Pharmacologic Treatment of CCU patients (Anti-thrombotic, anti-platelet, anti-ischemic, and other treatments)

Treatment Summary of Anti-Thrombotic and Anti-Platelet Agents in the CCU

Enoxaparin	30 mg IV load 1 mg/kg SC q 12 hours, with next dose 12 hours after first dose NOT STANDARD q12hr no weight cap
UFH	60 U/Kg IVP bolus (max initial bolus 4000 U) 12 U/kg/hr initial infusion (max initial infusion rate 1000 U/hr [10 ml/hr])
	UFH is preferable to enoxaparin for patients with Cr >2 mg/dl or CrCl <40-50 ml/min
	ENOXAPARIN SHOULD NOT BE HELD OR CHANGED TO UFH PRIOR TO CATH WITHOUT DISCUSSING WITH FELLOW AND ATTENDING FIRST
	Unless specified, enoxaparin and UFH should be stopped after PCI
ASA	324 mg load (4 baby aspirin) 325 mg after PCI if have stent placed
	for 81 mg dose, non-enteric coating should be used to ensure appropriate absorption
	DO NOT STOP ASA in patients going for bypass surgery; change to 81 mg
Clopidogrel	Indications: Ischemic ECG, Positive markers, Going to cath lab for likely PCI 300 mg load 75 mg daily afterwards
	AVOID IN PATIENTS WITH HIGH BLEEDING RISK: significant anemia, thrombocytopenia, multiorgan failure, or who are unlikely to undergo PCI within the next 24-48 hours (outside of weekends)
	STOP IMMEDIATELY in any patient going for bypass surgery
Prasugrel	Indications: STEMI patients (pre-PCI), high risk patients (determined after PCI—do not give prior to PCI for non-STEMI patients) Contraindications: elderly (75), low body wt (< 60 kg [132 lbs]), prior CVA or TIA, risk for bleeding), inability to give a history 60 mg po load 10 mg daily afterwards
	STOP IMMEDIATELY in any patient going for bypass surgery
GP IIb/IIIa Inhib	Indications: Positive markers without contraindications (recent CVA, CrCl <50ml/min, increased bleeding risk, thrombocytopenia, significant anemia) Cath lab emergently: Abciximab Cath lab > 4 hr: Eptifibatide
	Abiciximab infusion post PCI duration is 12 hours Eptifibatide infusion post PCI duration is 18 hours

Anti-Platelet Treatment

Aspirin

Studies have found no significant difference in outcomes for ASA doses ranging from 80 to 500 mg, although side effects increase with higher doses (BMJ 2002;324:71). In the ISIS 2 Trial, a loading dose of 162 mg continued out to 35 days had the same clinical benefit as Streptokinase.
However, higher loading doses may be of benefit, with minimal risk, especially in patients undergoing stenting

Patients who have stents implanted should be treated with 325 mg of ASA, with duration based on type of stent (1 month bare metal stent, 3 months for sirolumus, 6 months for taxus); thereafter the dose can be decreased to 81 mg (1 baby ASA). Because of the potential for inadequate absorption, the 81 mg dose should not be enteric coated. When used in combination with clopidogrel, bleeding increases with higher ASA dosages; therefore, in most cases, 81 mg of ASA may be the preferred dosage (except as noted above, such as patients who have recent stent placement).

Clopidogrel

Use of Clopidogrel in non-STEMI ACS is based primarily on two studies: CURE (NEJM 2001;345:494) and CREDO (JAMA 2002;188:2411). In CURE, patients with high-risk non-ST elevation ACS (positive markers or ischemic ECG changes) treated with clopidogrel had a significant reduction in death and MI at a mean 9 months of follow up. Reduction in events was noted within 24 hours of treatment initiation (2.1% to 1.4%). Benefit is greater in higher risk patients: (+) TnI, ischemic ECG changes, and less so in patients without these objective findings. It should be noted that patients with a history of coronary disease and a good story were initially included in CURE, but were dropped because of a low event rate.

In CREDO, patients who were treated with clopidogrel 300 mg loading dose > 12-15 hours before stent placement had a significant reduction in events compared to those without pre-treatment.

Therefore, patients who have positive markers, significant ECG changes (> 1mm ST depression or ischemic T wave inversion) or who are going to have coronary angiography with the anticipation that stenting will be performed should have clopidogrel started early (300 mg loading dose followed by 75 mg a day).

In patients who have contraindications to prasugrel, because it is very uncommon for patients having primary PCI to have to undergo emergency CABG, a 600 mg load should be given in the ED as soon as possible after identification (in the absence of contraindications).

Because of the increased risk of bleeding, its use should be avoided in patients with significant anemia, thrombocytopenia, multiorgan failure, or who are unlikely to undergo PCI within the next 24-48 hours (outside of weekends).

The duration of clopidogrel or prasugrel is a minimum of 1 month after a bare metal stent, and 12 months after a drug eluting stent, unless bleeding occurs or the patient needs a surgical operation. In addition, for most patients who have true ACS, clopidogrel should be continued for up to 1 year, if the patient is low risk for bleeding. Therefore it is important to determine the feasibity of the patient to maintain compliance (ie, do they have any non-cardiac surgery anticipated?)

Patients who are going to have bypass surgery should have treatment stopped as soon as possible, as bleeding is significantly increased in those in whom treatment was stopped < 5 days (Clopidogrel) or 7 days (prasugrel) before CABG.

The recently completed TIMI 28 (Clarity) and COMMIT Trials indicated that giving clopidogrel to patients with ST elevation was beneficial.

Studies have investigated higher loading doses (600 and 900 mg). Higher loading doses accelerate the time to peak platelet inhibition, but do not result in greater inhibition. However, there remains a substantial inter patient variability, which may relate to differences in absorbsion, conversion to its active metabolite, or both.

In patients who are already taking clopidogrel chronically, there appears to be benefit in reloading with an additional 300 mg po.

The ISAR-REACT-2 trial demonstrated that in ACS patients who are TnI (+) benefit from addition of a GP IIb/IIIa antagonist, even if given a 600 mg clopidogrel load.

Prasugrel

For patients who are coming in with STEMI the initial thienopyridine of choice for loading in the Emergency Department will be Prasugrel 60mg. For patients who have contraindications (age 75, weight < 60 kg, prior CVA or TIA), inability to provide a history, Clopidogrel will be given instead, with 600 mg as the loading dose. Prasugrel has improved efficacy over Clopidogrel with an absolute 2.2% and relative 19% reduction in the combination of Death, MI

or stroke. Risk reduction appeared greater in:

diabetic patients (absolute 4.8%, relative 30% reduction)
primary PCI (absolute 1.6%, relative 20%)
STEMI patients treated with lytics first (absolute 5.9%, relative 50%)
patients <65 yrs old (absolute 2.5%, relative 25%)

Patients who were older, particularly > 75, did not benefit.

The majority of the increase risk of bleeding with Prasugrel was seen in the elderly patients, and accrued overtime. There was no significant increased bleeding risk in the first 3 days (TIMI 38) or 30 days (TIMI 38 STEMI cohort).

Bleeding was increased, and was higher with:

prior stroke or TIA
increasing age
lower weight (<60 kg [132 lbs])
renal failure (Cr>2, CrCl < 30 m/min)

In addition, patients who underwent bypass surgery had a substantial increase in major bleeding, from 3.2% to 13.4%. Therefore, with the exception of patients with STEMI, it should not receive it without knowledge of the coronary anatomy.

In the overall cohort, half of the benefit from MI reduction was in the first 3 days (absolute 1%), and half from day 3 to day 450 (absolute 1.4%).

Most of the benefit seen in the Triton TIMI 38 STEMI subgroup appeared to accrue within the first month with a paralleling of curves after that time period. Therefore it appears that the first month after presentation is the highest risk period.

For patients in whom a subsequent contraindication is identified or in whom it is likely that compliance will be difficult, changing to Clopidogrel is recommended. Currently there are no specific guidelines on how this should be done. Both drugs act via irreversibly inhibiting the P2Y12 receptor, and a 60 mg dose of prasugrel results in >90% inhibition of this receptor. In talking to a number of the experts in the field, if the patient has been loaded with prasugrel, there is unlikely to be any benefit (or given the high degree of inhibition, any harm) with giving an additional loading dose of Clopidogrel.

For patients who on clopidogrel who are changed to prasurgel, loading with prasugrel will offer greater platelet inhibition, and should be strongly considered in the setting of recent stenting.

In summary,

1. prasugrel is likely to offer the greatest benefit in patients at high risk for recurrent ACS after PCI, including diabetics and STEMI patients.
2. Risk reduction is greatest in patients <65, with less benefit as age increased.
3. Risk of bleeding is significantly higher than with clopidogrel; subgroups with greater risk include
    - prior stroke or TIA (absolute contraindication)
    - lower weight (<60 kg or 132 lb)
    - women (likely due to lower weight)
    - increased age (particularly >75)
    - renal failure
4. Risk of bleeding was higher long term, with no significant increase in bleeding in the short term
5. Prasugurel should not be given unless the coronary anatomy is known, the only exception is patients with acute STEMI.
6. It is important to make sure that the patient has the ability to fill their prescription at the time of discharge, either at VCU, or determining their pharmacy carries prasugrel.

ANTI-PLATELET LONG TERM TREATMENT GUIDELINES

	ASA	Clopidogrel	Prasugrel
Medical management	81 mg forever	75 mg x 9-12 mo if low bleeding risk	10 mg x 9-12 mo if low bleeding risk
Post BMS	325 mg x 1 month, then 81	75 mg for at least 1 mo	10 mg for at least 1 mo

	mg		
Post DES	325 mg x 3 mo sirolumus, 6 mo paclitaxel, then 81 mg after	75 mg for 1 year	10 mg for 1 year

Beta-blockers
Although beta blockers clearly reduce events in the long term management of patients with MI, there is less data regarding their role in acute treatment. The largest study performed to date, the Chinese COMMIT Trial, found no benefit for early beta blocker initiation. Although there was a significant reduction in ventricular tachycardia and fibrillation, there was a significant increase in the incidence of shock. The overall benefit was therefore neutral. Worse outcomes were seen in patients who had:

clinical evidence of heart failure at the time of presentation
heart rate > 110 bpm
SBP <120 mmHg
were >70 yrs old

Therefore, patients who have clinical evidence of heart failure or other potential contraindications should not be treated acutely with beta blockers until an estimate of an ejection fraction can be obtained. Other potential contraindications include bradycardia, heart block, and severe asthma.

A key point to remember is start low, and go slow. Rather than IV Beta blockers, starting with a lower po dose (12.5 to 25 mg po) can be given. IV beta blockers should be avoided in STEMI patients until EF is known.
If additional anti-ischemic medication is needed IV Nitroglycerin can be used as this provides both treatment for heart failure as well as a reduction in ischemia through coronary vasodilatation.

We use 3 different BB: metoprolol, Toprol XL, and carvedilol. Some relative guidelines are:

Metoprolol used for most pts, can be be given q 8 or q 6 hrs acutely for higher risk pts who do not have CHF, who continue to have increased HR and/or BP

Toprol XL less up and down shift in serum concentrations, so may be of benefit in patients with moderate systolic dysfunction, especially if they have bronchospastic disease (asthma or COPD). Main downside is higher cost compared to the other 2 BBs.

Carvedilol typically used in patients with more severe systolic dysfunction, but now can be used in most patients, as it is generic. It is not beta selective, so metoprolol is the beta blocker of choice in patients with bronchospastic disease.

Atenolol is not routinely used as there is less information not its utility post MI, and because it is excreted renally, can result in significant bradycardia/heart block in patients with renal failure. Therefore, most patients post MI on atentolol should be changed to one of the above BBs.

Anti-Thrombotic Treatment
Glycoprotein IIb/IIIa Antagonists
Troponin positive patients appear to benefit preferentially from treatment with GP IIb/IIIa inhibitors. Because patients with significant ST depression have a high rule in rate, therapy is also recommended in these patients. Currently 2 different GP IIb/IIIa inhibitors are used; Integrilin (Eptifibatide) and Reopro (Abciximab). Both agents are given as a bolus followed by infusion.

For high-risk patients admitted to the CCU prior to angiography, the choice of GP IIb/IIIa is based primarily on timing of the cath.
Abciximab (Reopro) preferred agent for patients going urgently to the cath lab (i.e., within 4 hours) and for STEMI patients. It is not excreted through the kidneys, so it is not affected by renal failure. Treatment duration post PCI is 12 hours. Because of the potential for thrombocytopenia, platelet counts should be checked 2-4 hours and then 12-24 hours after initiation of a Reopro infusion. Strong consideration for stopping treatment should be given if platelet count decreases to < 100,000 and decreases by > 25% from pre-procedure. Prior to stopping it, the interventional attending or fellow should be contacted. It is the responsibility of the CCU to order and check the platelet count if the infusion is started before the patient goes to the cath lab

Integrilin preferred for those who are going to be treated for longer periods (i.e. admitted during the night or on weekend). It has a half life of 2-4 hours, so is the preferred agent in patients awaiting CABG. However, it is renally

excreted, and is contraindicated in patients with Cr >2 mg/dL or CrCl < 50 ml/min, Treatment duration post PCI is 12-18 hours. Integrilin is only rarely associated with thrombocytopenia.

GP IIb/IIIa treatment initiation should be discussed with the Cardiology fellow and/or attending prior to starting.

There is no indication for routine use of GP llb/llla inhibitors in patients after successful lytic treatment, other than to finish any infusion begun for PCI.

The recently completed ISAR-REACT-2 trial demonstrated that in high risk ACS patients (those with positive markers), even using a 600 mg clopidogrel load does not provide adequate protection, and that these patients benefit from addition of a GP IIb/IIIa antagonist.

Determining if and when to start a GP Iib/IIIa antagonist in the ACS patient (primarily integrillin, for more prolonged treatment :

1. Is the patient TnI positive? If not, then not likely to benefit
2. Are there any contraindications (CVA or TIA within 6 months, renal failure [crcl<50 ml/min), thrombocytopenia (plt<100 K), high bleeding potential?
3. What is the risk of the patient? Criteria include in addition to positive markers, is having significant ST depression, and/or recurrent CP (increases the risk of MI or death 3-4 fold), and baseline treatment at time of presentation. For example, if they are on nothing, then adding heparin, ASA, clopdiogrel, NTG and BB may prevent recurrent ischemia. In contrast, if the pt is on ASA, clopidogrel, BB, and has ischemic ECG changes, they have broken thru most of what you would give them, and the ischemic ECG changes puts them at a much higher risk; therefore, the risk/benefit ratio likely will shift more towards using a GP IIb/IIIa.

Enoxaparin and Unfractionated Heparin

Multiple studies have compared low molecular weight heparin with unfractionated heparin.
A meta-analysis of two large studies (ESSENCE {N Engl J Med 1997;337:447 and TIMI 11B Circulation 1999;100;1602) found that enoxaparin had a significant reduction in death and MI, or the combination of MI, and urgent revascularization, at 8 days that was maintained thru 42 days (Circulation 1999, 100;1602). Improved outcomes were seen early, with event curves separating by 8 hours after treatment initiation.

Use of a 30 mg IV bolus (studied in TIMI 11B) is safe and results in rapid achievement of anti-coagulation.

Small studies have found similar outcomes in patients having PCI when treated with enoxaparin or UFH (Circulation 2001;103:658). However, most studies were performed in patients who were anti-coagulated for a number of days prior to PCI. Therefore, given the timing of PCI in our patient population, it is important that the 30 mg IV loading dose be given to all patients. Dosing should remain q 12 hours based on the time of the initial dose for at least the first 4 doses or until after cath (ie, if the first dose is at 3 pm, the next one should be scheduled for 3 am, not 10 pm). A recent large trial SYNERGY (JAMA 2004) found that outcomes were non-significantly better in high risk ACS patients (2 of 3 of positive markers, age > 60, and ST depression) treated with enoxaparin. Patients who were randomized to switch from one anti-thrombotic to the other had a significant increase in bleeding. However, in the subgroup of patients (which made up 60% of the patients) who did not switch over to the opposite anti-thrombotic, enoxaparin was significantly better than UFH. This trial concluded that consistent therapy with enoxaparin is superior to UFH, but that switching from one drug to the other resulted in increased bleeding.

Enoxaparin is excreted through the kidneys, so enoxaparin should be avoided in patients with severe renal failure (Cr>2 mg/dL or CrCl<50 ml). It should be recognized that all Enoxaparin trials to date have excluded patients with Cr>2 mg/dL. In patients with renal insufficiency who are being treated with enoxaparin, anti-Xa activity should be monitored to make sure patients are not over anti-coagulated. Target values are anti-Xa activity of 0.5 to 1.2 (peak value, determined 4 hours after dose). Levels > 1.2 have been associated with increased bleeding risk without improved outcomes (J Am Coll Cardiol 1997;29:1474). For peak Anti-Xa values > 1.2, enoxaparin dose should decreased and rechecked 3 to 4 doses later.

Although there is no upper weight limit, pts >150 kg will require 2 injections, and UFH may be a better choice. For patients with excessive weights who are receiving prolonged treatment (ie, > 2-3 days) it may be useful to check an anti-Xa level. This is available M-F, if the test gets to the lab prior to 2 pm (it is not a send out lab), with results available that afternoon.

Unless specifically indicated, enoxaparin and UFH should be stopped after cath. One exception is the patient who has multivessel disease who is awaiting CABG. In that case, the patient should be restarted on UFH rather than

enoxaparin, as patients undergoing CABG who received Enoxaparin within 12-14 hours of surgery had a higher bleeding rate (Circulation 2002;106),

The effects of Enoxaparin are only partially reversed by protamine. An important advantage of enoxaparin compared to UFH is the lower rate of Heparin induced thrombocytopenia, so that for patients undergoing prolonged anti-coagulation, enoxparin may be preferred (in the absence of renal failure).

Diagnosis of HIT can be facilitated using the following criteria:

The "4 T's" Point System for Patients with Suspected HIT

Category	2 Points	1 Point	0 Points
Thrombocytopenia	>50% fall, or nadir of 20 to 100x10 9/L	30% to 50% fall, or nadir of 10 to 19x10 9L	<30% fall or nadir < 10x10 9L
Timing of Platelet Count Fall	Days 5 to 10 or ≤1 day if heparin exposure within past 30 days	>Day 10 or unclear (but fits with HIT), or ≤ 1 day if heparin exposure within past 30 to 100 days	≤ 1 day (no recent heparin)
Thrombosis or other Sequelae	Proven Thrombosis, skin necrosis or, after heparin bolus, acute Systemic reaction	Progressive, recurrent, or silent thrombosis, erythematous skin lesions	None
Other cause for Thrombocytopenia	None evident	Possible	Definite

*Points assigned in each of 4 categories are totaled, and the pretest probability of HIT by total points is as follow: 6 to 8 = high, 4 to 5 = intermediate; 0 to 3 = low. Adapted from Warkentin et al J Thromb Haemost. 2006 Apr;4(4):759-65.

For patients with presumed HIT, or with a prior history of HIT, there are three currently available treatment options. These include Argatroban, Bivalirudin (angiomax), and lepirudin (see Table below). Although all have been shown to be effective for treatment patients with HIT, the choice of a particular agent should be based on patient characteristics and treatment plan.
Dosing should be based on guidelines provided in the handout provided by pharmacy. Because these drugs are used infrequently, it is important to review the specific indications and treatment algorithms to prevent inadvertent dosing errors. Questions should be immediately referred to pharmacy or to the fellow/attending.

Prior diagnosis of HIT, now with presumed ACS (unstable angina or possible MI)
drug of choice--**bivalirudin**
There is substantial data on proper dosing and treatment of patients undergoing PCI or CABG being treated concurrently with bivalirudin. The primary contraindication is significant renal failure (CrCl < 30 ml/min).

Alternative agent--**lepirudin**
The best evidence for a heparin alternative in patients with true HIT is with lepirudin, unless there is significant renal failure (CrCl <30 ml/min).

Either of the above with severe renal failure (CrCl < 30 ml/min)
Drug of choice–**argatroban**
In contrast to the above agents, argatroban is metabolized primarily by the liver, so it is minimally affected by renal failure

Direct Thrombin Inhibitor	Plasma Half-Life	Clearance Mechanism	Dosage Bolus	Dosage Infusion	Dose adjustment in Renal Failure
Lepirudin	60 min	Renal	0.4 mg/kg	0.15 mg/kg/hr	Yes
Bivalirudin	20-30 min	80% plasma, 20% renal	0.15 mg/kg bolus	0.6 mg/kg/hr	Yes
Argatroban	39-51 min	Hepatic		2 ug/kg/min	No

Suggested dosing recommendations for each of the agents

Contrast Related Renal Failure
A number of scoring systems have been developed to predict contrast related acute renal failure. The most important predictors, which have been found in numerous studies, include age, baseline renal failure, diabetes, CHF, hypotension and dehydration. The contrast dose is also an important predictor, but is unlikely to be known prior to angiography. A number of methods have been shown in some (but not all) studies to reduce this risk. Prophylactic treatment should be considered in patients with Cr> 1.5 mg/dl or CrCl < 60 ml/min, and all diabetics

Pre-hydration—1/2 NS or NS, at least 1 ml/kg/hr for 12 hours prior to the procedure

N acetylcysteine—A number of different doses have been used: 600 mg bid for 4 doses,2 before and 2 after angiography is the one most commonly used here.

IV N acetylcysteine A recent randomized clinical trial demonstrated that 1200mg of IV Mucomist given every 12 hours for 4 doses was associated with a significant reduction in acute renal failure. STEMI patients are likely at increased risk for developing acute renal failure because of unknown renal status, inability to hydrate prior to the procedure, likely significant LV dysfunction as well as reduced cardiac output and shockincluding patients who had normal renal function and normal LV function. . Because the drug requires filtering, it is currently available in the cath lab and will be given to STEMI patients acutely. Giving the initial 2 doses IV, and then changing to po if it is determined the patient is low risk for acute renal failure (normal renal function, small dose of contrast, non-diabetic), given the increased cost of the IV preparation.

Coumadin— Often patients are admitted who have an increased INR. The following are recommendations on how to treat, in the presence or absence of bleeding. Treatment with Vitamin K should be either IV or PO, as SC injections has variable absorbsion, and is inferior to po.

Condition	Description
INR > 5.0 but < 9.0; no significant bleeding	Hold next 1-2 doses, monitor more frequently and resume at lower dose when INR therapeutic. Alternatively, give vitamin K (< 5 mg orally), particularly if increased bleeding risk. For more rapid reversal vitamin K (2 to 4 mg po) can reduce INR w/in 24 h. If INR still high, more vitamin K (1 to 2 mg po) can be given
INR > 9.0; no significant bleeding	Hold warfarin therapy and give vitamin K (5-10 mg po); INR will decrease in 24-48 h.
Serious Bleeding at any elevation of INR	Give vitamin K (10 mg by slow IV infusion), with fresh plasma or prothrombin complex concentrate, if necessary; recombinant factor VIIa can be given as alternative to prothrombin complex concentrate; vitamin K1 can be repeated every 12 h
Life-threatening bleeding	Give protrombin complex concentrate and vitamin K1 (10 mg by slow IV infusion); recombinant factor VIIa can be given as alternative; repeat if necessary, depending on INR

Common Pressors and Inotropic agents used in the ICU

Dobutamine—positive inotrope with mild vasodilator action. At low doses, may see mild improvement in contractility, which usually requires at least 5 ug/kg/min. At higher doses, heart rate increases as well. Has minimal immediate effects on wedge pressure. Does not require a central line.
Uses: cardiogenic shock, low output heart failure
Main side effects—increased heart rate, ventricular arrhythmias.
Half life—approx 5 minutes.
Contraindications—severe tachycardia, ventricular arrhythmias

Milrinone—vasodilator with mild inotropic effects. Can be considered a mix of dobutamine and nitroprusside. After IV bolus, pulmonary artery and wedge pressure decrease by about 20-25% within 15 minutes. Does not require a central line.
Uses: low output heart failure with elevated filling pressures
Main side effects: hypotension, ventricular arrhythmias
Half life—approx 2 hours
Contraindications: hypotension, significant renal failure

Norepinephrine and Dopamine—primarily vasopressors with inotropic effects as well. Dopamine has vasodilator at low doses (<5 ug/kg/min). Both require central venous access

Norepinephrine is likely the best initial choice, as it may have reduced tachycardia and arrhythmias, and has best clinical data behind it
Uses: hypotensive shock
Main side effects: tachycardia, ventricular arrhythmias, severe peripheral vasoconstriction
Half life: 5 minutes

Neosenephrine—pure alpha blocker without beta receptor properties. Requires a central line
Main use: shock with significant tachycardia
Contraindication: severely reduced EF or cardiac output—the severe peripheral vasoconstriction may worsen cardiac output significantly. **IT SHOULD ONLY RARELY BE USED IN PATIENTS WITH LOW EF OR LOW CARDIAC OUTPUT**. Can result in significantly reduced tissue perfusion.

Drug	Actions	Central Access required	Main Use	Main contra-indication
Dobutamine	Inotrope, mild vasodilator	No	Cardiogenic shock, low cardiac output	Severe tachycardia, ventricular arrhythmias
Milrinone	Vasodilator>> Inotrope	No	Severe CHF, low output failure	Renal Failure, low BP, ventricular arrhythmias
Dopamine	Inotrope, Vasoconstrictor	Yes	Hypotensive shock	Severe Tachycardia
Norepinephrine	Inotrope, Vasoconstrictor	Yes	Hypotensive shock	Severe Tachycardia
Neosenephrine	Pure alpha constrictor	Yes	Hypotensive septic shock, especially with severe tachycardia	Low cardiac output Low EF

Hypertensive Crisis Treatment

First rule is to determine if it is a hypertensive emergency (evidence of end-organ damage—CHF, CP,acute renal failure papilledema [yes, this diagnosis does require an opthalmascope]). About half of cases are related to non-compliance; in these cases, restarting po meds is a good idea.

Standard IV Medications Used

Labetolol—alpha and beta effects. Can be given IV (push and infusion) and PO. Should not be used in patients with significant LV dysfunction, CHF, bradycardia, or bronchospasm
Nitroprusside—pure vasodilator. Can cause reflex tachycardia. Thiocynate levels build up in patients with renal failure, levels should be checked q 24 hr (normal renal function) to q 12 hr (renal failure).
Nicardipine—useful in patients in whom Labetolol or Nipride are not desirable. Can cause reflex tachycardia, and levels can accumulate in renal failure.
Nitroglycerin—used in pts with pulmonary edema or chest pain/ischemia. May minimal BP effects in the absence of these conditions, and should not be used as a primary treatment for most pts with hypertensive emergency

Anti-Thrombotic Therapy

Heparin (for converting from LMWH to UFH or UFH to LMWH, page 2)

Enoxaparin

Contra-indications: renal failure (Cr > 2.0 mg/dL, CrCl < 50 ml/min)

Dose: 30 mg IV push, followed by 1 mg/kg SC. Dose should be repeated every 12 hours until coronary angiography is performed or for the first 48 hours (i.e., if the initial dose is given at 3 pm, the next doses should be given at 3 am).

Monitoring: There is no need to check PTTs, as it is relatively unaffected by enoxaparin

Special Considerations

In most cases there is no need to hold Enoxaparin in patients going to the cath lab. If it is stopped, consideration should be given to starting UFH.

Do not stop anti-coagulation in a patient going to the cath lab without discussing it with the fellow or attending.

Anti-coagulation should be stopped after PCI to reduce bleeding complications, unless specifically specified in Green sheet or cath lab. If there is a question, ask the fellow or attending

Timing

For the first 3-4 doses, do not change the time schedule (ie., if started at 5 pm, it should be ordered daily at 5 pm and 5 am).

Monitoring

Prolonged treatment in patients with mild renal insufficiency (creatinine 2 to 3.9 mg/dL or CrCl 30-60 mL) (for patients having bridge therapy to wafarin; in patients who are going to have a cath, would not use enoxaparin if Cr is > 2 mg/dL or CrCl<50 ml/min.)

Check anti-Xa activity 4 hours after the 3rd of 4th dose (this way the sample will be run that day)

Anti-Xa activity = 1.2 to 1.49, decrease enoxaparin dose by 20%,recheck after 3-4 doses

Anti-Xa activity $\geq$ 1.5, decrease enoxaparin dose by 30% and recheck after 3-4 doses.

Anti-Xa activity < 0.8 to 1.2, recheck at 5-7 days (if on continued therapy)

to estmiate CrCl (Cockcroft Gault) {(140-age)*(wt in kg}/(Serum Cr)*72}
For women, multiply by 0.85

Patient going for CABG

Stop enoxaparin once it is decided that the patient is going to have CABG, and change to UFH, starting with IV infusion (no bolus) 12 U/kg/hour 8 hours after last enoxaparin dose.

UFH

Indications: Known severe renal disease, on a IABP, awaiting CABG, or taking coumadin

Dose: 60 U/kg IV load (maximum 4000 U), followed by UFH infusion, 12 U/kg/hr (maximum 1000 U/hr

For patients taking coumadin, initiate infusion and adjust bolus based on PTT and INR

Monitoring: Check PTT at 6 hours, adjust per ACS Nomogram

Anti-Platelet Therapy

Aspirin

Indications: all ACS patients

Dose: Initial: 324 mg load with chewable ASA, then 81 mg/day

Chronic therapy doses 81-325 mg. Higher doses are associated with increased bleeding when used in combination with clopidogrel.

use 325 mg in patients with recent stent placement

Clopidogrel

Indications: Patients who have a true aspirin allergy

High risk ACS: (ST depression > 1mm, Deep T wave inversion not related to LVH, and positive markers)

Patients who are going to the cath lab for likely PCI

Dose: 300 mg po; 600 mg for STEMI patients not recieving prasugrel

Special Considerations:

Stop immediately if bypass surgery required.

Avoid in patients who have increased risk for bleeding (heme positive stools, platelet count < 100K, anemia, chronic coumadin use), multiorgan failure

Advantage in pre-treating patients prior to PCI if given > 12-15 hours before.

Glycoprotein IIb/IIIa Inhibitors

Indications: High risk ACS (ST depression or positive markers (not isolated T wave inversion)).

Special Considerations:

Initiate after discussion with CCU fellow or attending, as the choice of agent will be dependent on patient characteristics and timing of when the patient goes to the cath lab.

Stop 6-8 hours prior to going for bypass surgery.

Choices are:

Abciximab (Reopro) for patients going urgently to the cath lab. Not contraindicated in renal failure
Dose: 0.25 mg/kg bolus followed by 0.125 ug/kg/min (max 10 ug/min) for twelve hours post PCI
Monitoring: Platelet count should be checked at 2-4 hours and 12 hours after infusion initiation. Stop infusion for platelet count<100,000 or 25% decrease from baseline (check with fellow prior to stopping).

Eptifibatide, for all other patients. Relatively contraindicated if Cr> 2 mg/dL or CrCl<50 ml/min (would only give for the highest risk patients, and after discussing with attending as well as fellow) and contraindicated if Cr> 3 mg/dL (CrCl<30 ml/min)
Dose: 180 ug/kg bolus followed by 2 ug/kg/min infusion
Monitoring: check platelet count next am.

Guidelines for Changing Between UFH and Enoxaparin

Switching from UFH to LMWH

Stop UFH

Enoxaparin, 1 mg/kg SC immediately (no 30 mg IV bolus given)

Switching from LMWH to UFH

Hold am dose of enoxaparin

Start UFH, 12 U/kg/hr (1000 U max) without the bolus 8 hours after the last dose of enoxaparin.

Remaining on Enoxaparin

Sheaths can be removed 6-8 hours after the last SC dose of enoxaparin.

If IV enoxaparin given during PCI, sheaths can be pulled 4-6 hours after IV dose.

During PCI:

last dose of enoxaparin < 8hours:	no additional heparin given
last dose of enoxaparin 8-12 hours:	Enoxaparin, 0.3 mg/kg IV (consider increasing to 0.5 mg/kg IV if no GP IIb/IIIa given)
last dose of enoxaparin > 12 hours:	UFH, to ACT targeted to 150-200 sec