 mg/kg iv

3. **Percutaneous genitourinary**: high risk only (e.g., TURP)
   a. Ciprofloxacin 500 mg po or 400 mg iv [1,2]

4. **Vascular surgery**: femoral-popliteal artery bypass; abdominal aortic aneurysm repair; surgical procedures involving a groin incision; arterial surgery involving placement of a prosthesis.
   a. Cefazolin 1-2 g iv [1,2,3]
   b. Penicillin/cephalosporin allergic:
      Vancomycin 1 g iv or 15 mg/kg iv plus aztreonam 1 g iv [1,2]

5. **Obstetrics/gynecology**: numerous procedures
   a. Cefotetan 1-2 g iv [1,2] or cefoxitin 1-2 g iv [1,2] or cefazolin 1-2 g iv [1,2]
   b. Penicillin/cephalosporin allergic:
      Clindamycin 900 mg iv plus gentamicin 1.5 mg/kg iv [2]

6. **Gastrointestinal**
   a. Appendectomy (non-perforated): cefoxitin 1-2 g iv [1,2] or cefotetan 1-2 g iv [1,2]
   b. Colorectal: cefotetan 1-2 g iv [1,2] or cefoxitin 1-2 g iv [1,2]
      or cefazolin 1-2 g iv [1,2] plus metronidazole 500 mg iv [2]
   c. Hepatobiliary: cefotetan 1-2 g iv [1,2] or cefoxitin 1-2 g iv [1,2]
   e. Cephalosporin allergic:
      Clindamycin 900 mg iv [2] plus gentamicin 1.5 mg/kg iv [2]
      or ciprofloxacin 400 mg iv [2] plus metronidazole 500 mg iv [2]

7. **Neurosurgery**
   a. Craniotomy
      1. Cefazolin 1-2 g iv [1,2]
      2. Penicillin/cephalosporin allergic
         Vancomycin 1 g iv or 15 mg/kg iv [2]
   b. Spinal surgery: fusion, insertion of foreign material
      1 Vancomycin 1 g iv or 15 mg/kg iv [2] plus cefazolin 1-2 g iv [2]
      2. Penicillin/cephalosporin allergic:
         Vancomycin 1 g iv or 15 mg/kg iv [2] plus aztreonam 1 g iv [1,2]

8. **Orthopedic surgery**: total joint replacement and internal fixation of fractures
   a. Cefazolin 1-2 g iv q8h x 3 doses (including the pre-op dose) plus
      vancomycin 1 g iv or 15 mg/kg iv x 1 dose [1,2]
   b. Penicillin/cephalosporin allergic: aztreonam 1-2 g iv q8h x 3 doses (including the pre-op dose) plus vancomycin 1 g iv or 15 mg/kg iv x 1 dose

Footnotes

1 Cefazolin 2 g, Cefotetan 2 g, Cefoxitin 2 g, Aztreonam 2 g are suggested for patients weighing > 80 kg (175 lbs)
2 Except for cardiac procedures, surgical prophylaxis should not exceed a 24-hr duration
3 Vancomycin is recommended for (1) patients with a history of MRSA infection, (2) patients with previous hospital admission in the past year, and (3) nursing home residents.

INTERVENTIONAL RADIOLOGY PROCEDURES

1. Routine diagnostic and therapeutic vascular procedures:
   No antibiotic prophylaxis necessary

2. All prophylactic antibiotics should be given to the patient in the Radiology Department just prior to the procedure to ensure that maximum serum concentrations are present during the procedure itself.

3. Percutaneous abscess drainage
   a. Patients already on intravenous antibiotics: the antibiotics should be continued through the procedure. Appropriate antibiotics should then be selected on the basis of cultures taken from the abscess cavity.
   b. Patients not currently on intravenous antibiotics: selection of antibiotics for these patients should be handled in consultation with the house staff or attending physician. If questions arise, Infectious Diseases consultation can be obtained. Subsequent antibiotic should be selected on the basis of the cultures taken form the abscess cavity.

4. Biliary procedures
   a. Piperacillin/tazobactam 3.375 g iv
   b. Penicillin/cephalosporin allergic:
      Ciprofloxacin 400 mg iv plus Metronidazole 500 mg iv

5. Genitourinary procedures
   a. Ciprofloxacin 400 mg iv when the patient is on the table in Radiology
   b. Patients with special circumstances (e.g., prosthetic heart valves, arteriovenous malformations, etc.) will be handled on a case-by-case basis with Infectious Diseases consultation if appropriate.

TUBERCULOSIS LATENT INFECTION AND DISEASE

Washington University Division of Infectious Diseases, June 2013

SCREENING

1. High priority candidates for TB screening
   - Symptoms of TB (cough> 3 weeks, unintentional weight loss, night sweats. Also obtain CXR).
   - Close contacts of infectious TB
   - HIV/AIDS
   - Foreign-born from high prevalence countries (Latin America, Asia/Pacific Islands, Africa, Indian subcontinent, Eastern Europe, Russia)
   - Upper lobe fibrosis on CXR suggesting healed TB without treatment
   - End-stage renal disease
   - Diabetes mellitus
   - Silicosis
   - Head and neck cancer
   - Lymphoreticular malignancy
   - Immunosuppression (organ transplant or >15 mg/day predniSONE equivalent for > 30 days)
   - Medically underserved, low-income populations
   - Intravenous drug user (IVDU)
   - Health care workers (HCWs) serving high risk clients
   - Residents and employees of nursing homes, prisons, shelters
   - Homeless
   - Migrant workers
   - Post-gastrectomy or intestinal bypass surgery
   - Chronic malabsorption
   - < 90% ideal body weight

2. Intradermal Mantoux PPD (0.1 mL=5TU) interpreted at 48-96 hrs. Positive tests are defined by an induration of:

> 5 mm:	HIV or other significant immunosuppression; fibrotic lesions on CXR; recent contacts of infectious TB
> 10 mm:	High-risk groups based on demographics, medical illness or occupation
>15 mm:	No TB risk factors (Don't test people without risk factors)

3. Interferon Gamma Release Assay (IGRA), the T-Spot.TB and the Quantiferon Gold In Tube assay are licensed in the US. These are preferred for patients with a history of BCG vaccination.

4. For patients with a +PPD and no evidence of active TB, recommend treatment of latent TB infection (LTBI) as appropriate. See Tables 1 and 2. In Missouri a +PPD is reportable.

5. Treatment of LTBI is usually INH+vitamin B6. See Tables 2-4.

TABLE 1	HIGH PRIORITY CANDIDATES FOR TREATMENT OF LATENT TB INFECTION (LTBI) REGARDLESS OF AGE

- Close contacts of infectious TB cases
- Persons with HIV infection
- Recent skin test conversion (within 2 yrs)
- Persons with healed, untreated TB on CXR
- Intravenous drug users (IVDUs)
- Persons with medical risk factors for TB, see "Screening"
- Recent arrivals (<5 yrs) from high prevalence countries (Latin America, Asia/Pacific Islands, Africa, Indian subcontinent, Eastern Europe, Russia)
- Low-income, high-risk minority groups
- Residents and staff of high-risk congregate settings (correctional facilities, nursing homes, shelters, health care facilities)
- Children <4 yoa or children and adolescents exposed to high-risk adults

TABLE 2	ACCEPTABLE LTBI REGIMENS
INH	9-months preferred for all, required for HIV+, fibrosis, and children; 6-months acceptable for HIV-; daily or DOT twice weekly
RIF	Daily for 4-months. For INH-resistant contact or intolerance to INH
INH + Rifapentine	Once weekly for 12 weeks by DOT✎ Not recommended for patients with HIV on therapy, pregnant patients, or for exposure to INH or rifamycin resistant organisms. See: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm
MDR-TB contacts	MDR prophylaxis is based on susceptibilities of the source case organism. Consult a TB expert.

MANAGEMENT OF TB DISEASE

1. Manage patients with appropriate social support as outpatients.

2. Isolate the hospitalized patient in an appropriately ventilated room under negative pressure.

3. In patients with symptoms and radiographs consistent with TB, begin empirical therapy for tuberculosis with four drugs: isoniazid, rifampin, pyrazinamide, and ethambutol (see Tables 3-5). Check with health department regarding possible epidemiologic links to MDR-TB. **A negative skin test does not exclude TB**.

4. Smear results are available within 24 hours; cultures are final after 6-8 weeks. Negative smears do not exclude tuberculosis; cultures may become positive several weeks later. If the suspicion is high enough to start empirical therapy, medications should be continued at least until all cultures are negative. Treat culture negative patients who clinically respond to antituberculous therapy with at least four months of multi-drug therapy.

5. Submit AFB smear positive sputum specimens for DNA amplification testing (MTD). A positive MTD on a smear positive sputum specimen confirms the diagnosis of TB. Two negative MTD tests on two separate AFB smear positive sputum specimens suggests non-tuberculous mycobacteria and should be managed accordingly.

6. Report confirmed **and suspected** cases of tuberculosis to the health department serving the patient's residence. Reporting is required by law and gives patients access to medications free of charge. **Contact the health department prior to the patient's discharge so that DOT may begin immediately upon discharge**, and so the health department can initiate prompt contact investigation when appropriate.

IMPORTANT PHONE NUMBERS

St. Louis City Health Dept.	314-657-1525 Fax: 314-612-5267
St. Louis County Health Dept.	314-615-1630 Fax: 314-615-8346
St. Clair County Health Dept. (East St. Louis, IL)	618-233-6175 ext. 4480 Fax: 618-233-9356
Madison County Health Dept. (Wood River, IL)	618-692-8954 ext. 2 618-463-6957 after hours Fax: 618-251-9482
ID Phone Attendant System (Washington University Medical Center)	314-747-3535 (24 hrs)
Washington University ID Clinic	314-747-1206
Washington University Pulmonary Clinic	314-454-8917

7. **Place ALL patients on directly observed multi-drug chemotherapy (DOT) ("Standard of Care" for the State of Missouri)**. Intermittent twice or thrice weekly dosing should never be used without DOT. You must specifically request DOT at the time of reporting. Provide initial doses (5-7 days) of the medicines at discharge. Send prescriptions by FAX to the health department; the health dept. will then provide the remaining doses. Where DOT is unavailable, use of fixed-dose combination medications should be considered.

8. Obtain sputum samples monthly on all patients with positive smears/cultures until cultures convert to negative. Refer patients with persistently positive cultures to an appropriate expert (75% of patients are culture negative at 2 months; 95% at 3 months).

9. **Arrange medical follow-up for all patients started on medication for tuberculosis** to ensure that culture results are reviewed and that clinical response is assessed periodically. If serious side effects develop stop all medicines and consult an expert. The health department will provide basic medical management of tuberculosis; alternatively, arrange through the patient's primary physician, who must maintain close communication with health department/DOT workers.

10. Test all initial isolates of M. tuberculosis for antibiotic susceptibility and modify the regimen once these results are available. If the isolate is fully susceptible, ethambutol can be discontinued if on the daily regimen. If on an intermittent regimen, continue ethambutol for the entire 2-month initial phase.
11. **NEVER add a single drug to a failing regimen**.

Repeat susceptibility testing in patients who fail to respond to treatment or in whom cultures fail to convert to negative after 2 months of therapy. **Practitioners with experience in treating TB should supervise TB treatment**. Patients co-infected with HIV should be managed by an HIV expert. The presence of resistance to one or more components of the regimen and particularly to both INH and rifampin should prompt consultation with a TB expert.

TABLE 3 **ANTITUBERCULOUS MEDICATIONS**

Drug	Daily Dose (Max)	Twice Weekly Dose (Max)
Isoniazid (INH)	5 mg/kg (300 mg)	15 mg/kg (900 mg)
Rifampin (RIF)	10 mg/kg (600 mg)	10 mg/kg (600 mg)
Pyrazinamide (PZA)	15-20 mg/kg (2 g)	50 mg/kg (4 g)
Ethambutol (EMB)	15-20 mg/kg (1.6 g)	50 mg/kg (4 g)

1. See Tables 4, 5 for weight-based and renal dosing of pyrazinamide and ethambutol.
2. RIF and INH do not require renal dosing adjustment
3. Pyridoxine 50 mg/day or 100 mg/biweekly may be given with isoniazid.
4. Baseline evaluation should include: CBC, LFTs, visual acuity and color vision screen.
5. Monthly liver enzyme testing is suggested for age >35 yo, underlying liver disease, EtOH abuse, the peripartum period, or in patients with baseline LFT abnormalities.
6. All intermittent regimens must be directly observed.
7. Avoid pyrazinamide in pregnancy
8. Rifampin causes discoloration of urine, sweat, tears, and other body fluids; soft contact lenses may be permanently stained.

9. **Major adverse effects**

Isoniazid	hepatitis, neuropathy
Rifampin	drug interactions: oral contraceptives; warfarin; methadone; anticonvulsants; protease inhibitors; many others
Pyrazinamide	hepatitis, GI upset
Ethambutol	optic neuritis

TABLE 4 **PYRAZINAMIDE DOSES [1] ADULTS WEIGHING 40-90 KG**

	Ideal Body Weight (kg) [3]			Renal Dosing for CrCl < 30 ml/min or on HD
	40-55 kg	56-75 kg	76-90 kg	
Daily dose	1 g	1.5 g	2 g [2]	Avoid daily dosing. Use three times weekly dose (25 mg/kg/dose).
Three times weekly dose	1.5 g	2.5 g	3 g [2]	
Twice weekly dose	2 g	3 g	4 g [2]	

[1] Rounded to nearest whole tablet size. Pyrazinamide comes as a 500 mg tablet

[2] Maximum dose regardless of weight

[3] $IBW_{males} = 50\ kg + 2.3 \cdot (height\ in\ inches - 60)$
$IBW_{females} = 45.5\ kg + 2.3 \cdot (height\ in\ inches - 60)$

TABLE 5

ETHAMBUTOL DOSES [1] ADULTS WEIGHING 40-90 KG				
	Ideal Body Weight (kg) [3]			Renal Dosing for CrCl < 30 ml/min or on HD
	40-55 kg	56-75 kg	76-90 kg	
Daily dose, g (mg/kg)	0.8 g	1.2 g	1.6 g [2]	Avoid daily dosing. Use three times weekly dose (15 mg/kg/dose)
Three times weekly dose, g	1.2 g	2 g	2.4 g [2]	
Twice weekly dose, g	2.0 g	2.8 g	4 g [2]	

1 Rounded to nearest whole tablet size. Ethambutol comes as 100, 400 mg tablets

2 Maximum dose regardless of weight

3 $IBW_{males} = 50\ kg + 2.3 \cdot (height\ in\ inches - 60)$
$IBW_{females} = 45.5\ kg + 2.3 \cdot (height\ in\ inches - 60)$

TABLE 6

ANTITUBERCULOUS REGIMENS						
OPTION	TOTAL COURSE	INITIAL PHASE		CONTINUATION PHASE (for patients with an appropriate clinical response and pan-sensitive isolates)		
		Drug	Course	Drug	Course	Comments
Daily	6-9 months*	INH RIF PZA EMB	Daily for 8 weeks	INH RIF	Daily for 18-28 weeks	Continuation phase may be twice weekly by DOT
Twice Weekly	6-9 months*	INH RIF PZA EMB	Daily for 2 weeks; then twice/week for 6 weeks	INH RIF	Twice weekly for 18-28 weeks	Therapy must be directly observed. Twice weekly DOT should not be given to patients with advanced HIV disease (CD4< 100). Such patients should receive daily or 3x weekly DOT.

* 9 months is recommended for patients with cavitary disease when cultures are positive at 2 months, and in HIV+ patients who are slow to respond.

HEIP

HOSPITAL EPIDEMIOLOGY
INFECTION PREVENTION

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NATIONAL LEADERS IN MEDICINE

ISOLATION PRECAUTIONS QUICK REFERENCE GUIDE

Barnes-Jewish Hospital Department of Hospital Epidemiology and Infection Prevention, June 2013

This Quick Reference Guide is only a synopsis of the BJH Hospital Epidemiology and Infection Prevention Department policies. The policies may be viewed at http://bjcnet

GENERAL POLICY STATEMENTS

1. Standard Precautions measures always apply
2. Isolation Precautions should not be stopped without consulting an infection prevention specialist. Please call Infection Prevention (454-7560) with questions.
3. Perform hand hygiene with alcohol foam or antimicrobial soap upon entrance to and exit from a patient's room, between patient contacts, and when going from dirty to clean sites on a single patient
4. Minimize transport of patients in Isolation Precautions
5. Notify receiving service of Isolation Precautions if patient must be transported
6. Private room preferred for patients with large draining wounds, burns, and patients who soil the environment (e.g. incontinent, confused)

ISOLATION PRECAUTIONS

1. **Airborne with N95 respirator** - For patients with known or suspected/rule out TB
   a. Use a negative pressure room. Keep door closed.
   b. Wear N95 respirator (not a surgical mask) if entering room
   c. Discard mask after leaving room
   d. Limit visitors
   e. Avoid patient transport
   f. If patient transport is absolutely necessary, patient is to wear isolation (surgical) mask
   g. Instruct patient on respiratory etiquette
   h. Perform hand hygiene with alcohol foam or antimicrobial soap upon entrance and exit to patient's room and between patient contact

2. **Airborne without N95 respirator** - For patients with chicken pox, measles, disseminated herpes zoster or localized herpes zoster in immunocompromised patients (until dissemination is ruled out)
   a. Use negative pressure room - keep doors closed
   b. Employees/visitors who have not had Chicken Pox or Measles (or vaccine) cannot enter (not even with a mask)
   c. Persons immune to Chicken Pox or Measles do not need a mask
   d. Avoid patient transport
   e. If patient transport is absolutely necessary, patient is to wear a surgical mask and all skin lesions should be covered.
   f. Perform hand hygiene with alcohol foam or antimicrobial soap upon entrance and exit to patient's room and between patient contact

3. **Droplet** - For patients with suspected or confirmed diseases that are spread by respiratory droplets (i.e. influenza, meningococcal disease, pertussis)
   a. Keep doors closed
   b. Wear an isolation (surgical) mask if entering room
   c. Discard mask after leaving room
   d. Avoid patient transport
   e. If patient transport is absolutely necessary, patient is to wear isolation mask
   f. Perform hand hygiene with alcohol foam or antimicrobial soap upon entrance and exit to patient's room and between patient contact

4. **Contact** - For patients infected or colonized with highly contagious or multi-drug resistant organisms (see list below)
   a. Wear gown and gloves to enter room. NO EXCEPTIONS.

b. Use dedicated noncritical patient equipment (i.e. stethoscope, thermometer, BP cuff)
c. Remove gown and gloves before leaving room. Never reuse disposable barrier gown.
d. Perform hand hygiene with alcohol foam or antimicrobial soap upon entrance and exit to patient's room and between patient contact
e. Disinfect all surfaces daily and when visibly soiled
f. Avoid transporting patient out of room if possible
g. If transport is necessary, drape patient with a clean sheet or gown

Conditions requiring contact isolation

1. Multi-drug resistant bacteria
   - Methicillin-resistant Staphylococcus aureus (MRSA/ORSA)
   - Vancomycin-resistant enterococcus (VRE)
   - Extended spectrum beta-lactamase (ESBL) producing gram-negative bacilli and Carbapenemase resistant Enterobacteriaceae (CRE), e.g., Klebsiella pneumoniae carbapenemase (KPC) and New Dehli metallo-beta-lactamase (NDM-1)
   - Gram-negative organisms with intermediate sensitivity or are resistant to three or more of the following antibiotics:
     ✓ Ceftazidime or cefepime
     ✓ Any anti-pseudomonal beta-lactamase combination (e.g., piperacillin/tazobactam, ticarcillin/clavulanate)
     ✓ Any carbapenem
     ✓ Any fluoroquinolone
2. Clostridium difficile
3. Suspected or confirmed acute infectious diarrhea
4. RSV, parainfluenza virus or enteroviral infections in infants and young children (at BJH, this includes all community respiratory viruses in patients who are immunocompromised, i.e., Rhinovirus, Adenovirus)
5. Highly contagious skin infections or those that may occur on dry skin, including:
   - Herpes simplex virus (neonatal or mucocutaneous)
   - Impetigo
   - Major abscesses, cellulitis, decubiti, and burns (drainage uncontained)
   - Pediculosis and scabies
   - Staphylococcal scalded skin syndrome
   - Viral or hemorrhagic conjunctivitis (adenovirus); VZV if unable to contain drainage

DURATION OF ISOLATION PRECAUTIONS FOR SPECIFIC CONDITIONS

To remove any precautions, contact Infection Prevention at 454-7560		
Precaution Type	Infection	Duration
Airborne with N95 respirator; negative pressure ventilation (NPV) required	Presumed TB (high suspicion/risk)	Until all 3 criteria are met: at least 14 days drug therapy, clinical improvement, and 3 negative AFB smears (separate days). Patient may go home during this period if directly observed therapy arranged with local health department. Isolate patient if readmitted until compliance with therapy and negative smears confirmed. See TB Treatment section for health department phone numbers
	Rule out TB (low suspicion/risk)	3 negative AFB smears (separate days) OR 1 negative bronchial alveolar lavage (BAL) or bronchial washing

1 Non-immune persons stay out
2 Unless criteria for discontinuing isolation have been met, see "Discontinuing Contact Precautions"

To remove any precautions, contact Infection Prevention at 454-7560		
Precaution Type	Infection	Duration
Airborne without N95 respirator; NPV required	Chicken pox [1]	Until all lesions are crusted; minimum 5 days after onset of rash
	Disseminated zoster [1]	Until all lesions are crusted
	Localized zoster in immunocompromised patients [1]	Until dissemination is ruled out (i.e., no evidence of VZV pneumonia, hepatitis or multi-dermatomal disease after 72 hours of effective therapy)
	Measles [1]	4 days after start of rash (duration of illness if patient is immunocompromised)
Droplet	Influenza	Until patient is afebrile for 24 hours off antipyretics or 7 days from symptom onset, whichever is longer (duration is extended for immunocompromised patients)
	Meningitis (if N. meningitidis or H. influenza type B is suspected)	Until 24 hrs after start of effective therapy
	Mumps [1]	Until 9 days after onset of swelling
	Parvovirus B19	For 7 days for patients with transient aplastic crisis or red cell crisis (duration of hospital stay in immunodeficient patient)
	Pertussis	For 5 days after start of effective therapy
	Rubella	Until 7 days after onset of rash
Contact	Scabies/Lice	Until 24 hours after start of effective therapy (duration of admission for Norwegian scabies)
	Acute infectious diarrhea	Duration of illness (if norovirus, precautions should be in place until 48 hours after symptom resolution)
	MRSA/ORSA	Duration of present and future hospitalizations [2]
	Multi-Drug Resistant GNR/VRE	Duration of present and future hospitalizations [2]
	C. difficile	Until > 7 days of effective therapy and patient is free of diarrhea [2]
	Viral conjunctivitis (pink eye)	Duration of conjunctivitis

1 Non-immune persons stay out
2 Unless criteria for discontinuing isolation have been met, see “Discontinuing Contact Precautions”

CRITERIA FOR DISCONTINUING ISOLATION PRECAUTIONS

To remove any precautions, contact Infection Prevention at 454-7560	
Organism	Criteria
MRSA/ORSA	2 consecutive negative cultures from original site AND non-intact skin AND 2 consecutive negative nasal cultures
VRE	2 consecutive negative cultures from original site AND non-intact skin AND 2 consecutive negative stool cultures
Multi-Drug Resistant GNR/ CRE/KPC/NDM-1/ESBL	Duration of illness; if the patient is clinically cured, then no cultures are necessary. However, if the patient still has open wounds, has an ET tube, a tracheostomy or bronchiectasis that were culture positive before, that site must have a negative culture obtained off effective antibiotics for 48 hours
C. difficile	At least 7 days of therapy and free of diarrhea. No repeat testing is necessary
Suspected Influenza	Negative viral culture (final) or Negative Influenza PCR
Confirmed Influenza	No repeat testing necessary, see "Duration of Isolation Precautions For Specific Conditions"

CRE Carbapenemase resistant Enterobacteriaceae
KPC Klebsiella pneumoniae carbapenemase
NDM-1 New Dehli metallo-beta-lactamase
ESBL Extended-spectrum beta-lactamse

14-3-3 TESTS OF CSF FOR CREUTZFELDT-JAKOB DISEASE (CJD)

Because the prions of CJD are resistant to routine disinfection and sterilization, special handling of high risk substances (e.g., CSF, dura, nerve, and brain tissue) is necessary. It is very important to fully communicate when CSF specimens are sent for 14-3-3 testing in cases of suspected prion disease. Notify Lab Customer Service at 362-1470 prior to sending the specimen. All specimens should be labeled with the bright orange CJD sticker (available on 11400/11500 and in neuroradiology).

AIRBORNE PRECAUTIONS WITH N95 RESPIRATOR GUIDELINES FOR INITIATION AND FOLLOW-UP

Barnes-Jewish Hospital Department of Hospital Epidemiology and Infection Prevention, June 2013

HOW TO ISOLATE FOR TUBERCULOSIS (TB)

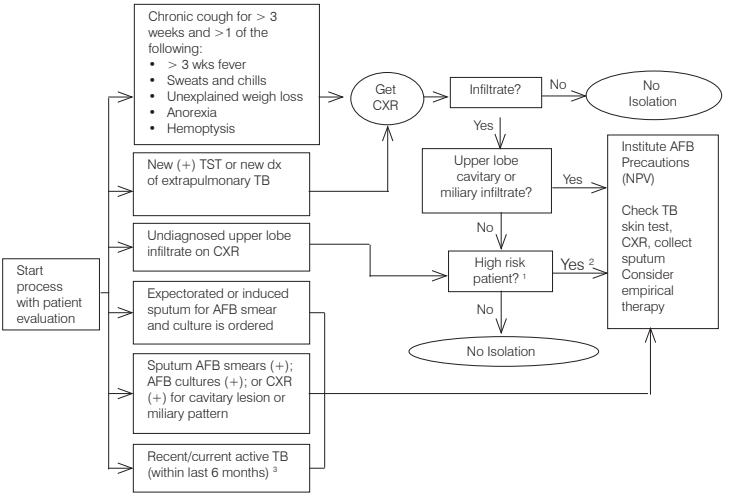
Airborne Precautions With N95 Respirator: for patients with known or suspected TB. See algorithm below.

- Use designated negative pressure room
- Keep doors closed at all times
- Healthcare workers wear an N95 respirator (not a surgical mask) if entering room
- Limit visitors
- Avoid patient transport out of room
- Patient to wear surgical mask (not an N95) for essential transport
- Instruct patient on cough etiquette

HOW TO DISCONTINUE AIRBORNE PRECAUTIONS

- **Contact Infection Prevention (454-7560) to discontinue AFB precautions**
- **Maintain airborne precautions with N95 respirators until the following criteria are met**

1. **Presumed TB (high suspicion/risk)**
   a. 14 days drug therapy, clinical improvement AND 3 negative AFB smears (separate days).
   b. Patient may be discharged during this period if arrangements made with local health department for direct observed therapy.
   c. Isolate patient if readmitted until compliance with therapy and negative smears confirmed.
2. **Rule-out TB (low suspicion/risk)**
   a. 3 negative AFB smears (separate days) or 1 negative BAL



1 High risk defined as:
- Hx of past (+) TB skin test; Dx of r/o TB; Hx of TB or TB exposure
- Members of groups with high prevalence for TB: foreign born (East Europe, Africa, S.E. Asia, S. America, Haiti), homeless, prisoners, nursing homes, shelters, alcoholic, healthcare workers, IVDU, HIV/AIDS)
- Medical conditions with increased risk for developing TB: malnourished (90% IBW); immunosuppression; use of TNF-alpha inhibitors; chronic renal failure; diabetes; HIV; silicosis; malignancy

2 HIV (+) patients with classic sxs/presentation of PCP do not need isolation

3 Until confirmation of adequate therapy and smear negative status can be confirmed

DISASTERS

DISASTER PREPAREDNESS
WEAPONS OF MASS DESTRUCTION

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DISASTER PREPAREDNESS AT BJH

Barnes-Jewish Hospital Department of Pharmacy, June 2013

BJH AND PHARMACY EMERGENCY PREPAREDNESS

1. All employees should familiarize themselves with the BJH Emergency Preparedness Mass Casualty Plan. The Plan contains emergency response procedures for command and control, security, triage, departmental roles. You may access the Plan only through the BJC LAN. Enter the URL below. Click on "For Employees" then "Emergency Preparedness and Safety".

   http://bjcnet

2. After the terrorist attacks of September 11, 2001, the Chemical/Biological Preparedness portion of the Mass Casualty Plan was modified by the BJH epidemiologists. Refer to the Chemical/Biological Preparedness Plan for specific guidelines related to patient and specimen transport, infection control and isolation, and healthcare worker cohorting.

3. The Pharmacy Disaster Plan can be found on Phred, the Pharmacy intranet site (see Drug Information Resources). Phred also contains web links to the CDC as well as back up copies of the CDC treatment plans. Other important toxicology references are located at the Drug Information Center (4-8399).

4. Pharmacy staff: in the event that computer or Internet connections are down, hard copies of the Pharmacy Disaster Plan as well as treatment guidelines for various biological and chemical agents can be found in the orange, emergency response tackle boxes, located in each of the primary pharmacy dispensing areas.

LINKS TO BIOTERRORISM INFORMATION

1. BJC Emergency Preparedness and Safety
   Click on "For Employees", then "Emergency Preparedness and Safety"
   http://bjcnet.carenet.org/

2. Centers for Disease Control
   http://emergency.cdc.gov/

3. St. Louis University Institute for Biosecurity
   http://biosecurity.slu.edu/

ANTHRAX PROPHYLAXIS

Source Of Information
These recommendations were adapted from the Centers for Disease Control. Because these recommendations are in flux, the Centers for Disease Control Bioterrorism website (http://emergency.cdc.gov/) should be consulted for updates.

Indications For Prophylaxis
1. Postexposure prophylaxis is indicated to prevent inhalational anthrax after a confirmed or suspected aerosol exposure.

2. When no information is available about the antimicrobial susceptibility of the implicated strain of B. anthracis, initial therapy with ciprofloxacin or doxycycline is recommended for adults and children. Use of tetracyclines and fluoroquinolones in children has adverse effects. The risks for these adverse effects must be weighed carefully against the risk for developing life-threatening disease. As soon as penicillin susceptibility of the organism has been confirmed, prophylactic therapy for children should be changed to oral amoxicillin 80 mg/kg of body mass per day divided every 8 hours (not to exceed 500 mg three times daily). B. anthracis is not susceptible to cephalosporins or to trimethoprim/sulfamethoxazole, and these agents should not be used for prophylaxis.

Prophylaxis Regimens
1. Adults - including pregnant women and immunocompromised patients.
   a. Initial regimen: ciprofloxacin 500 mg po bid
   b. Alternative: doxycycline 100 mg po bid
   c. Duration: 60 days (see alternatives below)

2. Children
   a. Initial regimen: ciprofloxacin 10-15 mg/kg po q12h Not to exceed 1g/day.
   b. Alternative: doxycycline by age and weight
      1. > 8 yrs and > 45 kg: 100 mg po bid
      2. > 8 yrs but < 45 kg: 2.2 mg/kg po bid
      3. < 8 yrs: 2.2 mg/kg po bid

Duration of Prophylaxis
1. Based on animal studies, inhalational anthrax is unlikely to occur after 60 days, hence the current recommended duration of prophylaxis for 60 days. Conflicting data exist as to the duration that anthrax spores remain viable in lungs. Some data suggest viability up to 100 days. If such a late infection were to occur, HHS scientists believe that the infection could be successfully treated, as were cases of inhalation anthrax that were identified early during the anthrax mail attacks. At the same time, HHS recognizes that some individuals may wish to take extra precautions, especially those whose exposure may have been especially high.

2. As a result, on December 18, 2001, HHS modified its recommendations for the duration of prophylaxis. Three durations are recommended:
   a. Current Recommendation - 60 days of antibiotic prophylaxis, accompanied by careful monitoring for illness.

   b. Option 1 - 100 days of antibiotic prophylaxis. This course would be intended to provide protection against the theoretical possibility that spores might cause infection up to 100 days after exposure. It should be accompanied by monitoring for illness or adverse reactions.

c. Option 2 - 100 days of antibiotic prophylaxis, plus anthrax vaccine as an investigational treatment (as 3 doses over a 4-week period). This is not currently an FDA-approved use of the vaccine, however the vaccine may provide additional protection by inducing an immune response to the anthrax organism. As an investigational new drug, the vaccine would need to be administered with the full informed consent of the individual as to possible risks. Individuals would also be asked to take part in a follow-up study measuring the effect of the vaccine when administered after exposure.

ANTHRAX TREATMENT

Source Of Information
These recommendations were adapted from the Centers for Disease Control. Because these recommendations are in flux, the Centers for Disease Control Bioterrorism website (http://emergency.cdc.gov/) should be consulted for updates.

Treatment of Inhalation Anthrax
1. A high index of clinical suspicion and rapid administration of effective antimicrobial therapy is essential for prompt diagnosis and effective treatment of inhalational anthrax.
2. Limited clinical experience is available and no controlled trials in humans have been performed to validate current treatment recommendations for inhalational anthrax.
3. Because of the mortality associated with inhalational anthrax, two or more antimicrobial agents predicted to be effective are recommended for therapy.
4. Agents with in vitro susceptibility that may be used in conjunction with ciprofloxacin or doxycycline include rifampin, vancomycin, imipenem, chloramphenicol, penicillin and ampicillin, clindamycin, and clarithromycin.
5. Cephalosporins, including 3rd generation cephalosporins, e.g., ceftriaxone and TMP/SMX should be avoided because of poor in vitro activity (based on susceptibility testing during the 2001 outbreak).
6. Historically, penicillins were used for the treatment and prophylaxis of anthrax. However, two theoretical concerns have arisen: a) B. anthracis may develop penicillinases b) beta-lactams penetrate poorly into macrophages where B. anthracis spores germinate. As a result, the CDC currently recommends using amoxicillin or amoxicillin/clavulanate only after susceptibility testing is supportive.
7. Toxin mediated morbidity is a major complication of systemic anthrax. Corticosteroids have been suggested as adjunct therapy for inhalational anthrax associated with extensive edema, respiratory compromise, and meningitis.
8. Raxibacumab, a recently approved monoclonal antibody that neutralizes the anthrax toxins, may be available through the federal government for the treatment of inhalation anthrax cases.
9. Consult with an infectious diseases specialist is highly recommended.

Treatment Regimens
1. **Adults** - including pregnant women and immunocompromised patients.
   a. Initial iv therapy: ciprofloxacin 400 mg iv q12h + 1-2 alternative antimicrobials (see 1e)
   b. Alternative: doxycycline 100 mg po bid + 1-2 alternative antimicrobials
   c. Switch to oral antimicrobial therapy when clinically appropriate
   d. Duration: 60 days (iv and po combined)
   e. The isolates associated with the 2001 outbreak were sensitive to rifampin, vancomycin, imipenem, meropenem, chloramphenicol, clindamycin, and aminoglycosides

2. **Children**
   a. Initial iv regimen: ciprofloxacin 10-15 mg/kg iv q12h + 1-2 alternative antimicrobials (see 1e). Ciprofloxacin dose not to exceed 1 g/day.

b. Alternative: doxycycline by age and weight + 1-2 alternative antimicrobials
   1. > 8 yrs and > 45 kg: 100 mg po bid
   2. > 8 yrs but < 45 kg: 2.2 mg/kg po bid
   3. < 8 yrs: 2.2 mg/kg po bid
c. Switch to oral antimicrobial therapy when clinically appropriate and based on susceptibility testing.
d. Duration: 60 days (iv and po combined)

Additional Comments

1. For gastrointestinal and oropharyngeal anthrax, use regimens recommended for inhalational anthrax
2. Ciprofloxacin or doxycycline should be considered an essential part of first-line therapy for inhalational anthrax
3. Initial therapy may be altered based on clinical course of the patient; one or two antimicrobial agents, e.g., ciprofloxacin or doxycycline, may be adequate as the patient improves
4. If meningitis is suspected, doxycycline may be less optimal because of poor CNS penetration
5. Because of the potential persistence of spores after an aerosol exposure, antimicrobial therapy should be continued for 60 days.
6. If iv ciprofloxacin is not available, oral ciprofloxacin may be acceptable because it is rapidly and well absorbed from the GI tract with non substantial loss by first-pass metabolism. Maximum serum concentrations are attained 1-2 hrs after oral dosing but may not be achieved if vomiting or ileus are present.
7. In children, ciprofloxacin dosage should not exceed 1 g/day
8. In an effort to balance the risk and benefit of tetracycline therapy in children, one should consider the American Academy of Pediatrics recommendation to treat young children with tetracyclines for serious infections, e.g., Rocky Mountain spotted fever. Using this analogous situation, most pediatric experts would use tetracyclines to treat a pediatric anthrax infection despite the risk of toxicity.
9. Although tetracyclines are not recommended during pregnancy, their use may be indicated for life-threatening illness. Adverse effects on developing teeth and bones are dose related; therefore doxycycline might be used for a short time (7-14 days) before 6 months of gestation.

NERVE GAS

General Information

1. The known nerve gases include sarin (GB), soman (GD), tabun (GA) and VX.
2. Nerve agents are the most toxic of the known chemical warfare agents. They are chemically related to organophosphate pesticides and exert their biological effects by inhibiting acetylcholinesterase.
3. The primary routes of exposure include inhalation, skin/eye contact, ingestion. The estimated LCT50 (the product of concentration times the time that it is lethal to 50% of the exposed population) by inhalation ranges from 10 mg-min/m3 for VX to 400 mg-min/m3 for tabun. For cutaneous exposure, death would be expected with 1 drop of VX or 1-10 ml of sarin, soman or tabun.
4. Manifestations of nerve gas exposure include rhinorrhea, chest tightness, pinpoint pupils, shortness of breath, excessive salivation and sweating, nausea, vomiting, abdominal cramps, involuntary defecation and urination, muscle twitching, confusion, seizures, flaccid paralysis, coma, respiratory failure, and death.
5. These signs and symptoms occur regardless of the route of exposure.

Mark 1 Kits

1. The military's Mark 1 Kits are designed to deliver atropine and pralidoxime (2-PAM) via autoinjectors.
2. Each Mark 1 kit contains 2 autoinjectors, one for each of 2 antidotes. Both antidotes should be administered in the field.
   a. Atropine 2 mg
   b. Pralidoxime (2-PAM) 600 mg
3. The kits are designed for use within the Hot Zone (area of biochemical agent contamination) and for self-administration. The kits are also designed to allow HAZMAT rescuers to administer antidotes while wearing protective gear and self-contained breathing apparatus (SCBA), which in general, makes rescuer movements limited.

DuoDote Kits

1. Single auto-injector kit designed to deliver:
   a. Atropine 2.1 mg
   b. Pralidoxime (2-pam) 600 mg
2. These are designed for use within the hot and warm zones and for self administration.
3. Emergency Department Physicians: Duodote Kits are available in the ED in the Disaster Pyxis Machine.

Hospital and Emergency Department Management

1. Because of the high toxicity, rapid absorption, and volatility of nerve gases, it is unlikely that a patient brought to the ED will have nerve agent on the skin. However, some nerve agent may remain in the hair or clothing. If decontamination has not already occurred, patients should be decontaminated prior to entering the treatment area.
2. The BJH Emergency Department has developed decontamination procedures in the event that victims arrive at BJH with contaminated clothing/skin.
3. Evaluate ABCs (airway, breathing, circulation).
4. Triage
   a. Patients who are conscious and have full muscular control will need minimal care.
   b. Patients who may have been exposed to liquid nerve agents must be kept under observation for at least 18 hrs.
   c. Patients with history of possible to exposure to vapor only (no liquid exposure), who have no signs of exposure by the time they reach the medical facility have not been exposed - because these effects occur within seconds to minutes after exposure. They can be discharged.
5. Patients exposed to vapor who have miosis and rhinorrhea will need no care unless:
   a. They have eye or head pain or nausea and vomiting. Under these circumstances topical atropine or homatropine in the eye should relieve the symptoms and the patient can be discharged within an hour or so.
   b. Or the rhinorrhea is very severe - under these circumstances, atropine im (2 mg adults, 0.05 mg/kg children), should relieve this and patient can be discharged in an hour or so.
   c. Topical atropine and homatropine should not be used routinely for miosis because they cause visual impairment for about 24 hrs.
6. For inhalation exposure
   a. Ventilatory support is essential.
   b. Following low-dose exposure, administration of antidotes and supplemental O2 may be adequate. Suction secretions from the upper airways.
   c. Marked resistance to ventilation is expected due to bronchial constriction and spasm. Resistance lessens after administration of atropine.
7. For skin exposure - skin must be decontaminated within minutes following exposure to nerve agents. See Pre-Hospital Management for decontamination procedures

Antidotes and Symptom Definitions

1. Doses - are based on age, refer toTable 1
2. Treatment is based on age, weight (for children, elderly/frail) and severity of symptoms

3. Mild to moderate symptoms include: localized sweating, muscle fasciculations, nausea, vomiting, weakness, dyspnea
4. Severe symptoms include: unconsciousness, convulsions, apnea, flaccid paralysis
5. ATR is atropine. Atropine is the prototypic antimuscarinic agent. ATR is available in 1 mg vials.
6. 2-PAM is pralidoxime. Pralidoxime is a cholinesterase reactivator and exerts its action on organophosphates by removing the phosphoryl group from the active site of the inhibited enzyme. 2-PAM also probably directly acts on cholinesterase and protects it from further organophosphate inhibition.
7. 2-PAM is available in 1 g vials. 2-PAM can be admixed and administered in three possible ways:
   a. 1 g in 20 ml sterile water (final concentration: 5% or 50 mg/ml solution) for slow iv push (not less than 5 minutes). Reference: package insert.
   b. 1 g in 3 ml sterile water or normal saline (final concentration: 333 mg/ml) for im injection. Reference: Poisondex.
   c. 1 g in 100 ml normal saline (final concentration: 1% or 10 mg/ml solution) can be given by slow iv infusion over 15-30 minutes. Reference: package insert.

Adverse Effects of Nerve Gas Antidotes

1. Atropine is the prototypic antimuscarinic agent. Therefore, adverse effects include: dry mouth, dry skin, blurred vision, cycloplegia, mydriasis, photophobia, anhidrosis, urinary hesitancy and retention, tachycardia, xerophthalmia and constipation. Other reported adverse effects include increased ocular tension, loss of taste, headache, nervousness, drowsiness, weakness, dizziness, flushing, insomnia, nausea, vomiting, and bloated feeling. Mental confusion and/or excitement may also occur, especially in geriatric patients. Hypersensitivity reactions have occurred, which may be due to preservatives (parabens) placed in certain formulations. Infants, patients with Down's Syndrome, and children with spastic paralysis or brain damage may be hypersensitive to the effects of antimuscarinic drugs.
2. 2-PAM is a cholinesterase reactivator. Although generally well tolerated, dizziness, blurred vision, diplopia, impaired accommodation, headache, drowsiness, nausea, tachycardia, hyperventilation, maculopapular rash, and muscular weakness have been reported. However, it is often difficult to differentiate the toxic effects produced by atropine or organophosphates from those of 2-PAM.
3. When atropine and 2-PAM are used concomitantly, signs of atropinism may occur earlier than when atropine is used alone. Excitement, confusion, manic behavior, and muscle rigidity have been reported following recovery of consciousness.
4. Rapid iv injection of 2-PAM may produce tachycardia, laryngospasm, muscle rigidity, and transient neuromuscular blockade. Therefore, the drug should be administered slowly, preferably by iv infusion. im injection may produce mild pain at the injection site.
5. 2-PAM may precipitate a myasthenic crisis in patients with myasthenia gravis.
6. Reference: American Hospital Formulary Service, 2012.

Nerve Gas Antidote Drug Interactions

1. Atropine
   a. Additive anticholinergic effects should be expected with phenothiazines, amantadine, antiparkinsonian drugs, glutethimide, meperidine, tricyclic antidepressants, muscle relaxants, certain antiarrhythmic agents (quinidine, disopyramide, procainamide), some antihistamines.
   b. Because atropine would be expected to slow GI motility, the oral absorption of other drugs may be impaired, including that of levodopa and digoxin. Slowing of GI motility may also increase the severity of GI mucosal lesions produced by wax-matrix preparations of potassium chloride (e.g., Slow-K).
   c. Atropine may also decrease gastric acid output and/or increase gastric pH, therefore drugs requiring gastric acid for oral absorption may be affected, including, but not limited to: ketoconazole.
2. 2-PAM - data are not available
3. Reference: American Hospital Formulary Service, 2012.

TABLE 1 **DOSAGES FOR NERVE GAS ANTIDOTES**

	Symptom Severity [1]	
	Mild-Moderate	Severe
Infants	ATR 0.05 mg/kg im or 0.02 mg/kg iv and 2-PAM 15 mg/kg iv slowly	ATR 0.1 mg/kg im or 0.02 mg/kg iv and 2-PAM 15 mg/kg iv slowly
Child (2-10 yrs)	ATR 1 mg im and 2-PAM 15 mg/kg iv slowly	ATR 2 mg im and 2-PAM 15 mg/kg iv slowly
Adolescents (>10 yrs)	ATR 2 mg im and 2-PAM 15 mg/kg iv slowly	ATR 4 mg im and 2-PAM 15 mg/kg iv slowly
Adult	ATR 2-4 mg im and 2-PAM 15 mg/kg iv (1 g) slowly	ATR 6 mg im and 2-PAM 15 mg/kg iv (1 g) slowly
Elderly/Frail 2	ATR 1 mg im and 2-PAM 5-10 mg/kg iv slowly	ATR 2 mg im and 2-PAM 5-10 mg/kg iv slowly

ATR=atropine, 2-PAM=pralidoxime. 1) Mild to moderate symptoms include: localized sweating, muscle fasciculations, nausea, vomiting, weakness, dyspnea. Severe symptoms include: unconsciousness, convulsions, apnea, flaccid paralysis. 2) In patients with normal renal function, the half-life of PAM is 0.8-2.7 hrs. Approximately 80-90% of an IV/im dose of PAM is excreted unchanged in urine, and thus, doses should probably be modified in patients with renal insufficiency. However, no specific dosage guidelines have been developed for this situation.

PLAGUE

Source Of Information

These recommendations were adapted from the Consensus Statement of the Working Group on Civilian Biodefense and are not necessarily approved by the FDA [JAMA 2000;283 (17):2281-90]. Because these recommendations are in flux, the Centers for Disease Control Bioterrorism website (http://emergency.cdc.gov/) should be consulted for updates.

Treatment of Plague

1. One antimicrobial agent should be selected for therapy. Therapy should be continued for 10 days. Prophylaxis is continued for 7 days. Oral therapy should be substituted when patient's condition improves.
2. Aminoglycosides and ciprofloxacin must be adjusted according to renal function (see Renal Dosing Guidelines in this handbook).
3. Evidence suggests that gentamicin, 5 mg/kg im or iv once daily, would be efficacious in children, although this is not yet widely accepted in clinical practice. Neonates up to 1 week of age and premature infants should receive gentamicin 2.5 mg/kg iv twice daily.
4. Other fluoroquinolones can be substituted at doses appropriate for age. Ciprofloxacin dosage should not exceed 1 g/day in children.
5. Chloramphenicol plasma levels should be maintained between 5-20 mcg/ml. Concentrations greater than 25 mcg/ml can cause reversible bone marrow suppression. Children younger than 2 years should not receive chloramphenicol. The oral formulation of chloramphenicol is no longer available in the United States.
6. Regardless of age, pregnancy or immune status, all patients should receive 10 days of therapy. Switch to oral antibiotics when clinically appropriate.

Plague Treatment Regimens

1. Adults
   a. Preferred choices
      1. Streptomycin 1 g im q12h or
      2. Gentamicin 5 mg/kg im or iv q24h (see extended interval dosing nomogram) or 2 mg/kg loading dose followed by 1.7 mg/kg im or iv q8h.

b. Alternatives
    1. Doxycycline 100 mg iv q12h or 200 mg iv q24h
    2. Ciprofloxacin 400 mg iv q12h
    3. Chloramphenicol 25 mg/kg iv q6h
2. Children
    a. Preferred choices
        1. Streptomycin 15 mg/kg im q12h (max dose 2 g) or
        2. Gentamicin 2.5 mg/kg im or iv q8h
    b. Alternatives
        1. Doxycycline > 45 kg, give adult dose; < 45 kg give 2.2 mg/kg iv q12h (max dose 200 mg/day)
        2. Ciprofloxacin 15 mg/kg iv q12h
        3. Chloramphenicol 25 mg/kg iv q6h
3. Pregnant women
    a. Preferred choices
        1. Gentamicin 5 mg/kg im or iv q24h or 2 mg/kg loading dose followed by 1.7 mg/kg im or iv q8h. At BJH, extended interval dosing is not routinely recommended in pregnant women because of altered pharmacokinetics.
    b. Alternatives
        1. Doxycycline 100 mg iv q12h or 200 mg iv q24h
        2. Ciprofloxacin 400 mg iv q12h
4. Immunocompromised patients - Treatment in this population has not been studied. Therefore, the Consensus recommendation is to administer antibiotics according to the guidelines developed for immunocompetent adults and children.

Prophylaxis of Plague

1. Prophylaxis of pneumonic plague is indicated in household, hospital or other close contacts of persons with untreated pneumonic plague. Close contact is defined as contact with a patient at less than 2 meters.
2. Treatment (vs. prophylaxis) should be initiated in the following situations. All persons developing a temperature > 38.5 C or a new cough.
3. Infants with tachypnea should receive immediate treatment.
4. Doxycycline is the first choice for postexposure prophylaxis. Fluoroquinolones could also be used based on studies in mice.
5. Prophylaxis should be given for 7 days.

Plague Prophylaxis Regimens : Preferred Choices

1. Adults
    a. Doxycycline 100 mg po bid
    b. Ciprofloxacin 500 mg po bid
2. Children
    a. Doxycycline > 45 kg, give adult dose; < 45 kg give 2.2 mg/kg po bid
    b. Ciprofloxacin 20 mg/kg po bid
3. Pregnant women
    a. Doxycycline 100 mg po bid
    b. Ciprofloxacin 500 mg po bid
4. Immunocompromised patients - Prophylaxis in these patients has not been studied. Therefore, the consensus recommendation is to administer antibiotics according to the guidelines developed for immunocompetent adults and children.
5. The Consensus states that oral chloramphenicol is an alternative drug for prophylaxis of plague, however, oral chloramphenicol is no longer available in the USA.

RADIATION

Source Of Information

These recommendations were adapted from the FDA. More information can be found at the CDC Bioterrorism website (http://emergency.cdc.gov/).

Threshold Thyroid Radioactive Exposures and Recommended Doses of Potassium Iodide for Different Age Groups				
Age Group	Predicted Thyroid Exposure (cGy)	KI Dose (mg)	Number of 130 mg tablets	Number of 65 mg tablets
Adults, > 40 yo	> 500	130	1	2
Adults, 18-40 yo	> 10	130	1	2
Pregnant or lactating women	> 5	130	1	2
Adolescents, 12-18 yo	> 5	65	1/2	1
Children, 3-12 yo	> 5	65	1/2	1
Children, 1 mo-3 yo	> 5	32	1/4	1/2
Birth - 1 month	> 5	16	1/8	1/4

Supersaturated Potassium Iodide (SSKI) solution is available from BJH Pharmacy at a concentration of 1 g KI/ml and can be diluted to achieve a solution which can serve as an alternative to KI tablets. Alternatively, several drops of SSKI in juice or water would result in an adequate daily adult dose.

RADIATION, CESIUM-137

Source Of Information

These recommendations were adapted from the CDC. More information can be found at the CDC website (http://emergency.cdc.gov/) as well as the Radiation Emergency Assistance Center/Training Site [REACTS/TS] (http://orise.orau.gov/reacts/med-countermeasures.htm). Additional information is also available from the EPA. http://www.epa.gov/radiation/

Prussian Blue

1. Other names: Ferric(III) hexacyanoferrate(II) “insoluble PB”
2. Prussian blue can remove select radioactive materials (cesium and thallium) from people’s bodies, but must be taken under the guidance of the Radiation Emergency Assistance Center/Training Site (REAC/TS) of the Oak Ridge Institute.
3. Since the 1960s, prussian blue has been used to treat people who have been internally contaminated with radioactive cesium (mainly Cs-137) or thallium (mainly Tl-201). Prussian blue can be given at any point after doctors have determined that a person is internally contaminated. Prussian blue will help speed up the removal of cesium and thallium from the body.
4. Prussian blue is not routinely available. When approved for use by REAC/TS it is supplied in 500 mg capsules that can be swallowed whole or mixed in liquid for children to drink. The amount to be taken depends on how badly a person is contaminated. Prussian blue must be taken 3-4 times a day for up to 150 days, depending on the

extent of the contamination, under the supervision of a doctor.
5. Patients should not take Prussian blue artist's dye in an attempt to treat themselves. This type of Prussian blue is not designed to treat radioactive contamination and is not manufactured in a germ-free area. People who are concerned about the possibility of being contaminated should contact their physician for treatment.

REACTS/TS Guidelines For The Use Of Prussian Blue

1. The internal burden of radiocesium should be ascertained after an accidental ingestion or inhalation by appropriate whole-body counting and/or by bioassay:
   a. Determine the magnitude of the radiocesium accident. The appropriate annual limit of intake (ALI) should be determined with health physics assistance from 10 CFR20. For Cs-137, this corresponds to 100 microCi for ingestion (3.7 E06 Bq) or 200 microCi (7.4 E06 Bq) for inhalation. For other radioisotopes of cesium, the appropriate ALI should be determined.
   b. An estimate of the magnitude of the accident may be determined by whole body counting, early stool or urine sampling, or by gastric lavage. Accidents in the DOE facilities complex are expected generally to involve either Cs-137 particulate inhalation or Cs-137 in a contaminated wound. In these cases, whole body counting or wound counting would be the preferred mode for initial determination of the magnitude of the accident.
   c. After an initial whole body or wound count, the treating physician should propose a prussian blue regimen based on the estimated body burden of Cs-137.
   d. The level of internal contamination should be categorized (e.g. low, intermediate, high). For initial treatment guidelines, REACTS/TS considers a low-level accident as 1-5 ALI, a moderate accident as 5-10 ALI, and a severe accident as greater than or equal to 10 ALI.
   e. The appropriate daily dose of prussian blue should be based on the suspected level of internal contamination (e.g. low: 3 g daily; intermediate: 3-10 g daily; high: 10-20 g daily). All administration should be three times daily.

2. In most cases requiring decorporation therapy, the extent of internal contamination is expected to be low to moderate (< 1-10 annual limits of intake, ALI). Prussian blue decorporation therapy for radiocesium in these cases should be initiated at an initial dosage of one gram TID and titrated as necessary. In order to judge the efficacy of treatment, the patient should be followed periodically with both urine and fecal bioassay and with whole-body counting.

TULAREMIA

Source Of Information

These recommendations were adapted from the Consensus Statement of the Working Group on Civilian Biodefense and are not necessarily approved by the FDA [JAMA 2001;285 (21):2763-73]. Because these recommendations are in flux, the Centers for Disease Control Bioterrorism website (http://emergency.cdc.gov/) should be consulted for updates.

Treatment of Tularemia

1. Treatment with streptomycin, gentamicin or ciprofloxacin should be continued for 10 days. However, treatment with doxycycline or chloramphenicol should be continued for 14-21 days.
2. Persons beginning treatment with intramuscular (IM) or intravenous (IV) doxycycline, ciprofloxacin can switch to oral antibiotic administration when clinically indicated.
3. Not listed in the CDC tularemia treatment guidelines, but considered part of routine practice at BJH: To avoid hematologic toxicity, chloramphenicol plasma levels should be maintained between 5-20 mcg/ml. Concentrations greater than 25 mcg/ml have been associated with reversible bone marrow suppression. Children younger than 2 years should not receive chloramphenicol. The oral formulation of chloramphenicol is

no longer available in the United States.
4. Treatment of tularemia using extended interval gentamicin dosing is not an FDA approved indication. Though extended interval aminoglycoside dosing is recommended in the Consensus for pregnant patients, this is not routine practice at BJH because of altered pharmacokinetics in this population.
5. Ciprofloxacin dosage should not exceed 1 g/day in children.

Treatment Regimens for Tularemia

1. Adults
   a. Preferred choices
      1. Streptomycin 1 g im q12h or
      2. Gentamicin 5 mg/kg im or iv q24h (see extended interval dosing nomogram)
   b. Alternatives
      1. Doxycycline 100 mg iv q12h
      2. Ciprofloxacin 400 mg iv q12h
      3. Chloramphenicol 15 mg/kg iv q6h
2. Children
   a. Preferred choices
      1. Streptomycin 15 mg/kg im q12h (max dose 2 g) or
      2. Gentamicin 2.5 mg/kg im or iv q8h
   b. Alternatives
      1. Doxycycline > 45 kg, give adult dose; < 45 kg give 2.2 mg/kg iv q12h (max dose 200 mg/day)
      2. Ciprofloxacin 15 mg/kg iv q12h
      3. Chloramphenicol 15 mg/kg iv q6h
3. Pregnant women
   a. Preferred choices
      1. Gentamicin 5 mg/kg im or iv q24h (see extended interval dosing nomogram) or 2 mg/kg loading dose followed by 1.7 mg/kg im or iv q8h. At BJH, extended interval dosing is not routinely recommended in pregnant women because of altered pharmacokinetics.
      2. Streptomycin 1 g im q12h
   b. Alternatives
      1. Doxycycline 100 mg iv q12h
      2. Ciprofloxacin 400 mg iv q12h
4. Immunocompromised patients - Treatment in this population has not been studied. Therefore, the Consensus recommendation is to administer antibiotics according to the guidelines developed for immunocompetent adults and children.

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PERSONAL NOTES

HOW DO I NAVIGATE THE TOOL BOOK?

The Tool Book has a table of contents and an index. If you are viewing on a tablet device, consult with your tablet's instruction manual for directions on how to navigate a book's table of contents. If you are viewing the PDF file, clicking on a page number within the table of contents or index will bring you to the desired page. The PDF file also has embedded bookmarks which can be viewed in Adobe Acrobat by clicking on the bookmark tab located on the left side of document window. Lastly, all URLs appearing with the PDF file are clickable and will take you to the specific website. BJC LAN hyperlinks are accessible only to BJH/Washington University users.

WHY CAN'T I FIND INFORMATION ON A SPECIFIC DRUG?

The purpose of the Tool Book is to provide drug information/policies specific to Barnes-Jewish Hospital. The intent has never been to replace other, more general drug information handbooks. See "How do I access other drug information?" below.

IS THE TOOL BOOK AVAILABLE IN COMPASS?

Yes. Within Compass, click on the blue "T" book icon located on the Compass menu bar.

HOW CAN I GET ANOTHER TOOL BOOK?

Only 2000 copies of the Tool Book are printed each year. It is made available free of charge as a service of the Department of Pharmacy. Priority is given to BJH house staff physicians, fellows, pharmacists, 3rd and 4th year medical students, 6th year PharmD students and selected nursing groups. Any remaining copies are available from the Drug Information Center on a first-come-first-served basis. When supplies run out, interested parties are directed to the handheld or online version, (see URL below). Annual distribution of the printed books occurs in mid-June during the new housestaff orientation sessions.

IS THE TOOL BOOK AVAILABLE ONLINE, IN PDF OR FOR TABLET DEVICES?

Yes, inside the Tool Book, see "Tool Book for Electronic Devices". Different file formats will be available for download from this website:

http://bjhtoolbook.wustl.edu/

HOW DO I ACCESS OTHER DRUG INFORMATION RESOURCES AT BJH?

Ask your pharmacist

Clinical pharmacists and unit-based pharmacists are assigned to certain physician teams and/or provide pharmaceutical care and drug information on various nursing divisions throughout the hospital. Staff pharmacists and pharmacy services are available 24 hours/day (South 362-5339, North 454-7449).

Drug Information Center

Room B830, North Campus
Phone: 314-454-8399
Hours: M-F 07:00-16:00

Phred: the Pharmacy Resources Directory

Phred is the Pharmacy Resources Directory (intranet site). It is available only on the BJH LAN. From any BJH clinical computer or Compass terminal, click on the "IV Guidelines" icon to launch Phred. Search Phred using the search window located at the top right side of the page. In 2012, Phred was moved to a new server. Please update your bookmarks to this new URL:

https://phred.carenet.org/

Formulary, Monographs, Patient Education Sheets

Available via Phred. From the desktop of any BJH clinical computer or Compass terminal, click on the "IV Guidelines" icon to launch Phred. On the top menu, click on "Home", then scroll half-way down the home page and click on "Drug Info Links". A list of multiple online resources will appear. To see drugs on the hospital's formulary, click on "**LexiComp & Drug Formulary**". The specific URL is:

https://online.lexi.com/lco/action/home

Micromedex 2.0

Micromedex is an online service which contains numerous drug monographs (both domestic and foreign) and information related to poison control, toxicology, IV compatibility, dosage form identification, patient teaching sheets and dosing tools. Within Compass, click on the Micromedex icon on the main menu bar. From any BJH clinical computer open a web browser and enter the following URL. This URL will not launch from handheld device browsers.

http://www.micromedexsolutions.com/micromedex2/librarian/