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Pharmacy Overview for Critical Care Nurses

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Objectives

- Discuss common pump errors
- Review titratable drips
  - Mechanism of Action (MOA)
  - Indication
  - Starting and max rates
  - Adverse effects
  - Monitoring
- Focus on heparin protocol
- Practice a calculation
- Apply to a patient case

Titratable Drips Discussed

- Vasopressors
- Inotropes
- Insulin
- Analgesics: opioids
- Sedatives
- Neuromuscular blockers
- Antiarrhythmics
- Antithrombotics
- Antihypertensives

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General Information

- Definition of titration
- Check vital signs every 15 min when actively titrating
- No IV drips may be run as an IVPB
- Choose CCA: ICU/IMC-card (or ICU-gen)

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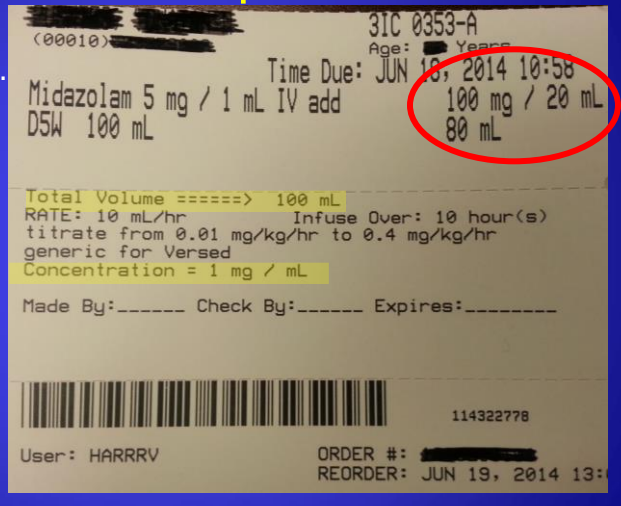
Common Pump Errors

- Choosing the wrong drug/conc. from the library (verify drip conc. matches pump conc.)
- Entering the wrong pt weight
- Choosing “Drug not in Library” and entering the wrong concentration from the label



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VASOPRESSORS

Norepinephrine

Epinephrine

Vasopressin

Dopamine

Phenylephrine

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General Guidelines for Pressors

- Treat hypovolemia induced hypotension with **fluids** PRIOR TO giving vasopressors
- Titrate one pressor at a time
- Central line
  - Monitor infusion site for extravasation
  - Antidote: phentolamine (an alpha-receptor antagonist) intradermally
- DO NOT administer sodium bicarbonate in the same line as any vasopressor (incompatible).

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Common Adverse Effects of Pressors

- Hypoperfusion (skin, kidneys, GI tract, etc), dysrhythmias, myocardial ischemia
- **Warning**: high doses can result in peripheral and mesenteric ischemia leading to digit loss and bowel necrosis
- If you are close to the max rate, it is time to add another pressor. Do NOT continue to increase the rate.

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Receptors

Receptor	Site	Action
Alpha-1 (α_1)	Smooth muscle (vascular, sphincters)	Smooth muscle contraction, vasoconstriction
Alpha-2 (α_2)	CNS	Inhibits norepinephrine release ↓HR, ↓BP
Beta-1 ($ß_1$)	Heart	↑contractility (inotrope), ↑ HR (chronotrope), ↑automaticity, ↑ conduction velocity
Beta-2 ($ß_2$)	Smooth muscle (vascular, bronchioles, intestine)	Vasodilation
Dopaminergic (D)	Vascular smooth muscle (renal, mesenteric, coronary)	Vasodilation
Vasopressin (V_1, V_2)	Kidney	↑ free water retention, ↑ SVR, vasoconstriction

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Vasopressors

Drug	Dose Range	Receptor	Effect
Dopamine (Intropin®)	1-5 mcg/kg/min 5-10 mcg/kg/min 10-20 mcg/kg/min	D>$ß_2$> $ß_1$ $ß_1$, $ß_2$>D> $α_1$ $α_1$> $ß_1$, $ß_2$>>D	Increase HR, contractility, and SVR
Epinephrine (Adrenalin®)	0.01-0.04 mcg/kg/min 0.05-1 mcg/kg/min	$ß_1$, $ß_2$ >> $α_1$ $ß_1$ > $α_1$, $ß_2$	↑↑HR, ↑contractility, ↓SVR↑ HR, ↑contractility, ↑SVR
Norepinephrine (Levophed®)	0.5-30 mcg/min 0.01-1 mcg/kg/min	$α_1$> $ß_1$ $α_1$>> $ß_1$	↑SVR, ↑contractility, ↓ HR,↑↑SVR
Phenylephrine (Neosynephrine®)	40-180 mcg/min	$α_1$	↑↑SVR
Vasopressin (Pitressin®)	0.01-0.04 units/min 2-4 units/hour	V_1, V_2	↑↑SVRwater resorption

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NorEPINEPHrine (Levophed®)

- Potent **alpha-1 agonist** activity, weak beta-1 activity (may see ↑ HR)
- **First line vasopressor for septic shock** (after fluids). Can also be used for other types of shock.
- WATCH for decreased cardiac output, reflex bradycardia, and chest pain or ventricular arrhythmias

Concentration	4 mg/250 mL (DS 8 mg/250 mL, QS 16 mg/250 mL) *May be mixed in the ICU in an emergency*
Starting Dose	0.01 mcg/kg/min (or 8 mcg/min)
Titration	Increase by 0.05 mcg/kg/min every 1 minute to maintain SBP greater than 90 mmHg (or as ordered)
Maximum Rate	3 mcg/kg/min (or 30 mcg/min)

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Vasopressin (Pitressin®)

- Other name: antidiuretic hormone (ADH)
- MOA: stimulates vasopressin receptor → vasoconstriction and free water retention (no inotropic or chronotropic effects)
- Indication:
  - **Second agent to add in septic shock (add to norepinephrine)**
  - Post-CABG
  - Not a stand-alone agent
- Watch for arrhythmia, asystole, or ↓ CO

Concentration	100 units/100 mL
Usual rate	2-4 units/hour
Titration	Fixed rate (not titrated).
Maximum Rate	6 units/hour

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EPINEPHrine (Adrenalin®)

- Has almost equal alpha-1, beta-1, and beta-2 agonist activity (↑ HR, CO, SV, and SVR)
- Indication:
  - Septic shock: preferred agent to add to norepi + vasopressin
  - Bradycardia, anaphylactic shock, cardiac arrest, post-CABG
- **WATCH for** HTN, dysrhythmias, tachycardia, hyperglycemia

Concentration	1 mg/250 mL (DS 2 mg/250 mL, QS 4 mg/250 mL) *May be mixed in the ICU in an emergency*
Starting Dose	0.01 mcg/kg/min
Titration	Increase by 0.05 mcg/kg/min every 1 minute to maintain SBP greater than 90 mmHg (or as ordered)
Maximum Rate	0.6 mcg/kg/min

Dopamine

- Indication:
  - Hypotension or symptomatic bradycardia
  - No longer recommended in septic shock
- DO NOT USE in patients with
  - Uncorrected tachyarrhythmias
  - Ventricular fibrillation

Concentration	Premix 800 mg/500 mL (DS 800 mg/250 mL)
Starting Dose	5 mcg/kg/min
Titration	Increase by 1-4 mcg/kg/min every 10 minutes Dose dependent effects: 5-10 mcg/kg/min (cardiac dosing/β1 receptors): increased renal blood flow, HR, cardiac contractility, cardiac output >10 mcg/kg/min (vasopressor dosing/α1 receptors) : vasoconstriction, increased blood pressure, HR
Maximum Rate	20 mcg/kg/min (greater doses may not improve BP but may increase arrhythmias)

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Dopamine

- No “renal dose” of dopamine
  - Low doses will increase UOP but do NOT improve or protect renal function
- Adverse effects
  - Common vasopressor ADRs, but especially tachycardia, tachyarrhythmias, and angina
  - These hamper clinical use and are more common with higher doses.
  - Studies have shown an increased mortality due to tachyarrhythmias in septic shock, and this is why dopamine is no longer recommended in septic shock (only to be used as a salvage drug).

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PHENYLephrine (Neosynephrine®)

- Acts as a pure alpha-1 agonist ONLY
- Indication:
  - Hypotension in patients with tachyarrhythmias (afib) since no B1 effects
  - Not recommended in septic shock Use as a second or third-line therapy to treat hypotension from shock resistant to other vasopressor agents (salvage therapy).
- Use extreme caution in HF or cardiogenic shock; ↑ SVR may significantly ↓ CO
- WATCH for ↓ CO, reflex bradycardia, severe peripheral and visceral vasoconstriction

Concentration	60 mg/100 mL
Starting Dose	100-180 mcg/min until BP stabilized
Titration	Increase by 10 mcg/min every 1 minute to maintain SBP > 90. Once BP stabilized, decrease to 40-60 mcg/min
Maximum Rate	180 mcg/min

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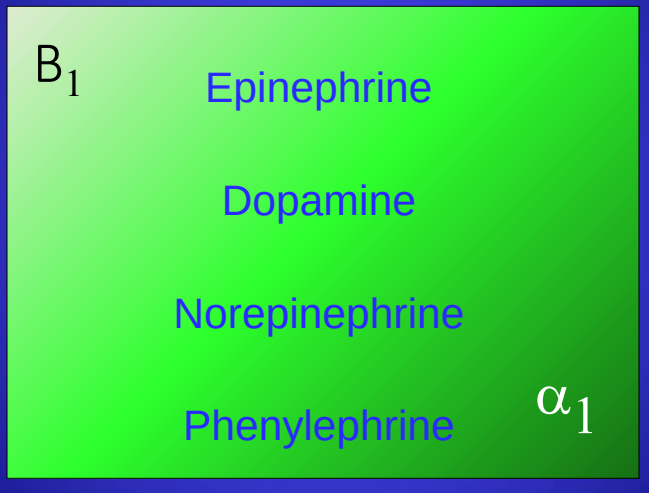
Vasopressors



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Application

- LT is a 78 year old man who presents to ER with AMS, SOB, cough with yellow sputum, and fever from a nursing home. He is diagnosed with sepsis secondary to HCAP.
- PMH: COPD, DM2, HTN
- VS: P 102 BP 78/34 RR 30 T 38.4 °C
- What is the first intervention you would recommend for the BP?
- After the intervention, BP is 83/42. What is your next recommendation?
- BP is 88/44. What now?

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INOTROPES

Recall that ionotropic refers to increased strength of contraction of heart muscle → increased cardiac output and stroke volume.

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Dobutamine (Dobutrex®)

- Potent beta-1 agonist: strong positive ionotropic activity
- Some beta-2 and alpha agonist activity. Because of B-2 activity, dobutamine *does not cause vasoconstriction* and may ↓ BP
- Indications
  - Septic shock: pts with low CO and high filling pressures (CI < 3 L/min/m^2 or $ScVO_2$ < 70%)
  - Cardiogenic shock. Vasopressors may need to be given to counteract arterial vasodilation.
- WATCH for: hypotension, hypertension, arrhythmias

Concentration	Premix 250 mg/250 mL (DS 500 mg/250 mL, QS 1000 mg/250 mL)
Starting dose	5 mcg/kg/min
Titration	Gradually adjust rate at 2-10 minute intervals according to Cardiac Index (CI) goal
Max Rate	20 mcg/kg/min (40 mcg/kg/min)

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Milrinone (Primacor®)

- MOA: inotrope (phosphodiesterase-3 inhibitor)
  - Dose-dependent VD can ↑ CO through SVR reduction
  - Lowering of PAP → beneficial in patients with pulmonary congestion due to LV dysfunction (pulmonary hypertension).
- Indication: acute decompensated heart failure, post-CABG, ↑ PAP
- Typical 1-3 hour delay in hemodynamic effects
- Rate requires adjustment for renal impairment
- WATCH for: arrhythmias, hypotension (esp. with LD), hepatotoxicity

Concentration	Premix 40 mg/200 mL
Maintenance dose	0.375-0.75 mcg/kg/min 50 mcg/kg loading dose over 10 min optional, hypotension likely
Titration	Titrate by 0.2 mcg/kg/min every 30 minutes to goal CI
Max Rate	0.75 mcg/kg/min

Application

- LT's BP is being maintained on two pressors. However, his $ScVO_2$ is 65%. You check his hemoglobin and it is 9 g/dL.
- What is your recommendation to improve his $ScVO_2$?

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INSULIN

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Insulin Regular

- Regular ONLY
- Indications:
  - DKA / HHNK
  - Post-op hearts
  - High doses of epinephrine infusions
- Flush with 20 mL to minimize adsorption to IV tubing
- Monitoring: goal BG 100-159. Check FSBS initially every hour
- Powerplans:
  - Protocol Hyperglycemia Management (XY)
  - Protocol Intensive Insulin Infusion
  - ENDO DKA PowerPlan

Concentration	100 units/100 mL
Starting rate	1-10 units/hour, depending on protocol severity ordered
Titration	Per protocol
Max rate	Per protocol. Notify provider if rate > 40 units/hr

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Application

- LT's blood glucose ranges from 190-280 mg/dL.
- What recommendation would you make to the physician?
- What medication is LT receiving that could affect his blood glucose?

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ANALGESICS

Fentanyl
Morphine
Hydromorphone

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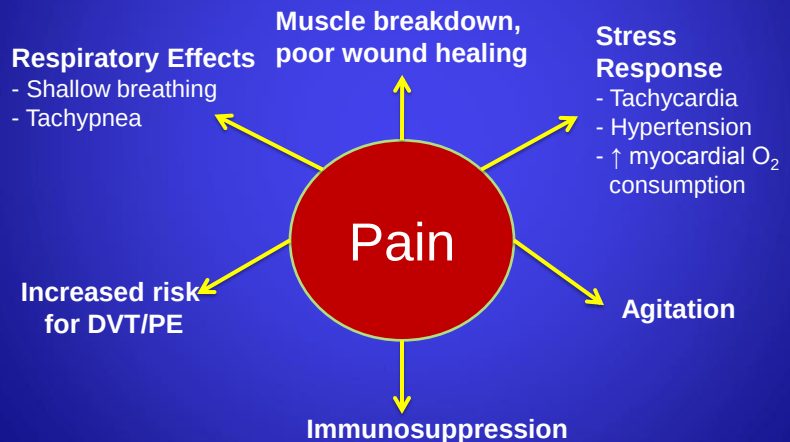
Analgesia

Physical Effects of Pain



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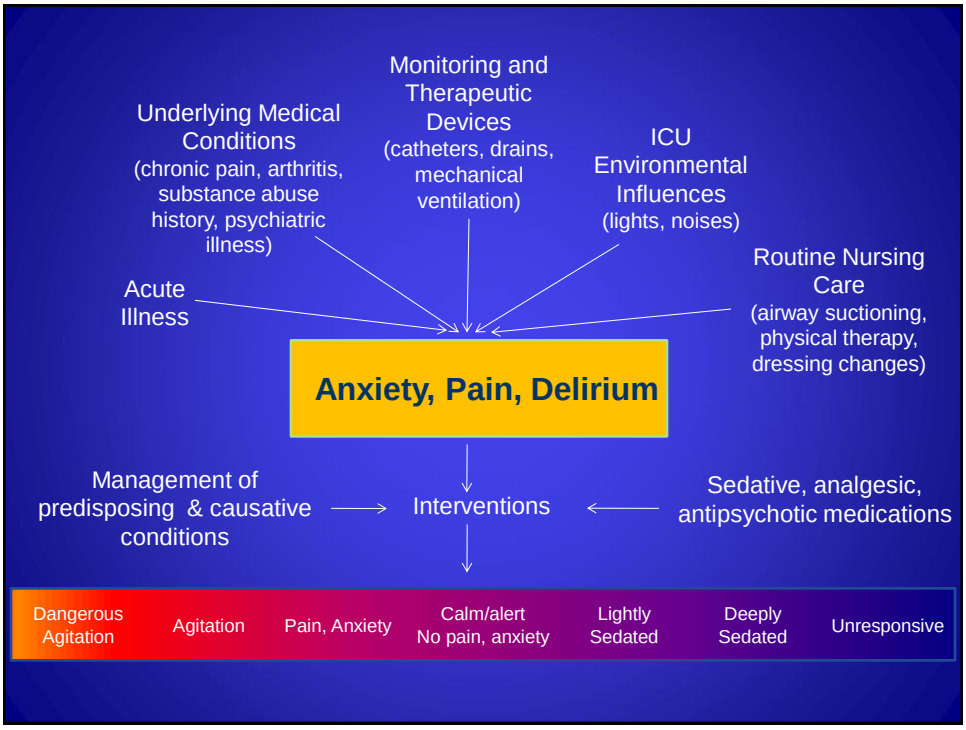

Pain

- Assess pain regularly
- Treatment
  - Nonpharmacological
    - Positioning of patient
    - Positioning of ventilator and feeding tubes
    - Heat or cold therapy
  - Pharmacological
    - Opioids (most common in ICU)
    - Non-opioid: APAP, NSAIDs

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Opioid Analgesics

- Fentanyl
  - Most rapid onset, shortest duration
    - Preferred in acutely distressed pts
    - Preferred in short procedures
  - Accumulation and prolonged effects in repeated dosing
- Morphine
  - Longer duration, intermittent doses may be given
  - Active metabolite: prolonged in renal insufficiency
  - Histamine release
  - Hypotension may result
- Hydromorphone
  - Duration similar to morphine
  - Lacks active metabolite or histamine release
  - Confused with morphine but is ~7 times stronger than morphine!
- Meperidine
  - Avoid due to potential for neurotoxicity
  - Normeperidine causes neuroexcitation (apprehension, tremors, delirium, seizures)
  - Interact with antidepressants (can cause serotonin syndrome)

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Analgesic Administration

- Preventing pain is more effective than treating established pain
- Administer on a scheduled or scheduled intermittent basis + PRN doses
- Patient Controlled Analgesia (PCA)
- Continuous Infusion- done through the PCA pumps at ISMC
- PRN only not as effective
- Monitor for respiratory depression, constipation (schedule stool softeners and/or laxatives as needed), hypotension

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SEDATIVES

Propofol
Midazolam
Lorazepam
Dexmedetomidine

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Sedative Selection

- *Sedate agitated patients only after adequate analgesia and treatment of reversible causes*
- 2002 SCCM Sedation Guidelines
  - Midazolam only for short-term sedation (< 2 days)
  - Lorazepam for long-term sedation (> 3 days)
  - Propofol for patients requiring intermittent awakenings
- 2013 version *non-benzodiazepine sedatives (propofol, dexmedetomidine) may be preferred to improve outcomes*

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Sedation Scale

Richmond Agitation Sedation Scale (RASS)	
+4	Combative
+3	Very agitated
+2	Agitated
+1	Restless
0	Alert and calm
-1	Drowsy
-2	Light sedation
-3	Moderate sedation
-4	Deep sedation
-5	Unarousable

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Propofol (Diprivan®)

- MOA: general anesthetic for sedation
- Shortest acting sedative (duration 10-15 min; accumulates over time
- Contraindications: egg allergy, no MV
- Administration
  - Vented tubing
  - Dedicated line (potential incompatibility and infection)
  - Strict aseptic technique must be used due to a high infection risk. Tubing and vial MUST be changed every 12 hours
- Green urine is rare but may occur due to phenolic metabolites

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Propofol (Diprivan®)

- WATCH for:
  - **Hypotension** (especially after bolus dosing)
  - **Bradycardia**
  - **Respiratory depression or apnea**
  - Pancreatitis- monitor triglycerides
  - Propofol-related infusion syndrome (PRIS)
    - Risk increases with increasing dose and duration
    - Syndrome of lactic acidosis, bradycardia, hyperlipidemia, and rhabdomyolysis
    - Incidence 1 %, mortality 33%

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Propofol (Diprivan®)

Usual Concentration	1000 mg/100 mL premixed and undiluted
Bolus Dose	NURSING CANNOT BOLUS DOSE
Starting Dose	5 mcg/kg/min
Titration	May increase by 5-10 mcg/kg/min every 5 minutes until at target sedation
Weaning	Decrease by 5-10 mcg/kg/min every 5 minutes. Abrupt discontinuation associated with anxiety, agitation, and resistance to mechanical ventilation.
Maximum Infusion Rate	50 mcg/kg/min (physician's order required for higher rates)

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Y-site Compatibility with Propofol

Drug	Y-site Compatible?
Amiodarone (Cordarone®)	NO
Diltiazem (Cardizem®)	NO
Dobutamine (Dobutrex®)	Yes
Dopamine	Yes
Epinephrine (Adrenalin®)	Yes
Eptifibatide (Integrilin®)	NO
Esmolol (Brevibloc®)	Yes
Fentanyl	NO
Heparin	Yes
Labetalol	Yes
Lorazepam	NO
Midazolam (Versed®)	NO
Morphine	Yes
Nicardipine (Cardene®)	NO
Nitroglycerin	Yes
Nitroprusside (Nipride®)	NO
Norepinephrine (Levophed®)	Yes
Phenylephrine (Neosynephrine®)	NO
Vasopressin (Pitressin®)	NO

Benzodiazepines

Midazolam (Versed)
Lorazepam (Ativan)

- MOA: binds to benzodiazepine receptors
- Indication: sedation
- Factors affecting intensity and duration of effect
  - Delayed emergence from sedation with prolonged administration (due to saturation of tissues) in elderly patients, hepatic dysfunction (all BZDs are metabolized by the liver), or renal insufficiency
  - Prior alcohol abuse and concurrent drug therapy may increase the dosages required
- Adverse effects
  - Respiratory depression and hypotension, especially when given with opioids
  - May also contribute to delirium
  - Potential for accumulation
- Reversal: flumazenil (Romazicon®) not recommended
  - Risk of inducing withdrawal after prolonged therapy
  - Reversal of patients on BZD for seizures or increased intracranial pressure could precipitate these events

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Midazolam (Versed®)

- Used most often for procedures requiring moderate sedation as IVP
- Rapid onset, short duration of action with single doses (useful for acute agitation)
- Accumulation and prolonged sedation due to active metabolite, especially in renal insufficiency

Concentration	100 mg/100 mL
Starting rate	1 mg/hr
Titration	Titrate by 2 mg/hr every 10 minutes to goal RASS
Max rate	10 mg/hr

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Lorazepam (Ativan®)

- Slightly slower onset than midazolam, less useful for acute agitation
- Infusion is not readily titratable due to half life of ~8 hours
- Commonly used to treat alcohol withdrawal and seizures
- Solvent is propylene glycol. May cause reversible acute tubular necrosis, lactic acidosis, and hyperosmolar states

Concentration	40 mg/50 mL
Starting rate	1 mg/hr
Titration	Titrate by 2 mg/hr every 10 minutes to goal RASS
Max rate	10 mg/hr

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Dexmedetomidine (Precedex®)

- MOA: selective α_2-agonist sedative, small analgesic properties
- Patients remain sedated when undisturbed, but arouse readily---does not work well as monotherapy for sedation
- Indication
  - Short-term sedation of mechanically ventilated patients with anticipated early extubation
  - ISMC ICU use restricted for 24 h for extubation

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Dexmedetomidine (Precedex®)

- ADRs: hypotension (24-56%), hypertension with bolus doses, bradycardia (5-42%), can be severe
- Caution with vasodilators or drugs that ↓ HR
- Expensive: 3x propofol

Concentration	200 mcg/50 mL
Starting rate	0.2 mcg/kg/hr Optional loading dose: 1 mcg/kg over 10 min (omit if concern for hemodynamic compromise)
Titration	0.1 mcg/kg/hr every 15 minutes to RASS of 0 to -2. Allow 15 minutes for peak effect after each dosage change. *Abrupt discontinuation should be avoided (nervousness, agitation, HA, rapid ↑ BP).*
Maintenance	0.2-1.4 mcg/kg/hr

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NEUROMUSCULAR BLOCKERS

Cisatracurium

Succinylcholine

Rocuronium

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NMBAs

- NMBAs have NO analgesic or amnestic effects
- Patients may appear comfortable, but analgesia and sedation MUST BE USED
- Indications
  - All other modalities must be tried first- NMBAs should be a last resort
  - Facilitate mechanical ventilation: used for both rapid sequence intubation (RSI) and ventilator asynchrony
  - Acute respiratory distress syndrome (ARDS)
  - Therapeutic hypothermia after cardiac arrest

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NMBA Monitoring

- Sedation: BIS monitor (keep BIS 40-60)

Sedation Level	BIS value	Level of Consciousness
	0	Flat line EEG, absence of brain activity
Deep Sedation	20-40	Burst suppression
Deep Sedation	40-60	Low probability of explicit recall Unresponsive to verbal stimulus
Moderate Sedation	60-80	Responds to loud commands or mild prodding/shaking
Anxiolysis	80-90	Responds to normal voice
Anxiolysis	90-100	Awake

- Paralysis: Peripheral Nerve Stimulator (2:4)

No. of twitches	Approximate % receptors blocked
0	100
1	90
2	75-80
3	75
4	0

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NMBA Checklist

Before starting a NMBA make sure:

- ✓Scheduled or continuous analgesia
- ✓Scheduled or continuous sedation
- ✓DVT prophylaxis
- ✓Stress ulcer prophylaxis
- ✓Eye drops or ointment
- ✓Not receiving corticosteroids (prolonged paralysis)

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Cisatracurium (Nimbex®)

- Most common paralytic infusion at ISMC
- Metabolism not affected by renal or hepatic disease

Concentration	200 mg/100 mL
Starting rate	0.5 mcg/kg/min
Titration	Titrate by 1 mcg/kg/min every 10 minutes to goal train-of-four of 2:4
Max rate	10 mcg/kg/min

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Rapid Sequence Intubation (RSI)

– Definition: using a sedative (often etomidate) along with a NMBA to quickly achieve readiness for endotracheal intubation

– Associated with an improvement in intubating conditions and reduction in hypoxemia and complications (aspiration, traumatic intubation, dental injury)

- **Succinylcholine:**
  - 1-1.5 mg/kg once (~100 mg in a 70 kg adult)
  - Avoid when depolarizing effect can cause increase in extracellular potassium (sustained muscle weakness, prolonged immobility, renal failure)
- **Rocuronium:**
  - 1-1.2 mg/kg once
  - Used in RSI when succinylcholine is contraindicated
  - Duration much longer than succinylcholine (60-80 min); may not be appropriate for difficult intubations or mask ventilation as hypoxemia can occur

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Application

- LT continues to decline and develops respiratory failure and ARDS as a complication of HCAP/sepsis. His SCr is 3.4. The pulmonologist wants to start a paralytic.
- Which paralytic would you recommend and what other recommendations would you make?

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ANTIARRHYTHMICS

Diltiazem
Amiodarone
Esmolol

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Diltiazem (Cardizem®)

- MOA: non-dihydropyridine CCB
- Indications:
  - Lower the ventricular response in A-fib, Atrial flutter, and SVT
- WATCH for:
  - Bradycardia
  - Hypotension

Concentration	125 mg/125 mL
Bolus dose	A bolus dose of 0.25 mg/kg (in adults usually 10-20 mg) may be given over 2 minutes. May be repeated once at 0.35 mg/kg after 15 minutes.
Starting dose	5-10 mg/hr
Titration	Titrate by 5 mg/hr every 15 minutes up to 15 mg/hr
Max Rate	15 mg/hr

Amiodarone

- MOA: class III antiarrhythmic agent that slows intra-cardiac conduction.
- Indication:
  - Ventricular arrhythmias (VT, Vfib)
  - Rapid ventricular rates associated with SVT, Afib
  - Conversion from atrial fibrillation RVR (particularly if little response to BB or CCB)
- 0.22 micron filter required
- Infuse through dedicated IV line (central preferred)
- Contraindication: 2nd or 3rd degree AV heart block, bradycardia, cardiogenic shock
- WATCH for: bradycardia and hypotension, QT prolongation

	Usual Concentration	Rate (mg/min)	Rate (mL/hr)
Loading Dose	150 mg/ 100 mL D5W	15 mg/min	600 mL/hr for 10 minutes
Slow Loading Dose	450 mg/250 mL D5W	1 mg/min	33.3 mL/hr for 6 hours
Maintenance Dose	450 mg/250 mL D5W	0.5 mg/min	16.7 mL/hr for 18 hours

Esmolol (Brevibloc®)

- MOA: short acting β1-selective beta-blocker
- Indication: SVT, HTN, atrial fibrillation/flutter
- Contraindication: HF, cardiogenic shock, bradycardia, 2nd or 3rd degree heart block, hypotension
- WATCH for: bradycardia and hypotension

Concentration	2500 mg/250 mL (DS 2000 mg/100 mL)
Bolus dose	500 **mcg**/kg loading dose over 1 minute. Loading dose may be repeated up to three times per physician order.
Starting dose	50 mcg/kg/min
Titration	Titrate by 50 mcg/kg/min every 4 minutes to patient response
Weaning	Decrease the infusion rate in increments to 25 mcg/kg/min after therapeutic dose has been reached
Max Rate	200 mcg/kg/min

Application

- LT is improving due to his excellent care and is able to come off all his IV drips except for norepinephrine. You notice that his HR is 128 with irregularly irregular R-R and no p waves.
- What recommendations would you make?

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ANTIHYPERTENSIVES

Nicardipine

Nitroprusside

Nitroglycerin

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Nicardipine (Cardene®)

- MOA: dihydropyridine calcium channel blocker
- Indication: antihypertensive, HTN crisis, ischemic stroke
- Contraindication: aortic stenosis (may ↓ coronary perfusion → ischemia)
- Peripheral or central line
- WATCH for: hypotension, reflex tachycardia, headache, peripheral edema

Concentration	50 mg/250 mL
Starting dose	5 mg/hr
Titration	Titrate by 2.5 mg/hr every 15 minutes to patient response. Do not abruptly discontinue. Abrupt withdrawal may cause rebound angina in patients with CAD.
Max Rate	15 mg/hr

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Nitroprusside (Nipride®)

- MOA: direct vasodilator potent arterial vasodilator
- Indications: usually LAST OPTION for hypertensive crisis, ischemic stroke, HF, post-CABG
- Cyanide toxicity at high infusion rates for long periods of time. Use with caution in hepatic or renal impairment
- Light sensitive: keep drug and tubing covered
- WATCH for:
  - **Excessive hypotension**: do not leave the bedside while titrating. Sudden and extreme decreases in systolic blood pressure have been associated with this infusion. Monitor BP every 5 minutes during titration.
  - **Cyanide toxicity**: monitor for cyanide toxicity via metabolic acidosis and SVO2
    - Initial symptoms: flushing, tachycardia, tachypnea, headache, and dizziness.
    - Worsening toxicity: loss of consciousness, coma, hemodynamic compromise, arrhythmias, seizures, apnea, cardiac arrest, and death.
  - Thiocyanate toxicity: in renal impairment, prolonged infusion (>3 days), dose ≥4 mcg/kg/ minute
  - Headache, Nausea

Concentration	50 mg/250 mL . *May be mixed in the ICU in an emergency*
Starting dose	0.3 mcg/kg/min
Titration	Increase by 0.5 mcg/kg/min every 3-5 minutes to effect or until headache/nausea occurs
Max Rate	10 mcg/kg/min (rarely need greater than 4 mcg/kg/min). When administered by prolonged infusion faster than 2 mcg/kg/minute, cyanide is generated faster than an unaided patient can handle.

Nitroglycerin

- MOA: coronary vasodilator and peripheral venodilator (reduces preload)
- Indication: angina, hypertension, CHF, and pulmonary hypertension
- Contraindications:
  - Head trauma or ICH
  - Within 24 hours of sildenafil (Viagra®) or vardenafil (Levitra®) or within 48 hours of tadalafil (Cialis®). May cause severe hypotension, MI, or death
- WATCH for:
  - Hypotension
  - Lightheadedness, headache (common)
  - Tachycardia
  - Flushing of the face and neck

Concentration	Premix 50 mg/250 mL
Starting dose	5 mcg/min IV
Titration	Increase by 5 mcg/min every 3-5 minutes to 20 mcg/min. If no response at 20 mcg/min, increase by 10 mcg/min every 3-5 minutes.
Max Rate	200 mcg/min

Application

- Two weeks later LT was discharged to LTAC, but he returns to the ER after one week with crushing chest pain and BP 240/172. The plan is to go to the cath lab.
- In the meantime, what is your recommendation for his BP?
- What are your HTN recommendations after placement of 2 stents?

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ANTITHROMBOTICS

Heparin

Bivalirudin

Eptifibatide

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HEPARIN PROTOCOL

Cheri Walker, PharmD, BCPS & Ann-Marie McCormick, RN, CCRN
February 2016

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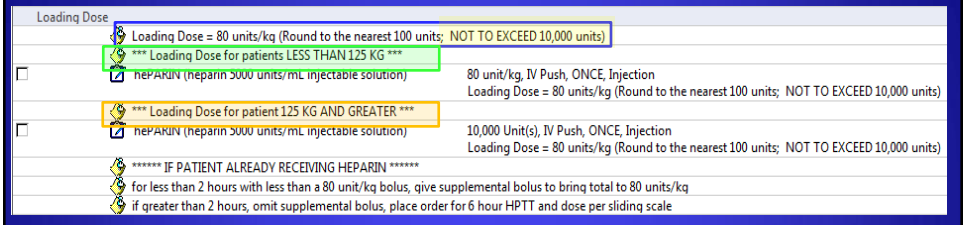
Heparin

- MOA: Potentiates antithrombin III and inactivates thrombin
- Indication: anticoagulant for DVT/PE or in ACS
- Monitor: HPTT 6 hours after initiation and each rate change (keep 42-70), S/S bleeding, H/H
- Antidote: protamine sulfate

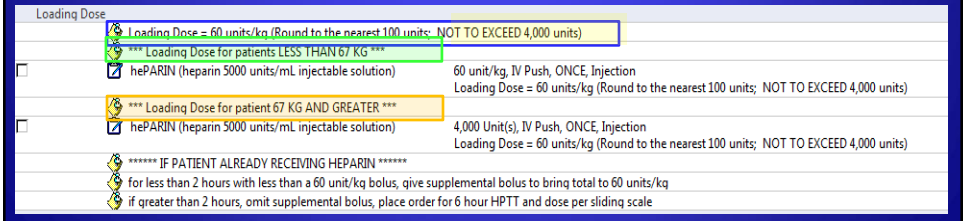
	DVT/PE	ACS
Concentration	Premix 25,000 units/500 mL	
Loading Dose	80 units/kg (round to nearest 100 units), max 10,000 units	60 units/kg, round to nearest 100 units, max 4000 units
Maintenance dose	18 units/kg/hr (round to nearest 50 units), not to exceed 1500 units/hr	12 units/kg/hr (round to nearest 50 units), max 1000 units/hr
Titration	Per protocol	
Max Rate	Per protocol (sliding scale calculates for maximum weight in kg)	

Loading Dose

DVT/PE



ACS



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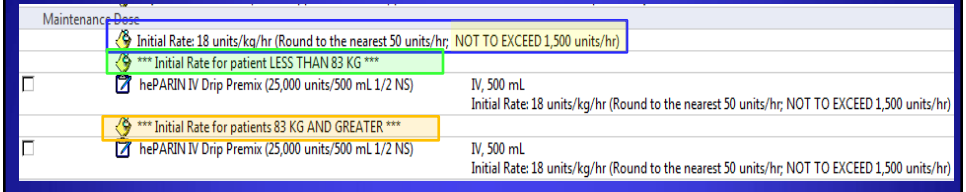
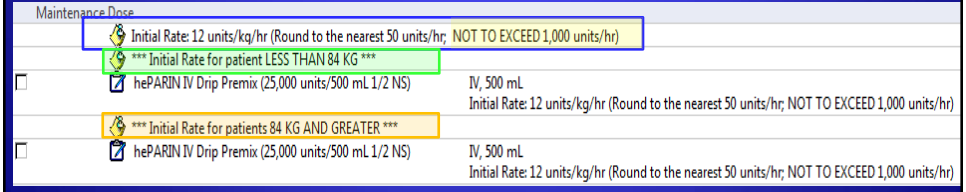
Initial Rate

DVT/PE



ACS



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Titration

- Pharmacist calculates and enters patient specific doses in order comments
- Bolus dose and rates vary based on HPTT, patient weight, and protocol (VTE vs. ACS)

Heparin for VTE: titration for 70 kg patient	
HPTT < 32	5600 unit bolus and INCrease infusion BY 300 units/hour
HPTT 32 - <35	4200 unit bolus and INCrease infusion BY 200 units/hour
HPTT 35 - 40	2800 unit bolus and INCrease infusion BY 150 units/hour
HPTT 40 - 41	NO bolus; INCrease infusion BY 50 units/hour
HPTT 42 - 70	NO CHANGE; Recheck HPTT in 6 hrs. After two that result in no rate change, order HPTT next morning
HPTT 71 - 75	NO bolus; DECrease infusion BY 50 units/hour
HPTT 76 - 85	NO bolus; DECrease infusion BY 100 units/hour
HPTT 86 - 90	NO bolus; DECrease infusion BY 150 units/hour
HPTT 91 - 110	HOLD INF x 1 hr, then resume at rate lower BY 200 units/hour
HPTT > 110	HOLD INF and notify physician promptly

Heparin for ACS: titration for 70 kg patient	
HPTT < 32	4000 unit bolus and INCrease infusion BY 200 units/hour
HPTT 32 - <35	3500 unit bolus and INCrease infusion BY 150 units/hour
HPTT 35 - 41	2800 unit bolus and INCrease infusion BY 100 units/hour
HPTT 42 - 70	NO CHANGE; Recheck HPTT in 6 hrs. After two that result in no rate change, order HPTT next morning
HPTT 71 - 78	NO bolus; DECrease infusion BY 50 units/hour
HPTT 79 - 85	NO bolus; DECrease infusion BY 100 units/hour
HPTT 86 - 90	NO bolus; DECrease infusion BY 100 units/hour
HPTT 91 - 110	HOLD INF x 1 hr, then resume at rate lower BY 200 units/hour
HPTT 111 - 155	HOLD INF x 90 min, then resume at a rate lower BY 200 units/hour
HPTT > 155	HOLD INF x 90 min, then resume at a rate lower BY 300 units/hour

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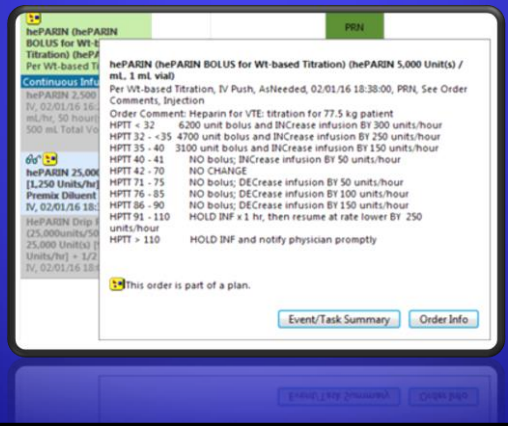
Titration

Scroll over heparin order to see titration rates



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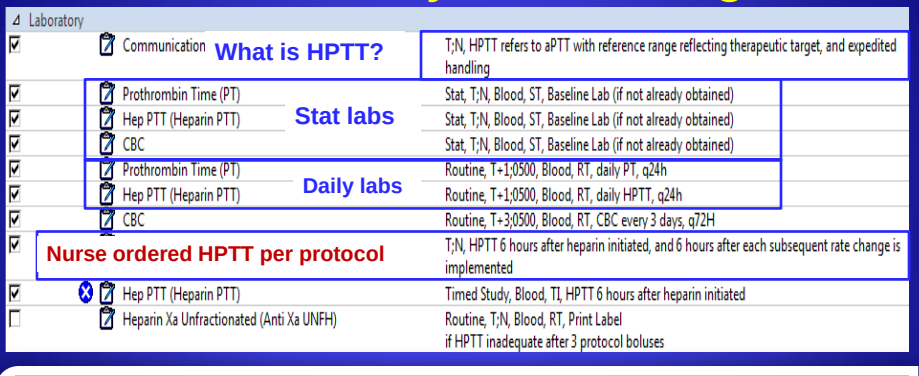
Laboratory Monitoring



HPTT 42 - 70 sec: NO CHANGE in rate. Recheck HPTT in 6 hours. **After two HPTT values that result in no rate change, order HPTT next morning.**

Please make sure to check labs q 6 hours until you reach NO Change X 2 then you may change to q day HPTT

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HPTT Labels

- If more than one HPTT is ordered at a time, ensure that the time on the label matches the time the level was drawn.
  - Levels have been reported at the wrong time due to label mismatch.
  - This can cause patient harm by leading to incorrect dose adjustments.

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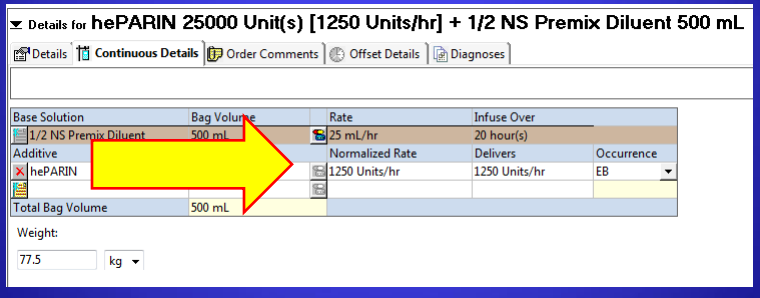
Rate Documentation

How to document rate changes on the MAR

- Go to heparin order (Modify heparin order)
- Change unit rate to desired units per hour per protocol
- Pharmacy will change the rate on the MAR

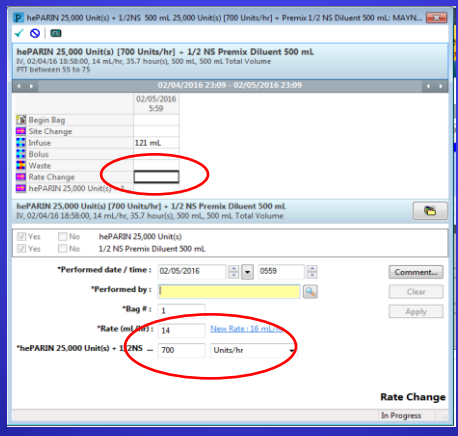
Rate Documentation

- Modify unit rate to desired units per hour per protocol



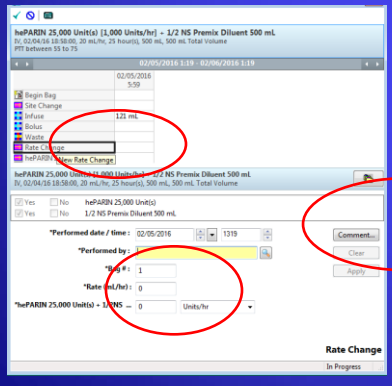
Rate Documentation

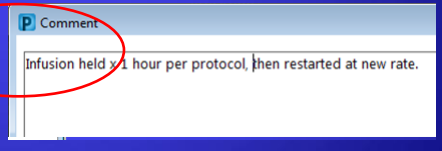
- Document as rate change in the MAR



Holding Infusion due to HPTT

- If HPTT 91 – 110, the order states to “HOLD INFUSION x 1 hr, then resume at a rate lower BY 200 units/hour”
- Document as rate change to zero and add comment about holding dose x 1 hr
- After holding for one hour, document rate change with new infusion rate. Modify the heparin order with the new rate.

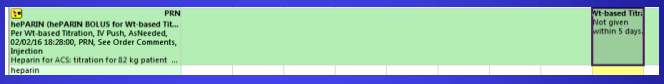




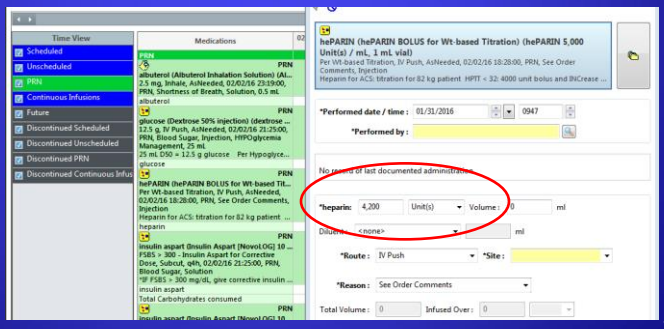
Bolus Documentation

How to document bolus on the MAR

- Bolus dose is located in the PRN orders on the MAR



- Scan your heparin and document units given per protocol.



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Heparin Titration Problem

- WZ is on a heparin drip at 1300 units/hr. The 24 hour HPTT is 33. What should you do?

HPTT < 32	5600 unit bolus and INCrease infusion BY 300 units/hour
HPTT 32 - <35	4200 unit bolus and INCrease infusion BY 200 units/hour
HPTT 35 - 40	2800 unit bolus and INCrease infusion BY 150 units/hour
HPTT 40 - 41	NO bolus; INCrease infusion BY 50 units/hour
HPTT 42 - 70	NO CHANGE; Recheck HPTT in 6 hrs. After two that result in no rate change, order HPTT next morning.
HPTT 71 - 75	NO bolus; DECrease infusion BY 50 units/hour
HPTT 76 - 85	NO bolus; DECrease infusion BY 100 units/hour
HPTT 86 - 90	NO bolus; DECrease infusion BY 150 units/hour
HPTT 91 - 110	HOLD INF x 1 hr, then resume at rate lower BY 200 units/hour
HPTT > 110	HOLD INF and notify physician promptly

- Bolus 4200 units, document in MAR
- Modify order per protocol and increase infusion to 1500 units/hr.
- Order HPTT 6h after rate change.

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Heparin Titration Problem

- HPTT rechecked after 6 hours is 45. The current rate is 1500 units/hr. What should you do?

HPTT < 32	5600 unit bolus and INCrease infusion BY 300 units/hour
HPTT 32 - <35	4200 unit bolus and INCrease infusion BY 200 units/hour
HPTT 35 - 40	2800 unit bolus and INCrease infusion BY 150 units/hour
HPTT 40 - 41	NO bolus; INCrease infusion BY 50 units/hour
HPTT 42 - 70	NO CHANGE; Recheck HPTT in 6 hrs. After two that result in no rate change, order HPTT next morning.
HPTT 71 - 75	NO bolus; DECrease infusion BY 50 units/hour
HPTT 76 - 85	NO bolus; DECrease infusion BY 100 units/hour
HPTT 86 - 90	NO bolus; DECrease infusion BY 150 units/hour
HPTT 91 - 110	HOLD INF x 1 hr, then resume at rate lower BY 200 units/hour
HPTT > 110	HOLD INF and notify physician promptly

- No change in rate
- Order new 6 hr HPTT. If level is 42-70, *NO CHANGE* required and confirm AM HPTT has been ordered.

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ANTITHROMBOTICS

Heparin

Bivalirudin

Eptifibatide

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Bivalirudin (Angiomax®)

- MOA: direct thrombin inhibitor
- Indication: anticoagulant for ACS, HIT
- Target aPTT 42-70 seconds, check 2 hours after initiation and every 4 hours until in range x 2 consecutively

	PCI	HIT
Concentration	250 mg/500 mL	
Bolus	0.75 mg/kg x 1 prior to PCI	None
Starting dose	1.75 mg/kg/hr during procedure and 4 hours after procedure May be continued up to 10 hours after procedure at 0.2 mg/kg/hr	CrCl > 60 mL/min: 0.15 mg/kg/hr CrCl 30-60 mL/min: 0.08 mg/kg/hr CrCl < 30 mL/min: 0.04 mg/kg/hr CRRT: 0.03-0.07 mg/kg/hr
Titration	Not titrated or per orders	Per protocol
Max Rate	1.75 mg/kg/hr	0.3 mg/kg/hr without checking for coagulation abnormalities

Eptifibatide (Integrilin®)

- MOA: GP 2b3a inhibitor
- Indication: antiplatelet for ACS or PCI
- Contraindicated: SCr > 4 or on dialysis (don't use CrCl in computer b/c have to use ABW)
- Before PCI, concomitant heparin or enoxaparin recommended (not usually after)
- DO give with aspirin and a P2Y12 (clopidogrel, prasugrel)
- WATCH for: S/S bleeding, platelet count

Concentration	Premix 75 mg/100 mL
Bolus dose	180 mcg/kg, not adjusted based on renal function (max 22.6 mg) over 1-2 minutes
Starting dose	CrCl > 50 mL/min: 2 mcg/kg/min CrCl <= 50 mL/min or SCr 2-4: 1 mcg/kg/min
Titration	Not titrated. Continue until discharge, CABG, or up to 72 hours (total infusion time <96 hours)
Max Rate	CrCl > 50 mL/min: 15 mg/hr CrCl <= 50 mL/min or SCr 2-4: 7.5 mg/hr

Application

- After receiving the two stents, LT is admitted to the ICU.
- Which antithrombotic may he still be receiving?

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Calculation Practice

- You want to start a norepinephrine drip on a 60 kg female at 0.2 mcg/kg/min using the standard concentration (4 mg/250 mL).
- How many mcg/min is that?
- How many mL/hr is that?

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Calculation Answers

Calculate mcg/min

$$\frac{0.2 \text{ mcg}}{\text{kg}} \times 60 \text{ kg} = \frac{12 \text{ mcg}}{\text{min}}$$

Calculate mL/hr

$$\frac{12 \text{ mcg}}{\text{min}} \times \frac{1 \text{ mg}}{1000 \text{ mcg}} = \frac{0.012 \text{ mg}}{\text{min}}$$

$$\frac{0.012 \text{ mg}}{\text{min}} \times \frac{60 \text{ min}}{\text{hour}} \times \frac{250 \text{ mL}}{4 \text{ mg}} = \frac{45 \text{ mL}}{\text{hour}}$$

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For More Information

Person	Number
Critical Care Pharmacy Specialist: Cheri Walker	1-1398
Infectious Diseases Pharmacy Specialist: Ann Nguyen	6-7258
Cardiology Pharmacy Specialist: Kristin Montarella	1-1331
ICU mobile pharmacist	1-1401
Central pharmacy	6-7255
IV room	6-7261

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