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The Clinical Challenge of Heart Failure: Comprehensive, Evidence-Based Management of the Hospitalized Patient With Acute Myocardial Decompensation

Part II: Outcome-Effective Treatment and Prophylaxis Against Venous Thromboembolic Disease (VTED)

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The approach to managing heart failure (HF) is multi-factorial, and includes hemodynamic support; close monitoring of vital signs, metabolic status, and cardiac rhythm; and administration of pharmacologic agents belonging to a number of therapeutic classes. Historically, the pharmacotherapeutic approach to HF has focused on a number of agents—both oral and intravenous—with the capacity to decrease intravascular volume, reduce afterload, and/or improve left ventricular (LV) function.

To achieve both hemodynamic and symptomatic goals in a broad group of patients, ranging from those with decompensated HF to individuals with pulmonary edema and cardiogenic shock (CS), a number of so-called workhorse agents for managing HF have been pressed into service in the emergency department (ED) setting. They include diuretics, oxygen, morphine, nitroglycerin (NTG), nitroprusside, angiotensin-converting enzyme inhibitors (ACEIs), digoxin, vasodilators, beta-blockers (β-blockers), angiotensin receptor blockers (ARBs), and inotropic agents.

Recently, the therapeutic options for managing HF have expanded to include such newer agents as nesiritide, a recombinant DNA manufactured form of endogenously synthesized b-type natriuretic polypeptide. In addition to managing deteriorations in cardiac function and ejection fraction, clinicians are focusing on the need to prevent VTED, in particular, deep venous thromboembolism (DVT) and pulmonary embolism (PE), as part of the overall management approach to hospitalized patients.

Part II of this two-part series outlines a systematic approach to managing patients with HF in the ED setting. Initial stabilization approaches are outlined in detail, and a systematic approach to pharmacologic therapy is highlighted. The benefits, risks, and indications for newer therapeutic options are discussed in detail, with a focus on improving clinical outcomes and reducing length of hospital stay.

—The Editor

Initial Stabilization Measures

Stabilization measures aimed at maintaining airway control and ensuring adequate ventilation should take precedence during the initial phase of patient management. Clearly, any patient with signs or symptoms of heart failure (HF) is a candidate for supplemental oxygen, which

should be administered promptly on an empiric basis. Patients who appear to be in impending respiratory failure, who are unable to oxygenate, are ventilating poorly, or cannot protect their airways should be evaluated promptly for eligibility regarding endotracheal or nasotracheal intubation.

As emphasized, oxygen administration may improve clinical status and should be considered for all patients with suspected decompensated HF. Therapy may be guided by the results of pulse oximetry. Supplemental oxygen also can accelerate relief of dyspnea and frequently relieves the anxiety of hypoxia. Because hypoxia presents a more immediate risk than hypercarbia, oxygen should not be withheld due to concerns about carbon dioxide retention. When carbon dioxide retention is likely to complicate management (i.e., patients with chronic obstructive pulmonary disease [COPD]), arterial blood gas analysis is helpful for guiding subsequent therapy, including the need for intubation in patients with acute carbon dioxide retention. Selecting an appropriate oxygen delivery device is based on patient needs. Patients with minimal dyspnea may be able to oxygenate adequately with a nasal cannula, whereas patients with CS and/or extreme respiratory distress may require endotracheal intubation.

Non-invasive positive pressure ventilation (NPPV) can be a temporizing measure in properly selected patients. Bilevel positive airway pressure (BiPAP) and continuous positive airway pressure (CPAP) are the most commonly used modalities. BiPAP involves delivery of separately controlled inspiratory and expiratory pressures via face mask, while CPAP delivers constant pressure throughout the respiratory cycle. To be eligible for a trial of NPPV, patients must be monitored closely and hemodynamically stable and mentally appropriate. In addition, they must be able to protect their airway and clear secretions.

NPPV has been studied most extensively in patients with COPD exacerbation. In this setting, NPPV may offer a mortality benefit over invasive mechanical ventilation. The data is controversial in acute cardiogenic pulmonary edema. The use of NPPV may result in decreased rates of endotracheal intubation; however, mortality appears to be unchanged. In addition, one study showed that patients treated with CPAP had higher rates of myocardial infarction (MI) than patients treated with BiPAP.[1] Consequently, there is no consensus regarding the precise role of NPPV in patients with acute pulmonary edema (APE).

Intravenous (IV) access is mandatory for all HF patients. Significant electrolyte abnormalities can occur as the result of aggressive diuretic therapy. Since HF patients are at risk for ventricular arrhythmia, prompt treatment may be required. Delaying therapy to attempt vascular access may have adverse consequences.

The initial approach to the patient with HF requires simultaneous assessment of vital signs, cardiovascular laboratory parameters, radiographic studies, and overall evaluation of the patient's clinical status. Initial treatment decisions are based on the acuity of presentation, determination of volume status, and systemic perfusion. Although most patients presenting to the ED are symptomatic, patients who present with minimal symptoms may undergo an initial period of evaluation before treatment is initiated. Typically, initial evaluation should include the following steps:

1. Evaluation of airway, degree of respiratory distress, and need for mechanical ventilation;
2. Assessment of circulation by blood pressure (BP), mentation, pulses, and skin temperature;
3. Expeditious physical exam and history with attention to cardiopulmonary systems;
4. Evaluation of oxygenation and ventilation by pulse oximetry and arterial blood gas (ABG), if indicated;
5. Assessment of cardiac rhythm by monitoring, and evaluation for ischemia by 12-lead electrocardiogram (ECG);
6. Chest x-ray—portable if necessary;

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Table 1. Initial Therapy for Acute Pulmonary Edema (APE)

1. Sit the patient upright with legs dependent (to reduce venous filling), if possible.
2. Administer 100% oxygen.
3. Administer nitrates if systolic BP > 100.
   - Sublingual nitroglycerin 0.4 mg q 1-5 minutes (monitor BP closely)
   - IV nitroglycerine or nitroprusside if needed.
4. Administer IV furosemide (or ethacrynic acid if sulfa allergy)
5. Administer IV morphine 2-6 mg (if no respiratory acidosis/depression)
6. Cardioversion to restore sinus rhythm

7. Blood drawn for complete blood cell count (CBC), electrolytes, B-natriuretic peptide level (BNPL), cardiac enzymes, and possibly digoxin levels (especially with worsening renal function or drug interaction); and

8. Placement of a urinary catheter to monitor fluid output in seriously ill and unstable patients;

Management Strategies for Specific Categories and Patient Risk Groups with Heart Failure

Cardiogenic Shock. CS requires immediate intervention, which will be concurrent with the clinical challenge of gathering historical, physical, and diagnostic data. Although unavailable in the ED, Swan-Ganz catheterization may be necessary to guide therapy and confirm myocardial dysfunction as the cause of shock. Urgent cardiology consultation is mandatory and will facilitate prompt echocardiographic and, when necessary, invasive evaluation of myocardial function. Bioimpedance monitoring also may be a useful adjunct. Because approximately 20% of patients with CS develop hypotension without pulmonary congestion, a small fluid challenge (100-250 ccs NS) may be appropriate. If pulmonary congestion is present, this intervention should be omitted. Almost all patients will require intubation and sedation to protect the airway and decrease oxygen demand associated with increased work of breathing. Therapy with agents that may lower BP (ACEIs, diuretics, nitrates, and β-blockers) should be withheld.

If there is no improvement in systemic perfusion after fluid challenge, and in the setting of hypotension with pulmonary congestion, inotropic agents should be considered. In particular, inotropic therapy will be required if there is no improvement in tissue perfusion after fluid bolus. These agents may stabilize the patient and preserve perfusion while other interventions aimed at restoring cardiac function (e.g., PTCA, intra-aortic balloon pump [IABP], CABG) are being considered and/or mobilized. Agents with pure inotropic activity, or inotropic and vasodilator properties (i.e., milrinone, dobutamine), are inadequate in the setting of shock. Optimal therapy requires agents with both vasopressor and inotropic activity (e.g., dopamine). However, combination therapy with a vasopressor (i.e., dopamine) and a pure inotrope (i.e., dobutamine) may be more effective than use of either agent alone.[2]

Patients with CS may require prompt revascularization by either percutaneous procedures or emergency CABG. The placement of an intra-aortic balloon pump can serve as a bridge until such therapies are available. In the case of acute MI complicated by a right ventricular (RV) infarction, hypotension is treated with vigorous IV fluids. However, cardiac output will not increase if fluid therapy causes RV distension (causing compromise of the LV cavity) or produces an unacceptably high increase in pulmonary capillary wedge pressure (PCWP). Dobutamine and/or therapy with IABP is the next line of therapy in such patients. Finally, because hypotension may result from preload reduction, the clinician should be cautious with medications that produce this hemodynamic effect (e.g., NTG, loop diuretics, etc.).

Acute Pulmonary Edema. The failing heart is sensitive to increases in afterload. In some HF patients, when systolic BP is elevated to the 150 mmHg systolic range, pulmonary edema will ensue. Prompt BP reduction often will break the downward spiral of pulmonary edema and avoid the need for intubation. Although diuretic therapy is important, it is critical to lower BP and cardiac filling pressures. These authors recommend that initial therapy consist of repeat doses of sublingual (SL) NTG, provided there is adequate BP. In APE, NTG is placed sublingually, at the rate of one per minute (each tab is 0.4 mg) until IV NTG can be started. Following this maneuver, IV NTG then is titrated rapidly upward until BP is controlled. If pressures remain elevated, or clinical improvement is not achieved, conversion to IV nitroprusside may be required.

IV furosemide or bumetanide are the preferred diuretics in the setting of APE. Ethacrynic acid is useful if the patient has a serious sulfa allergy. These agents are characterized by quick onset; diuresis can be expected 10-15 minutes after the use of IV furosemide. If urine output is inadequate after 20-30 minutes, the diuretic dose should be increased and repeated. Diuretics also may have an early effect as weak venodilators. IV morphine may be helpful to venodilate and to decrease respiratory distress and circulating catecholamine levels. *(See Table 1.)*

When hypertrophic obstructive cardiomyopathy (HOCM) occurs concurrently with APE, special attention is required. These patients have dynamic outflow obstruction that is exacerbated by increases in cardiac contractility or heart rate. Conditions of decreased preload or afterload also can worsen the obstructive gradient. Consequently, ideal therapy for HOCM in the setting of APE will decrease the outflow gradient by slowing the heart rate and myocardial contractility. This can be accomplished with IV β-blockers, a pharmacotherapeutic intervention best left to the cardiologist in the intensive care unit/critical care unit (ICU/CCU) environment. If shock is present, the pressor of choice is phenylephrine. Phenylephrine vasoconstricts the peripheral vascular tree without increasing cardiac contractility.

Decompensated HF. Patients in this group have stable vital signs, adequate oxygenation and ventilation, and organ function at or near baseline. The majority will require diuresis with an IV loop diuretic, supplemental oxygen, education about low-salt diet, and therapy aimed at lowering BP to acceptable levels. Some patients can be followed in a clinical

Table 2. Contraindications to Angiotensin-Converting Enzyme Inhibitors (ACEIs)

- Angioedema
- Progressive azotemia (> 3 mg/dL, especially if progressively increasing)
- Bilateral renal artery stenosis
- Systemic hypotension (systolic blood pressure < 80, especially in ambulatory patients)
- Hyperkalemia
- Pregnancy
- Hemodynamic instability
- Intolerance secondary to **severe** cough

Table 3. ACEIs/ARBs for Chronic Systolic Heart Failure Agents*

DRUG	START	TARGET DOSE	TRIAL DATA
CAPTOPRIL			
	6.25 mg tid	50 mg tid	SAVE
LISINOPRIL			
	2.5 mg qd	40 mg qd	ATLAS
ENALAPRIL			
	5 mg qd	20 mg qd	SOLVD
RAMIPRIL			
	2.5 mg qd	10 mg bid	AIRE
LOSARTAN			
	50 mg qd	50 mg bid	ELITE
VALSARTAN			
	40 mg bid	160 mg bid	Val-HeFT

* Dosing data from major clinical trials

decision unit, while others will require admission to the hospital or ICU.

Multiple large-scale clinical trials have provided clinicians with an evidence-based approach to managing stable, systolic dysfunction HF. The principal drugs from which the clinician should choose include β-blockers, ACEIs, angiotensin-receptor blockers (ARBs), hydralazine/nitrates, diuretics, digoxin, and spironolactone. In general, the hemodynamic management of chronic systolic HF focuses on maintaining the lowest possible BP to allow mentation, ambulation, and urination.[3]

One common misunderstanding about the management of HF pertains to the timing for initiating individual therapeutic agents. HF patients with clinically stable disease and mild symptoms may benefit most from the addition of a new drug to their medical regimen. All HF patients without contraindications should be on an ACEI and a β-blocker, even in the setting of stable disease and minimal symptoms. The neurohormonal antagonism requirements of HF therapy are different from other disease states, where the impetus to expand therapy is driven primarily by continuing symptoms.

Pump Failure Without Signs of Shock. If systemic congestion persists despite nitroprusside therapy and IV diuretics, IV inotropes may be required. Although several agents are available for treatment of acute HF, each drug has unique properties, hemodynamic effects, and potential side effects. The emergency physician should be familiar with the use of dobutamine and milrinone, although the ICU environment, where invasive monitoring is possible, is the optimal setting for monitoring such therapy. Typically, however, dopamine is reserved for patients with signs of shock.

Pharmacotherapeutic Strategies and Specific Agents for HF

Therapeutic options for HF have evolved dramatically during the past decade. Interestingly, some unexpected approaches have characterized some of these new clinical paradigms. For example, the place of β-blockers in the therapeutic arsenal has evolved from one of absolute contraindication to that of a central role as cornerstone agents. The use of ACEIs and powerful loop diuretics such as furosemide has decreased the morbidity of this debilitating disease, while ACEIs have decreased mortality rates as well. Many patients with HF now can enjoy a longer life, relatively free from daily congestive symptoms previously attributed to this syndrome.

ACE-Inhibitors. Vasodilators, which are used to "unload" the heart and improve pump function, have been studied extensively. However, it is clear that all vasodilators used in HF are not created equal. While powerful agents (e.g., amlodipine, flolan) have failed to benefit patients with HF, less potent vasodilators such as ACEIs have altered the natural history of this condition.

Put simply, ACEIs are the cornerstone of pharmacological therapy for HF. In the absence of contraindications, all patients with HF should be treated with an ACEI. There also is strong evidence that patients with asymptomatic LV dysfunction derive benefit from ACEIs.[4] In placebo-controlled studies, ACEIs have been shown to decrease the overall mortality rate and combined end-point of death or hospitalization in HF.[5] For example, use of enalapril leads to a 31% decrease in one-year mortality in class IV patients and a 16% mortality reduction in class II and III patients.[6] ACEIs appear to be superior to both ARBs and the combination of hydralazine and isosorbide.[7-9]

It should be stressed that the salutary effects of ACEIs on HF are not explained fully by their vasodilating properties. These agents exert clinical effects primarily by suppressing levels of angiotensin II and augmenting levels of endothelium-protective bradykinins. The long-term effects of ACE-inhibition include prevention of ventricular remodeling, a benefit that persists despite failure chronically to suppress angiotensin II levels. All patients with systolic HF should receive ACEIs, except those who meet exclusionary criteria summarized in Table 2.

ACEI-induced angioedema occurs as a result of increased bradykinin production precipitated by ACE-inhibition. Treatment in the ED is similar to that of routine angioedema, and includes permanent cessation of ACEI use. The presence of cough during ACEI therapy should prompt a search for other causes (pulmonary congestion, infection, bronchospasm) before these symptoms are ascribed to drug-related side effects. If no other cause for cough is identified, then cessation of ACEIs should be con-

Table 4. Contraindications to Beta-Blockers

- Unstable hemodynamics, or congested and requiring IV diuresis (most ED patients)
- Severe bronchospastic airway disease
- Symptomatic bradycardia
- Advanced heart block
- Acute vascular insufficiency or worsening claudication/rest pain
- Class IV stable HF (therapy should be provided by HF specialist)
- Inotropic therapy/cardiogenic shock
- Severe conduction system disease (unless protected by a pacemaker)

Table 5. Beta-Blockers for Chronic Systolic Heart Failure*

DRUG	STARTING DOSE	TARGET DOSE	TRIAL DATA
Metoprolol xl/cr	12.5 mg qd	100 mg qd	MERIT-HF
Carvedilol	3.125 mg bid	25-50 mg bid	US-TRIALS COPERNICUS
Bisoprolol	1.25 mg qd	10 mg qd	CIBIS II

* Dosing data from major clinical trials

sidered, and if the symptoms are drug-related, they will disappear within 1-2 weeks. If the cough is not severe, patients should be educated about the significant benefits of these drugs and encouraged to continue therapy. In patients who are unable to take ACEIs, ARBs or a combination of hydralazine and isosorbide dinitrate, with or without spironolactone, should be considered strongly.

Diuretics. Diuresis may sensitize patients to the hypotensive effect of ACEIs, and therefore, ACEI therapy should be delayed during aggressive diuresis. Hyponatremia may be a sign of heightened renin-angiotensin-aldosterone system (RAAS) activation, and may predict ACEI-induced hypotension. In the absence of postural symptoms, hypotension is relatively well-tolerated. In patients who experience symptomatic hypotension with the first doses of ACEI, diuretic doses can be decreased and the ACEI continued. Additionally, the use of diuretics activates the RAAS, and concurrent use of ACEIs helps to blunt this effect. The development of mild azotemia during ACEI therapy should be tolerated as long as the patient does not have bilateral renal artery stenosis, oliguria, acute renal failure from other causes, or serum creatinine greater than 3 mg/dL.

Potassium balance and renal function should be followed carefully in patients who are started on ACEIs. In general, low doses should be started and titrated up to the same doses used in major trials. However, recent data suggest that even lower doses of ACEIs are effective in reducing mortality.[10] These agents work by inhibiting neurohormonal pathways and, therefore, may take weeks to months to exert symptomatic benefit. Even in the absence of symptomatic improvement, ACEI therapy should be continued for the long-term effects on LV remodeling and overall mortality benefit. *(See Table 3 for dosing guidelines.)*

Angiotensin Receptor Blockers. ARBs were developed to directly inhibit the adverse effects of angiotensin II. These agents also were developed with the hope that they would have fewer effects on bradykinin metabolism and produce a lower incidence of side effects than ACEIs. The therapeutic effects of ARBs are due to blockade of the angiotensin receptor subtype AT1. Stimulation of the AT1 receptor by angiotensin II promotes aldosterone release, LV remodeling (including apoptosis), arterial vasoconstriction, and renal damage.[11] Because inhibition of these effects is associated with vasodilation, ARBs are effective and are among the most well-tolerated agents for treatment of hypertension. In addition, they are more effective than β-blockers (such as atenolol) at reducing LVH.[12] ARBs also may decrease proteinuria and have a renoprotective effect in patients with diabetes.[13] Cough and angioedema are reported less frequently with ARBs than with ACEIs.

Some authors have suggested that ACEIs may be superior to ARBs for reducing cardiac mortality due to their ability to inhibit bradykinin breakdown. Bradykinins are presumed to have a vascular protective and vasodilatory effect. Whether theory translates into clinical effect has been the subject of intensive recent study. It is notable that there are currently no prospective, randomized, placebo-controlled trials that have studied whether ARBs are associated with a mortality benefit compared to placebo in patients with HF.[14] Clearly, more data is needed before ARBs are recommended for the treatment of HF in patients who are otherwise tolerant to ACEIs.

Beta-blockers. Once contraindicated in HF, β-blockers currently are advocated for management of patients with HF because of studies suggesting impressive mortality reduction data, as well as evidence for symptomatic relief that is comparable to, and in some cases eclipses, benefits observed with some ACEIs. One study found metoprolol led to a 34% reduction in one-year overall mortality for class II-III HF patients.[15] In addition, there was a 41% decrease in sudden death compared to placebo. Other large-scale trials evaluating β-blockers have yielded similar results. Benefit has been shown for patients with NYHA class II, III, and IV HF.[16] Norepinephrine levels are elevated in HF and contribute to myocardial hypertrophy, increased afterload, and coronary constriction. β-blockers are thought to exert their clinical effect via reductions in sympathetic nervous system activity. All of the major studies evaluating β-blockers in HF have included patients who already were taking ACEIs.

Although carvedilol (a combined α- and β-blocker) improves mortality rates in class IV patients, the use of β-blockers in these patients is best left to an HF specialist. Because therapy can be initiated only in the absence of fluid overload, and preferably in patients with stable disease, it may be problematic for the emergency physician to have all the data required to initiate these drugs in the acute setting. As with ACEIs, patients should be started on β-blockers even if they are clinically stable. The benefits of β-blockers lie in their ability to prevent sudden death and

Table 6. Diuretics for Acute Heart Failure

AGENT	DOSING (IV)	EFFECT	SIDE EFFECTS
FUROSEMIDE			
	No prior use: 40 mg IVP **If prior use:** Double last 24-hour usage (max 180 mg) **If no effect by 20-30 min:** Re-double dose	• Diuresis starts within 15-20 min • Duration of action is 4-6 hrs	• Reduced K+ and Mg++; • Hyperuricemia; ototoxicity • Sulfa allergy; hypovolemia; • Pre-renal azotemia; • Myalgia
BUMETANIDE			
	1-3 mg 1 mg ~ 40 mg furosemide	• Diuresis starts within 10 min • Peak action at 60 min	Same as above
TORSEMIDE			
	10-20 mg	• Diuresis starts within 10 min • Duration of action is 6-8 hrs • Better oral bioavailability than furosemide	Same as above
ETHACRYNIC ACID			
	50 mg	Similar to furosemide	• Same as above • Non-sulfa agent • Increased ototoxicity
METOLAZONE			
	5-10 mg po 20-30 min before IV furosemide	Additive to loop diuretic	• Similar to furosemide except no ototoxicity • Has liver disease caution

improve overall mortality. Upon initiation of β-blockers, patients may complain of increased fatigue. However, since benefits occur even in the absence of subjective improvement, patients should be encouraged to continue their β-blocker regimen.

All patients with HF should be considered for β-blocker therapy, except in those situations listed in Table 4. Therapy begins with low doses, and patients should be monitored closely for signs of deterioration. Daily weights are important. If weight increases, the dose of diuretic can be increased, or therapy with the β-blocker may be decreased or deferred. Doses should be titrated upward to the levels used in most clinical trials. β-blockers can take months to provide symptom improvement. *(See Table 5 for dosage recommendations.)*

For patients who develop brochospasm and pulmonary symptoms, the clinician should be sure that congestion is not playing a role. Bradycardia can develop and should prompt dose reduction or withdrawal if it is symptomatic or of advanced degree (second or third degree). Other drugs that act on the conduction system (i.e., clonidine, calcium channel blockers, digoxin) may have to be discontinued to allow continuation of β-blocker therapy. Some patients may develop symptomatic hypotension on β-blockers, especially if they also are taking ACEIs. The clinician often can adjust the dosage of the ACEI or diuretic to ameliorate these symptoms. Additionally, dosing of the ACEI and β-blocker can be separated by a couple of hours. Agents with peripheral vasodilating effects (carvedilol) may have to be changed to agents without this effect (metoprolol) if hypotension is a problem.

The strategy for patients currently being treated with β-blockers who present with worsening HF symptoms should be considered on an individual basis. In the absence of tissue hypoperfusion or pulmonary edema, clinicians may consider continuation of β-blockers, although the dose may have to be reduced or diuretics may need to be increased. If β-blockers need to be withheld, they should be re-instituted at low doses as soon as the patient is hemodynamically stable and is back to his/her baseline weight.

The acutely decompensated patient who presents to the ED and already is receiving β-blocker therapy presents a difficult management problem. Termination of the β-blocker may cause clinical deterioration. However, higher doses of β-blockers may compromise tenuous hemodynamics. The optimal compromise may be a short course of an IV inotrope, such as milrinone, to provide hemodynamic support, while using other measures to stabilize hemodynamics (e.g., IV diuretics and vasodilators).

Digoxin. Recognized as beneficial for HF for more than 200 years, this foxglove alkaloid functions by inhibiting myocardial cellular membrane Na+/K+ ATPase. Digoxin generally is used for patients with HF and atrial fibrillation. However, β-blockers may be more effective than digoxin in controlling the ventricular response in patients with atrial fibrillation.[9] Digoxin also can be used to improve clinical symptoms when therapy with ACEIs and β-blockers is initiated. This may be helpful, as the clinical

effect of ACEIs and β-blockers may take some time to manifest. Digoxin also may be considered when therapy with ACEIs, β-blockers, and diuretics fails to control symptoms of HF.

In this regard, it should be emphasized that, although therapy with digitalis does not produce a mortality benefit, it may decrease symptoms and the incidence of hospitalization for symptoms associated with HF.[17] Digoxin should not be discontinued in patients who are not receiving other HF therapies, and levels should be monitored closely if there is concomitant renal insufficiency. Physicians should be aware of important drug interactions between digoxin and such other agents as amiodarone, spironolactone, verapamil, or macrolides. Electrolyte levels must be monitored periodically because derangements increase the risk of digitalis toxicity. Typically, digoxin is started at a dose of 0.125 mg per day. There is a trend toward using lower doses of digoxin, and the practice of using the highest tolerable dose no longer is recommended.[9] Elderly patients, as well as those with renal insufficiency, should be maintained at low doses and even considered for every-other-day dosing.

Digoxin toxicity may produce cardiac arrhythmia (e.g., heart block, ectopic, and re-entrant rhythms); gastrointestinal symptoms such as nausea or vomiting; and neurologic complaints, including visual disturbances (in only 10%), disorientation, and confusion. The arrythmogenic effect of digitalis toxicity is secondary to increased automaticity associated with cellular calcium overload in combination with AV conduction block. Typical arrythmias include paroxysmal atrial tachycardia with AV block and atrial fibrillation with slow ventricular response. Serum levels are helpful if they exceed 2 ng/mL**,** but toxicity can occur at lower levels, especially with hypokalemia or hypomagnesemia. Quinidine, verapamil, spironolactone, flecainide, propafenone, and amiodarone may increase digoxin levels; if one of these drugs is added to the regimen, the dose of digoxin should be decreased. For rate control of atrial fibrillation, doses in excess of 0.25 mg daily are not recommended.

Diuretics. Patients with systemic or pulmonary congestion should receive loop diuretics. Diuretics provide rapid symptomatic relief in HF. These agents also sensitize patients to the hemodynamic effects of ACEIs by decreasing intravascular volume. Note that diuretics are not indicated as monotherapy for HF.[18,19] No study has documented a mortality benefit of diuretics (except spironolactone). Once signs and symptoms of congestion have resolved, a fixed maintenance dose should be continued to prevent recurrence of symptoms and to preserve the new "dry" body weight.

Loop diuretics promote water and sodium excretion, and are efficacious, except in cases of severe renal dysfunction (creatinine clearance less than 5 mL/min). This compares to distal tubule diuretics (thiazides, metalozone, and potassium-sparing agents), which are less effective and lose activity with moderate renal dysfunction (creatinine clearance less than 30 mL/min).[18] Ethacrynic acid is the only loop diuretic that can be used in patients with sulfa allergy.

For dyspnea secondary to pulmonary congestion, furosemide is an inexpensive and efficacious loop diuretic. An equivalent dose equal to twice the patient's daily usage, up to a maximum of 180 mg, can be administered intravenously. If the patient previously has not been on a loop diuretic, 40 mg is an adequate initial dose. If bumetadine is used, 1 mg of bumetadine equals 40 mg furosemide.[20] Some patients require the addition of a thiazide diuretic, such as metalozone, to maintain effective diuresis. Metolazone can be given 20-30 minutes prior to furosemide. *(See Table 6.)* The physiological rationale for combined diuretic therapy—a loop and thiazide diuretic—may be explained by the action of these agents on different sites in the nephron.

Hypokalemia can be quite severe in patients undergoing aggressive diuresis, and therefore, HF patients should be monitored carefully and/or switched to a loop diuretic plus a potassium-sparing agent. Electrolytes should be monitored closely in any patient on IV diuretics (especially if the patient is also on digoxin). A widening QT interval may suggest hypocalcemia, hypokalemia, or hypomagnesemia. Loop diuretics rarely have been associated with hyperuricemia and the precipitation of gout. Ototoxicity is rare, but may be seen when diuretics are used in conjunction with aminoglycoside antibiotics.

Urinary response to diuretics should be monitored. In more symptomatic patients who are unresponsive to initial IV diuretics, the dose may be doubled and administered again in 30-60 minutes. In stable patients, if urine output is inadequate 2-3 hours after IV bolus furosemide, the physician should consider doubling and repeating the diuretic. If urinary output still is limited, hospitalization is necessary. Adequate urinary output should exceed 500 ccs within two hours, unless the creatinine exceeds 2.5 mg/dL; in that case, two-hour urine output goals are halved. *(See Table 6.)* Diuretic response correlates with prognosis. Patients with poor diuresis in the setting of APE have a four-fold increased acute mortality.[21] In a retrospective study, less than 1 liter of net fluid output was more common in HF patients who subsequently failed outpatient observation unit management.[22]

Outpatient diuretic use ideally is guided by daily measured body weight. Diuretic complications are common, and consist of electrolyte abnormalities, hypertension, azotemia, and neurohormonal activation. Resistance to diuretics occurs, but may be overcome by IV use or by combination of multiple diuretics.

All patients taking diuretics should limit their sodium intake to fewer than 3 g per day. In addition, they should be advised against taking agents that antagonize diuretic action, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2 (COX-2) inhibitors, especially rofecoxib.[9] Those with severe systemic congestion will require IV diuretics, as bowel wall edema can preclude proper absorption of oral agents. The diuretic dose should be titrated dependent on symptoms and stabilization of body weight. The duration of action of oral loop diuretics is approximately six hours.

Proper use of diuretics can relieve patients of congestive symptoms that would otherwise limit them from tolerating therapy with β-blockers. In this way, diuretics are key drugs in HF, as they pave the way for the efficacious and tolerant use of ACEIs and β-blockers. *(See Table 6 for a summary of diuretic characteristics.)*

Spironolactone. The RALES study demonstrated a significant mortality benefit with the aldosterone antagonist spironolactone in patients with class III and IV HF.[23] Because there was a 30%

Table 7. Vasodilators for Acute Heart Failure

AGENT	DOSING	TITRATION	SIDE EFFECTS
NITROGLYCERIN SUBLINGUAL			
	0.4 mg SL q 1-5 min	Blood pressure symptoms	• Hypotension • Headache
NITROGLYCERIN INTRAVENOUS			
	0.2-0.4 mcg/kg/min (starting dose)	Blood pressure symptoms	• Hypotension • Headache
NITROPRUSSIDE			
	0.1-0.2 mcg/kg/min (starting dose) 10 mcg/kg/min (maximum)	Blood pressure symptoms	• Hypotension • Possibility of coronary steal • Cyanide toxicity • Thiocyanate toxicity
NESIRITIDE			
	2 mcg/kg bolus then infusion of 0.01 mcg/kg/min	Titration usually unnecessary	• Hypotension

decrease in all-cause mortality, the trial was terminated early. Most patients were on ACEIs and a diuretic. Patients who also were taking β-blockers and digoxin had a significant mortality reduction. The major side effects in the trial were hyperkalemia and gynecomastia. Current recommendations for spironolactone are limited to patients who remain symptomatic, despite ACEI, β-blocker, digoxin, and diuretics. Patients with creatinine greater than 2.5 mg/dL, or potassium greater than 5 mmol/L, should not receive spironolactone. Lastly, the use of spironolactone in patients with mild HF (stage I-II) is not recommended.

Vasodilators. Selecting optimal treatment for HF requires determining perfusion status and estimating the degree of pulmonary congestion. Patients who are vasoconstricted will benefit from vasodilators; those with congestion require diuretics.[24] The most common presentation of HF in the ED is the vasoconstricted/congested patient for whom treatment with vasodilators and diuretics will generate the best outcomes. This strategy, because it decreases PCWP and increases cardiac output, is likely to produce the best clinical results in chronic HF, in which mortality rates are linked predictably to the PCWP.[25] *(See Table 7 for a summary of commonly used vasodilators.)*

Prior to aggressive treatment with vasodilators, the physician should ascultate for and inquire about murmurs of HOCM or aortic stenosis, since these patients may become hypotensive after administration of arterial or venous vasodilators. In any patient who becomes acutely hypotensive after the administration of nitrates, the physician should consider the differential diagnosis listed in Table 8.

Nitroglycerin. NTG has benefits in HF, provided there is adequate systolic BP, and especially if there is hypertension. A fast-acting, systemic arterial and venous dilator, NTG decreases mean arterial pressure by reducing afterload, and diminishes preload. The coronary vasodilation effects of NTG also may decrease myocardial ischemia, and thereby, improve cardiac function.

NTG can be administered through the IV, SL, or transdermal route. NTG paste may be used for less critical presentations. One inch is placed on the chest wall with a non-absorbent backing material. IV NTG is initiated at 10-20 mcg/min and rapidly is increased by 5-10 mcg/min, titrated to BP and symptomatic improvement. High doses may be required in the acute setting (usually greater than 100 mcg/min).

The most important complication, hypotension, is more likely to occur with volume depletion and RV infarct. It usually resolves after cessation of NTG. If this fails to improve BP, a small fluid bolus (e.g., 250 ccs) may be required. Headache is frequent, but acetaminophen usually is adequate for relief. Meth-hemoglobinemia has been reported with use of high doses of NTG.

Nitroprusside. When further afterload reduction is required (i.e., continued high systemic BP), IV nitroprusside usually is indicated and effective. It is a more potent arterial vasodilator than NTG. Hemodynamic effects include decreased BP, decreased LV filling pressure, and increased cardiac output. Some have suggested that nitroprusside may promote a vasodilation that results in blood being shunted away from the coronary arteries (the so-called "coronary steal"). The clinical relevance of this coronary steal has not been studied formally, but some clinicians recommend simultaneous use of a low dose of IV NTG if recent ischemia or severe CAD is suspected.

The starting dose is usually 0.1-0.2 mcg/kg/min, then titrated up every 5-10 minutes based on BP and clinical response. It also is used to decrease systemic vascular resistance (SVR), as guided by hemodynamic data. The major complication is hypotension. Long-term use (for more than several days at high dose) is associated with thiocyanate toxicity, especially in patients with renal failure. Cyanide toxicity has been reported with high doses (greater than 10 mcg/kg/min) of nitroprusside.

Nesiritide—A New Advance in HF Therapy

Nesiritide is the first medication approved for HF by the U.S. Food and Drug Administration in more than a decade. Pharmacologically, it consists of the recombinant DNA manufactured form of endogenously synthesized B-type natriuretic polypeptide (BNP). Consequently, when given as a therapy, its use represents an amplification of the natural compensatory mechanism for neurohormonal and hemodynamic derangements that occur in

Table 8. Possible Causes of Hypotension after Initiating Therapy with Nitrates

- Right ventricular infarction
- Aortic stenosis
- Hypertrophic obstructive cardiomyopathy
- Anaphylaxis
- Cardiogenic shock
- Intravascular volume depletion

HF. As a neurohormonal antagonist,[26] nesiritide serves as a counterpoint to the RAAS; it antagonizes the sympathetic nervous system and causes decreases in aldosterone and endothelin levels.

Background. Understanding the clinical importance of neurohormonal antagonism in HF therapy represents a major shift in the management of HF patients. Historically, relief of congestion with diuretics has represented the main thrust of HF therapy in the ED. While diuretics still are important for acute relief of congestion, they provide symptomatic relief, but without improvements in the mortality rate. Studies with a combined population of more than 20,000 patients—evaluating the role of ACEIs, β-blockers, and other agents—have demonstrated that neurohormonal antagonism is required for mortality improvement. Direct neurohormonal antagonism represents one significant and specific advantage of nesiritide over currently available inotropes and vasodilators used for ED-based therapy of HF.

As a rule, ED patients who present with HF are dyspneic and congested and require prompt IV diuresis. There is theoretical support for the use of a neurohormonal antagonist in combination with diuretics for HF. First, the pathophysiological consequences of successful diuresis are intravascular volume loss and sodium depletion. Ultimately, the patient is decongested, but the consequence is a maximally stimulated neurohormonal axis. Unchecked, this compensatory neurohormonal activation attempts to restore the patient to his pre-diuresis state by vasoconstriction and retention of sodium and water. The use of a neurohormonal antagonist, such as nesiritide, at the time of diuresis, blunts the degree of compensatory neurohormonal activation.

In addition to being an effective neurohormonal antagonist, nesiritide also has direct effects on fluid homeostasis. It is both a weak diuretic and a natriuretic. After an IV infusion, both urinary sodium and volumes increase, but without a statistically significant increase in urinary potassium or creatinine clearance. It is important to note that although nesiritide has diuretic effects, it still is necessary to combine this agent with a loop diuretic to ensure adequate diuresis for treatment of decompensated HF.

Finally, of special clinical significance to the emergency physician are the acute hemodynamic effects of nesiritide, which causes vasodilation of both the systemic veins and arteries. This leads to a rapid and predictable decrease in right atrial pressure (RAP), pulmonary artery pressure (PAP), PCWP, SVR, and mean arterial pressure (MAP), with subsequent increases in the stroke volume index (SVI) and the cardiac index (CI).[27,28] These effects are beneficial in the decompensated HF patient, and the resulting hemodynamic improvements translate into a synergistic

Table 9. Nesiritide Effect Summary

HEMODYNAMICS
- Decreases afterload
- Decreases preload
- Vasodilator (including corornary arteries)

DIURETIC
- Promotes free water loss
- Promotes sodium loss
- Minimal kaliuretic effect

SYMPTOMATIC IMPROVEMENT
- Dyspnea
- Global clinical status

IMPORTANT LACK OF EFFECT
- Not inotropic
- Not arrhythmogenic

NEUROHORMONAL ANTAGONIST
- Endothelin
- Sympathetic nervous system
- Renin angiotensin system

augmentation of other therapeutic components of standard HF treatment, i.e., diuretics, NTG, etc. *(See Table 9.)*

Clinical Effects. Several prospective studies have evaluated the clinical effects of nesiritide. The PRECEDENT trial evaluated the effects of varying doses of nesiritide or dobutamine on cardiac ectopy.[29] Dobutamine-treated patients had ectopy rates as high as 13%, whereas the nesiritide group had ectopy rates of only 6%. Although 5% of the dobutamine group suffered cardiac arrest, no nesiritide patients did. The rate of ventricular tachycardia was 22% with dobutamine, compared to 7% with nesiritide. Another study, evaluating six-month survival following short-term nesiritide therapy, showed a marked decrease in death rates compared to dobutamine.[30] Similar favorable trends were observed for nesiritide as far as readmission rates and total cost of care.

Studies suggest nesiritide is superior to the most commonly used inotropes for HF. Compared to NTG, the most commonly used vasodilator for HF, nesiritide had a better decrease in PCWP, superior dyspnea score at three hours, and lower rates of headache and hypotension. At 24 hours, the nesiritide group had less dyspnea, and the global clinical evaluation was better than with NTG. Adverse event rates were similar in regard to myocardial infarction, ventricular tachycardia, and symptomatic hypotension.[31]

Safety in ACS

In the United States, underlying CAD is one of the most common causes of HF. Therefore, in patients presenting to the ED with signs and symptoms of decompensated HF, underlying ACS must be considered in the differential diagnosis. In a retrospective review[30], the Cleveland Clinic found that 14% of decompensated HF patients in the ED ultimately "rule in" for ACS with a positive troponin. Whether the elevated cardiac markers were a precipitant or a consequence of the decompensated HF was unclear. However, any medication for use in ED patients with decompensated HF should be safe in the occurrence of concurrent ACS.

There is little published data specifically evaluating the safety of nesiritide in ACS. However, its physiologic profile would suggest it is safe when used in the HF patient who ultimately is found to have an underlying ACS. An important management strategy in the treatment ACS is to minimize myocardial oxygen demand (MVO_2), thus limiting the size of a potential infarction. This is accomplished by controlling the major determinates of (MVO_2), i.e., heart rate and afterload (MAP), with β-blockers. β-blockers are contraindicated in the acutely congested HF patient requiring IV diuresis. Nesiritide, with neither inotropic (tension-inducing)[32] nor chronotropic (HR-increasing) effects, should not increase MVO_2. The lack of inotropic and chronotropic activity suggests there may be an increased margin of safety using this agent if there is coincident underlying ACS in an HF patient. Prospective studies will be required to evaluate this hypothesis.

Other characteristics of nesiritide also suggest safety in HF patients with a concurrent acute coronary ischemic syndrome. Nesiritide functions to decrease systolic BP (decreasing MAP), the other major determinant of MVO_2. As a result, it should provide benefit as long as hypotension is avoided. Finally, nesiritide is an epicardial coronary artery vasodilator.[33] While nesiritide is not indicated for the primary treatment of ACS, the characteristic of coronary vasodilation increases safety for use in decompensated HF. In summary, the early use of nesiritide in ED patients with suspected decompensated HF is not dependent upon the return of negative cardiac enzymes. Nesiritide may be initiated early in the course of the ED visit, based on congestive HF symptoms, and before the results of lab investigation are known. If the patient ultimately is diagnosed with acute MI, the clinician has the option of discontinuing nesiritide therapy and replacing this agent with standard ACS therapy (e.g., NTG, heparin, or low molecular weight heparin [LMWH], etc.).

Finally, nesiritide may be used in acute decompensated HF without CS. It should be used concurrently with ACEIs, β-blockers, and diuretics. Recommended dosing is to administer an initial bolus of 2 mcg/kg followed by a fixed dose of 0.01 mcg/kg/min IV. The most common complication is hypotension, with an overall rate of 4%.

Vasodilators and Inotropic Agents

Hydralazine/Isosorbide Dinitrate (ISDN). The combination of hydralazine and ISDN has the advantage of producing preload and afterload reduction, while at the same time achieving protective effects against ventricular remodeling.[9] The V-HeFT trial demonstrated that in HF, the combination of hydralazine plus ISDN resulted in significant mortality reduction compared with placebo. However, the V-HeFT-II study showed that enalapril-treated patients had better long-term outcomes than patients treated with the combination of hydralazine and ISDN.[7] Because of this, the use of hydralazine and ISDN should be considered only in patients who have proven to be intolerant to ACEIs. Moreover, therapy with the combination of hydralazine/ISDN can be cumbersome and can result in significant side effects (i.e., drug-induced lupus, hypotension, gastrointestinal complaints, and headache). As a result, some clinicians prefer to use ARBs prior to hydralazine/ISDN in patients who are unable to take ACEIs. There is no data to support the use of hydralazine or ISDN as single agents in the management of stable, compensated HF.

The dose of hydralazine typically is started at 10-25 mg TID and titrated up to a maximum of 300 mg per day. ISDN is started at 10 mg TID and titrated to a maximum dose of 240 mg per day. If once-a-day nitrate dosing is desired, isosorbide mononitrate can be used starting at 30 mg, with a maximum daily dose of 240 mg.

Morphine Sulfate. Morphine can be used in APE, provided there is adequate BP. It is used to reduce overall anxiety, decrease adrenergic responsiveness of vascular beds, as a venodilator, and to treat pain associated with myocardial infarction. Dosing is 2-5 mg IV, initially, titrated to clinical effect. Since it is a respiratory and central nervous system (CNS) depressant, morphine use should be avoided if there is significant respiratory depression (e.g., respiratory acidosis) or altered sensorium. Naloxone should be available if needed. Complications include hypotension, hypoventilation, sedation, nausea, and vomiting. Hypotension is particularly likely if there is a concurrent RV infarct.

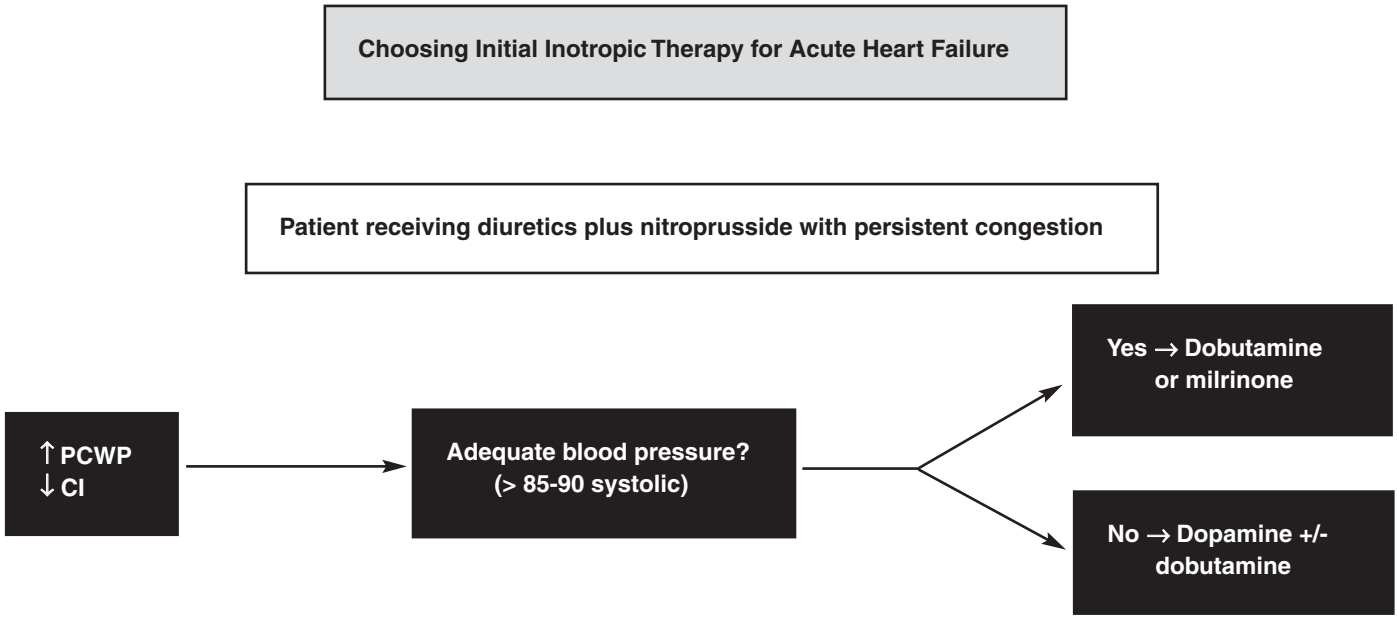
Inotropic therapy. Since inotropic therapy improves cardiac performance, it would appear that it would be of value in patients with HF. As a class, these drugs augment myocardial function by improving contractility, and some agents decrease SVR through vasodilation. In the short term, these effects improve cardiac output. Inotropes are used most appropriately as a bridge to definitive therapy. Unfortunately, despite the short-term hemodynamic effects, no lasting improvement in symptoms or clinical outcomes has been documented with these agents.[18,34] In fact, long-term IV therapy with inotropes has produced increased mortality rates.[18,33,35,36] Consequently, chronic use cannot be recommended.

Nevertheless, there are appropriate uses for inotropic therapy. In patients on chronic β-blocker therapy who present with congestive findings as a result of dietary or non-compliance issues, inotropes may be used as temporizing therapy. In this population, for whom it may not be prudent to stop β-blockers, inotropes may serve as a bridge to hemodynamic stability. Inotropes can be used while awaiting the placement of an LV assist device or heart transplant. *(See Table 10.)*

The use of intermittent (so-called "holiday") inotropic therapy for chronic HF is not recommended.[9] Studies have been sparse, but appear to show a trend toward increased mortality in patients treated with intermittent therapy with either IV or oral inotropes.[9] A distinction between intermittent inotropic therapy for stable end-stage HF must be distinguished from long-term, home inotropic therapy for end-stage HF. The latter group of patients is often inotrope-dependent, in that they could not be weaned from inotropes during their hospitalization. Even though long-term inotropic therapy likely will not provide clinical benefit (and even may lead to harm), withdrawal of the inotrope would result in prompt decompensation.

Dopamine. A first-line agent for CS, dopamine has dose-dependent effects. At doses less than 2.5 mcg/kg/min, dopaminergic stimulation dilates renal, cardiac, and splanchnic vessels. In the range of 2.5-5 mcg/kg/min, β1 effects predominate. When doses exceed 5-10 mcg/kg/min, both α and β1 effects occur. Finally, as dosing increases above 10 mcg/kg/min, α tone pro-

Table 10. Inotrope Characteristics



AGENT	MECHANISM	DOSING	COMMENTS
DOBUTAMINE			
	β-1 > β-2 > α-1	0.5-20 mcg/kg/min IV	• Primarily β-1 stimulation • Less vasodilation than milrinone • Less effective if β-receptor downregulation • Quicker onset than milrinone
MILRINONE			
	Phosphodiesterase inhibitor (↑ cellular cAMP) Vasodilator	Load 50 mcg/kg IV over 10 min Maintenance: 0.375-0.75 mcg/kg/min IV	• Risk of hypotension especially when use loading dose • Needs adjustment for renal insufficiency • Effective in states of β-receptor downregulation • Possibly less ischemic potential than dobutamine
DOPAMINE			
	Low Dose 1-2 mcg/kg/min primarily D-1 **Medium Dose** 2-10 mcg/kg/min IV β-1 > α-1 > β-2 **High Dose** 10 mcg/kg/min IV α-1 > β-1 > β-2	See Mechanism	• Agent of choice when shock or unacceptable hypotension • Prefer a central line to prevent skin extravasation • Lower doses promote renal blood flow • Can ↑ PCWP • Goal is to bring systolic blood pressure to acceptable range

Key:
PCWP = Pulmonary capillary wedge pressure
CI = Cardiac index
D-1 = Dopamine receptor
cAMP = Cyclic adenosine-monophosphate

gressively increases. Dosing usually begins at 3-5 mcg/kg/min and is titrated up to 20-50 mcg/kg/min, to maintain BP. Complications include arrhythmia, extremity gangrene, and tachycardia at high doses (which increases myocardial oxygen demand and may extend ischemia).

Dobutamine. Dobutamine usually is used for acute HF with signs of poor perfusion, but systolic BP greater than 90 mHg. It is primarily a β1-agonist, with weak β2 stimulation. The net effect increases cardiac output and lowers systemic vascular resistance, with little change in BP. Started at 3-10 mcg/kg/min,

dobutamine is titrated to 20-40 mcg/kg/min. Complications include arrhythmia, nausea, and headache. If there is an inadequate response to this agent alone, dopamine may be added to support BP. Dobutamine is used in the hemodynamic management of acute HF to improve myocardial contractility. It also is used in the setting of right-sided myocardial infarction when volume infusion fails to improve cardiac output.

Overall, dobutamine has the hemodynamic effects of reducing PCWP, increasing CI, producing a small dose-dependent increase in heart rate, and decreasing SVR. Dobutamine is fairly neutral in its effect on BP, and can be expected to increase only minimally the mean arterial pressures. Therefore, it may be preferred in the HF patient with borderline hypotension.

Chronic HF can result in a state of β-receptor downregulation.[37] As a result, dobutamine may not exert the desired inotropic response in some patients. These patients may require the addition of milrinone (which can be used with dobutamine). In addition, patients with hypotension may require the addition of dopamine to preserve tissue perfusion.

Dobutamine is initiated at 0.5 mcg/kg/min and titrated up to the usual dosage of 2.5 to 20 mcg/kg/min. Hemodynamic monitoring during titration is required to observe the desired effect of increased CI and decreased PCWP.

Milrinone. Milrinone is a phosphodiesterase inhibitor. Inhibition of the phosphodiesterase enzyme results in an increase in intracellular levels of cyclic adenosine-monophosphate (cAMP) and calcium. Increased levels of intracellular cAMP enhances myocardial contractility and promotes peripheral vascular smooth muscle relaxation, resulting in arterial and venous vasodilation. In this regard, milrinone is considered to function as both an ionotrope and a vasodilator. Milrinone especially is effective in patients with chronic severe HF who may not respond well to dobutamine because of β-receptor downregulation.

Milrinone has a longer half-life than dobutamine and must be given as a loading dose to facilitate prompt hemodynamic effect. The typical loading dose is 50 mcg/kg given over 10 minutes, followed by a maintenance infusion at 0.375-0.750 mcg/kg/min. The loading dose can cause excessive hypotension. Milrinone is extensively renally cleared and the dose must be reduced in renal insufficiency. There is some suggestion that milrinone may have a more favorable effect on myocardial oxygen demand than dobutamine.[38] Therefore, it may be preferred over dobutamine when patients require inotropic support in the setting of suspected ischemia or known severe CAD.

Patients must be monitored closely for hypotension and arrythmias. Long-term use of milrinone has been associated with an increase in mortality. Thus, the main use of milrinone is short-term treatment (usually fewer than 72 hours) of severe acute HF that has persisted despite diuretics and nitroprusside. Milrinone also is used for hemodynamic support after cardiac surgery.

Anticoagulation

Outpatient Therapy. The risk of thromboembolism in the clinically stable outpatient with HF is low, and is estimated to be 1-3% per year. It is greatest in patients with low ejection fractions.[39,40] While many physicians use warfarin in HF, there is insufficient data to suggest an optimal or precise approach.[18,41] However, in the absence of contraindications, patients with atrial fibrillation should be anticoagulated and should receive sufficient warfarin to maintain an international normalized ratio (INR) between 2.0 and 3.0.[41] Other patient subgroups, especially those with low ejection fractions, LV dysfunction, and previous history of AMI, may be considered for long-term oral anticoagulation therapy.

There is evidence to suggest the syndrome of HF may predispose to a hypercoaguable state. Several large-scale trials are underway to determine if the use of antiplatelet and/or anticoagulant (i.e., warfarin) drugs is warranted in patients with LV dysfunction in the absence of atrial fibrillation. Most authors would give warfarin if there is significant LV dysfunction in the presence of atrial fibrillation, LV thrombus, or prior embolic event.[41]

Inpatient Therapy. While the majority of literature regarding deep venous thrombosis (DVT) and pulmonary embolism prophylaxis is derived from post-surgical patients, recent publications have identified specific subgroups of medical patients who also are at moderate- to high-risk for thrombotic complications.[42-44] These include HF, mobile intensive care unit (MICU) admissions, and those with acute coronary syndromes. In the MEDENOX trial comparing the LMWH enoxaparin to placebo in hospitalized medical patients, administration of enoxaparin 40 mg subcutaneously once daily was shown to decrease the rate of venographically documented DVT in patients with HF by as much as 63%. In particular, restricted patients with HF are at greater risk for sustaining the morbid sequelae and complications associated with DVT. Accordingly, the threshold for empirical prevention of DVT in this patient population must be balanced against the relatively low risk of serious complications associated with anticoagulant-mediated prophylaxis. The supplement to Part I of this series discussed in detail the mandate to prevent VTED. The screening and risk-stratification algorithm is presented in this section to help clinicians identify patients who should be prophylaxed with enoxaparin. *(See Insert.)*

Therapeutic Approaches to Be Avoided in HF

Calcium Channel Blockers (CCBs). CCBs are not recommended routinely in HF.[18,41] Short-term use may result in pulmonary edema and CS, while long-term use may increase the risk of worsening HF and death.[45-48] These adverse effects have been attributed to the negative inotropic effects of CCBs. If necessary, amlodipine, which has no clear adverse effect on mortality, may be used preferentially for compelling clinical reasons (e.g., as an antianginal agent despite maximal therapy with nitrates and β-blockers).

Non-Steroidal Anti-Inflammatory Drugs. As a rule, NSAIDs should be avoided in HF.[18,41] They inhibit the effects of diuretics and ACEIs, and can worsen cardiac and renal function.[18] The routine use of aspirin for CAD, with concurrent ACEI treatment, is controversial. In a retrospective subset analysis of 464 HF and CAD patients on ACEIs and/or ASA, 5-year mortality was 24% with both agents. This compared to a 34% 5-year

Table 11. Indications for Admission to Cardiac ICU in Patients with HF

- Worsening hypoxemia or increasing oxygen requirements
- Hypercarbia
- Myocardial ischemia (by ECG or cardiac enzymes)
- Concomitant severe infection (i.e., pneumonia, sepsis)
- Evidence of end organ dysfunction (oliguria, obtundation)
- Severe structural/valvular lesions (aortic stenosis, HOCM)

death rate if ACEIs were used alone (p=0.001).[49] Further data is needed for comprehensive treatment recommendations.

Antiarrhythmics. Since patients with HF are particularly sensitive to the pro-arrhythmic and cardiodepressant effects of the commonly used antiarrhythmics, suppression of asymptomatic ventricular arrhythmias usually is unnecessary. Furthermore, their use does not prevent sudden cardiac death. If there has been resuscitation from sudden death, ventricular fibrillation, or sustained ventricular tachycardia, electrophysiologic stimulation testing, and consideration for an implantable device is warranted.[18]

Class I antiarrhythmics (quinidine, procainamide, flecanide, encainide) should not be used in HF, except for immediate treatment of life-threatening ventricular arrhythmias.[18,41,50,51] Some class III agents (e.g., amiodarone) do not increase the risk of sudden death.[52,53] Therefore, class III agents are preferred for atrial arrhythmias.[18] However, due to toxicity, amiodarone is not recommended for routine use to prevent sudden death in patients already treated with mortality reducing drugs (ACEIs, β-blockers).[18]

Sudden Death/Ventricular Arrhythmias.

The diagnosis of HF is an important risk factor for sudden death. Ventricular arrhythmias are common in these patients, and PVCs are seen in 95% of patients with dilated cardiomyopathy. Non-sustained ventricular tachycardia occurs in 30-40%. Sudden death risk increases proportionally to ejection fraction deterioration and the severity of HF,[54] and occurs in 10-40%[54-56] of HF patients. Progressive pump failure is the fatal event in approximately 50%.

Since arrhythmia is common in HF, neither Holter monitoring nor electrophysiologic studies predict individuals at risk for sudden death,[56] so therapy is guided by symptoms. Syncope, resuscitation after cardiac arrest, sustained ventricular tachycardia, symptomatic non-sustained ventricular tachycardia, and ventricular fibrillation suggest aggressive management. Prophylactic administration of antiarrhythmics is not effective, and may increase mortality.[50]

Patient Disposition

Cardiogenic Shock. Patients presenting with CS have high short-term mortality, require aggressive circulatory support, and may benefit from pulmonary artery catheterization. Hence, they require ICU admission. Furthermore, patients with CS should be evaluated for emergency revascularization to correct any potential cardiac ischemia.

Acute Pulmonary Edema. APE frequently requires ICU admission. A small subset of patients will improve greatly while still in the ED. In these, admission to a non-ICU monitored bed may be feasible, but only if nursing staffing ratios are adequate to ensure that hemodynamic monitoring is vigilant and other precipitants of APE are excluded (e.g., myocardial infarction). Because transient hypertension can result in precipitous hemodynamic instability, close monitoring is needed. *(See Table 11 for ICU admission indications.)*

Decompensated HF. Decompensated HF patients usually require hospital admission, IV diuresis, vasodilator therapy, titration of medicines, and correction of any potentially reversible causes of their decompensation. All patients with new onset HF, evidence of myocardial ischemia, poor social support, hypoxemia, hypercarbia, concurrent infection, respiratory distress, syncope, or symptomatic hypotension should be admitted to the hospital. Patients who have mild symptoms that resolve with therapy; normal lab, x-ray, and ECG evaluation; and a strong social situation, and who are likely to comply with outpatient follow up, may be discharged from the ED. More significant symptoms, inadequate response to therapy, or a poor social situation suggest hospital admission is required.

Stable fluid-overloaded patients with a prior HF diagnosis may be admitted to a non-monitored setting or an ED observation unit. Intensive short-stay therapy has beneficial effects in the prevention of repeat visits. To realize the benefit of fewer revisits, it is important for the ED observation unit to have an HF protocol established. It should address specific therapy, as well as education and social issues.[57]

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Physician CME Questions

59. Which of the following therapies should be avoided in heart failure?
    A. β-blockers
    B. Calcium channel blockers
    C. Dobutamine
    D. Nitroglycerin

60. Which of the following statements is true regarding diuretics?
    A. Diuretics should not be given to patients with systemic or pulmonary congestion.
    B. Diuretics fail to provide rapid symptom relief in HF.
    C. Diuretics sensitize patients to the hemodynamic effects of ACEIs.
    D. Diuretics are effective in cases of severe renal dysfunction.

61. All of the following drugs have been shown to reduce mortality in heart failure *except*:
    A. dobutamine.
    B. captopril.
    C. spironolactone.
    D. metoprolol.

62. Spironolactone should be considered in the management of heart failure in which of the following patient?
    A. A 68-year-old female with NYHA III systolic heart failure, on furosemide, metoprolol, and lisinopril
    B. A 72-year- old male with NYHA III systolic heart failure and a serum creatinine of 3.8 gm/dL due to diabetic nephropathy
    C. A 59-year-old male with NYHA II systolic heart failure, on prinivil and metoprolol
    D. A 70-year-old female with NYHA IV systolic heart failure, chronic renal failure and a baseline serum potassium of 5.9 mmol/L

63. Inotropic therapy should:
    A. be considered as temporizing therapy in patients on chronic β-blocker therapy who present to the ED with congestive findings from dietary or non-compliance issues.
    B. be used intermittently for chronic HF.
    C. be recommended for chronic use in HF because long-term IV therapy has been shown to decrease mortality rates.
    D. not be considered appropriate for use while awaiting placement of an LV assist device or heart transplant.

64. Contraindications to using ACEIs for HF include:
    A. systemic hypotension.
    B. hemodynamic instability.
    C. hyperkalemia.
    D. All of the above.

65. In studies evaluating nesiritide's effects in the treatment of acute heart failure, nesiritide was found to:
    A. have a better decrease in PCWP compared to NTG.
    B. have lower rates of ventricular tachycardia compared to dobutamine.
    C. have a marked decrease in death rates at six months compared to dobutamine.
    D. have less ectopy than dobutamine.
    E. All of the above

66. Which of the following is true regarding pharmacotherapeutic strategies for HF?
    A. Use of ACEIs and powerful loop diuretics has decreased the

morbidity of HF.

B. Options for HF have failed to evolve during the past decade.
C. ACEIs have no effect on mortality rate.
D. β-blockers are contraindicated.

Emergency Medicine Reports
CME Objectives

To help physicians:

- quickly recognize or increase index of suspicion for specific conditions;
- understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- be educated about how to correctly perform necessary diagnostic tests;
- take a meaningful patient history that will reveal the most important details about the particular medical problem discussed;
- apply state-of-the-art therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;
- understand the differential diagnosis of the entity discussed;
- understand both likely and rare complications that may occur;
- and provide patients with any necessary discharge instructions.

In Future Issues:

Community Acquired Pneumonia

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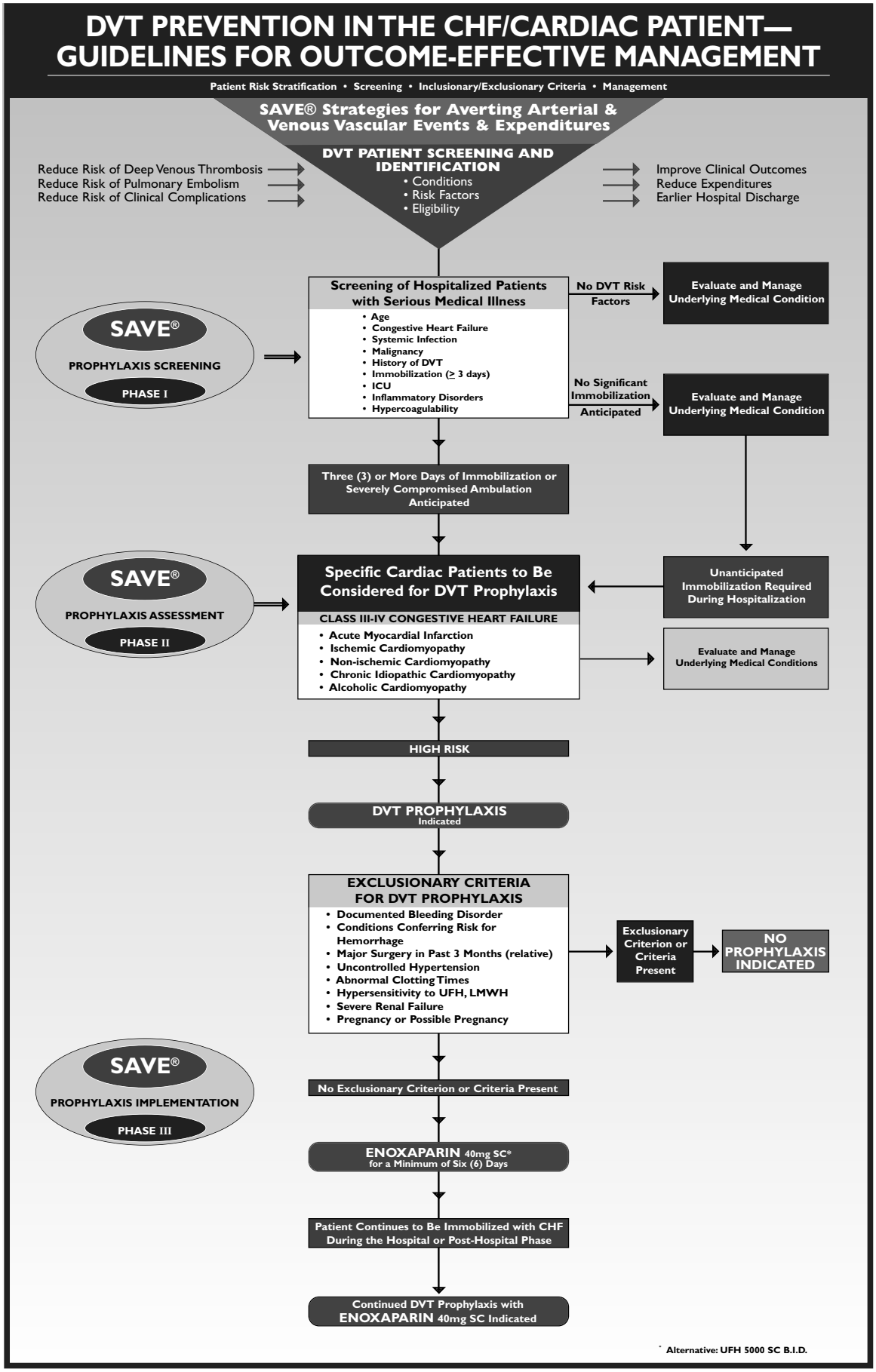
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• Systemic Infection
• Malignancy
• History of DVT
• Immobilization (≥ 3 days)
• ICU
• Inflammatory Disorders
• Hypercoagulability
No DVT Risk Factors
Evaluate and Manage Underlying Medical Condition
No Significant Immobilization Anticipated
Evaluate and Manage Underlying Medical Condition
Three (3) or More Days of Immobilization or Severely Compromised Ambulation Anticipated
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CLASS III-IV CONGESTIVE HEART FAILURE
• Acute Myocardial Infarction
• Ischemic Cardiomyopathy
• Non-ischemic Cardiomyopathy
• Chronic Idiopathic Cardiomyopathy
• Alcoholic Cardiomyopathy
Unanticipated Immobilization Required During Hospitalization
Evaluate and Manage Underlying Medical Conditions
HIGH RISK
DVT PROPHYLAXIS Indicated
EXCLUSIONARY CRITERIA FOR DVT PROPHYLAXIS
• Documented Bleeding Disorder
• Conditions Conferring Risk for Hemorrhage
• Major Surgery in Past 3 Months (relative)
• Uncontrolled Hypertension
• Abnormal Clotting Times
• Hypersensitivity to UFH, LMWH
• Severe Renal Failure
• Pregnancy or Possible Pregnancy
Exclusionary Criterion or Criteria Present
NO PROPHYLAXIS INDICATED
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Emergency Medicine Reports
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Heart Failure Part II

Initial Therapy for Acute Pulmonary Edema (APE)

1. Sit the patient upright with legs dependent (to reduce venous filling), if possible.
2. Administer 100% oxygen.
3. Administer nitrates if systolic BP > 100.
   - Sublingual nitroglycerin 0.4 mg q 1-5 minutes (monitor BP closely)
   - IV nitroglycerine or nitroprusside if needed.
4. Administer IV furosemide (or ethacrynic acid if sulfa allergy)
5. Administer IV morphine 2-6 mg (if no respiratory acidosis/depression)
6. Cardioversion to restore sinus rhythm

Possible Causes of Hypotension after Initiating Therapy with Nitrates

- Right ventricular infarction
- Aortic stenosis
- Hypertrophic obstructive cardiomyopathy
- Anaphylaxis
- Cardiogenic shock
- Intravascular volume depletion

Contraindications to Angiotensin-Converting Enzyme Inhibiltors (ACEIs)

- Angioedema
- Progressive azotemia (> 3 mg/dL, especially if progressively increasing)
- Bilateral renal artery stenosis
- Systemic hypotension (systolic blood pressure < 80, especially in ambulatory patients)
- Hyperkalemia
- Pregnancy
- Hemodynamic instability
- Intolerance secondary to **severe** cough

Nesiritide Effect Summary

HEMODYNAMICS
- Decreases afterload
- Decreases preload
- Vasodilator (including corornary arteries)

DIURETIC
- Promotes free water loss
- Promotes sodium loss
- Minimal kaliuretic effect

SYMPTOMATIC IMPROVEMENT
- Dyspnea
- Global clinical status

IMPORTANT LACK OF EFFECT
- Not inotropic
- Not arrhythmogenic

NEUROHORMONAL ANTAGONIST
- Endothelin
- Sympathetic nervous system
- Renin angiotensin system

ACEIs/ARBs for Chronic Systolic Heart Failure*

DRUG	START	TARGET DOSE	TRIAL DATA
CAPTOPRIL			
	6.25 mg tid	50 mg tid	SAVE
LISINOPRIL			
	2.5 mg qd	40 mg qd	ATLAS
ENALAPRIL			
	5 mg qd	20 mg qd	SOLVD
RAMIPRIL			
	2.5 mg qd	10 mg bid	AIRE
LOSARTAN			
	50 mg qd	50 mg bid	ELITE
VALSARTAN			
	40 mg bid	160 mg bid	Val-HeFT

* Dosing data from major clinical trials

Indications for Admission to Cardiac ICU in Patients with HF

- Worsening hypoxemia or increasing oxygen requirements
- Hypercarbia
- Myocardial ischemia (by ECG or cardiac enzymes)
- Concomitant severe infection (i.e., pneumonia, sepsis)
- Evidence of end organ dysfunction (oliguria, obtundation)
- Severe structural/valvular lesions (aortic stenosis, HOCM)

Diuretics for Acute Heart Failure

AGENT	DOSING (IV)	EFFECT	SIDE EFFECTS
FUROSEMIDE			
	No prior use: 40 mg IVP **If prior use:** Double last 24-hour usage (max 180 mg) **If no effect by 20-30 min:** Re-double dose	• Diuresis starts within 15-20 min • Duration of action is 4-6 hrs	• Reduced K+ and Mg++; • Hyperuricemia; ototoxicity • Sulfa allergy; hypovolemia; • Pre-renal azotemia; • Myalgia
BUMETANIDE			
	1-3 mg 1 mg ~ 40 mg furosemide	• Diuresis starts within 10 min • Peak action at 60 min	Same as above
TORSEMIDE			
	10-20 mg	• Diuresis starts within 10 min • Duration of action is 6-8 hrs • Better oral bioavailability than furosemide	Same as above
ETHACRYNIC ACID			
	50 mg	Similar to furosemide	• Same as above • Non-sulfa agent • Increased ototoxicity
METOLAZONE			
	5-10 mg po 20-30 min before IV furosemide	Additive to loop diuretic	• Similar to furosemide except no ototoxicity • Has liver disease caution

Contraindications for Beta-Blockers

- Unstable hemodynamics, or congested and requiring IV diuresis (most ED patients)
- Severe bronchospastic airway disease
- Symptomatic bradycardia
- Advanced heart block
- Acute vascular insufficiency or worsening claudication/rest pain
- Class IV stable HF (therapy should be provided by HF specialist)
- Inotropic therapy/cardiogenic shock
- Severe conduction system disease (unless protected by a pacemaker)

Beta-Blockers for Chronic Systolic Heart Failure*

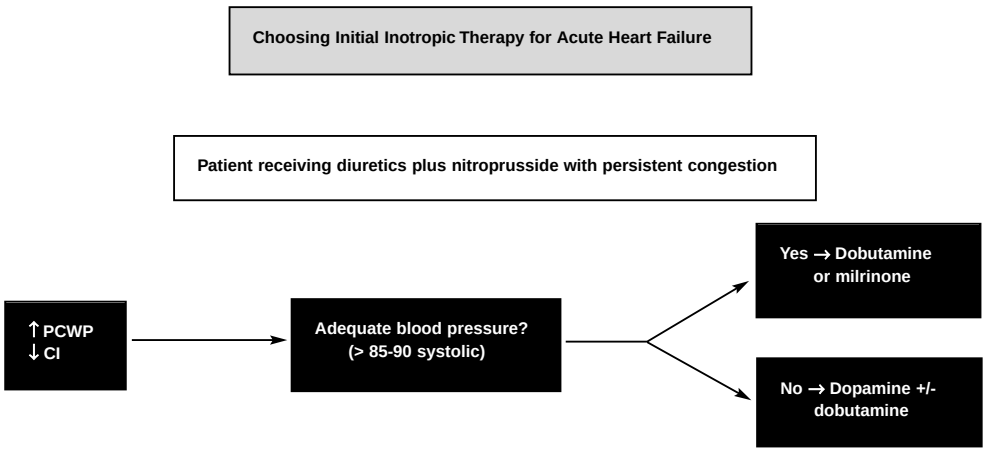
DRUG	STARTING DOSE	TARGET DOSE	TRIAL DATA
Metoprolol xl/cr	12.5 mg qd	100 mg qd	MERIT-HF
Carvedilol	3.125 mg bid	25-50 mg bid	US-TRIALS COPERNICUS
Bisoprolol	1.25 mg qd	10 mg qd	CIBIS II

* Dosing data from major clinical trials

Vasodilators for Acute Heart Failure

AGENT	DOSING	TITRATION	SIDE EFFECTS
NITROGLYCERIN SUBLINGUAL			
	0.4 mg SL q 1-5 min	Blood pressure symptoms	• Hypotension • Headache
NITROGLYCERIN INTRAVENOUS			
	0.2-0.4 mcg/kg/min (starting dose)	Blood pressure symptoms	• Hypotension • Headache
NITROPRUSSIDE			
	0.1-0.2 mcg/kg/min (starting dose) 10 mcg/kg/min (maximum)	Blood pressure symptoms	• Hypotension • Possibility of coronary steal • Cyanide toxicity • Thiocyanate toxicity
NESIRITIDE			
	2 mcg/kg bolus then infusion of 0.01 mcg/kg/min	Titration usually unnecessary	• Hypotension

Inotrope Characteristics



AGENT	MECHANISM	DOSING	COMMENTS
DOBUTAMINE			
	β-1 > β-2 > α-1	0.5-20 mcg/kg/min IV	• Primarily β-1 stimulation • Less vasodilation than milrinone • Less effective if β-receptor downregulation • Quicker onset than milrinone
MILRINONE			
	Phosphodiesterase inhibitor (↑ cellular cAMP) Vasodilator	Load 50 mcg/kg IV over 10 min Maintenance: 0.375-0.75 mcg/kg/min IV	• Risk of hypotension especially when use loading dose • Needs adjustment for renal insufficiency • Effective in states of β-receptor downregulation • Possibly less ischemic potential than dobutamine
DOPAMINE			
	Low Dose 1-2 mcg/kg/min primarily D-1 **Medium Dose** 2-10 mcg/kg/min IV β-1 > α-1 > β-2 **High Dose** 10 mcg/kg/min IV α-1 > β-1 > β-2	See Mechanism	• Agent of choice when shock or unacceptable hypotension • Prefer a central line to prevent skin extravasation • Lower doses promote renal blood flow • Can ↑ PCWP • Goal is to bring systolic blood pressure to acceptable range

Key:
PCWP = Pulmonary capillary wedge pressure
CI = Cardiac index
D-1 = Dopamine receptor
cAMP = Cyclic adenosine-monophosphate

Supplement to Emergency Medicine Reports, April 8, 2002: "The Clinical Challenge of Heart Failure: Comprehensive, Evidence-Based Management of the Hospitalized Patient with Acute Myocardial Decompensation. Part II: Outcome-Effective Treatment and Prophylaxis Against Venous Thromboembolic Disease (VTED)." Authors: **W. Frank Peacock, MD**, Emergency Department Clinical Operations Director, The Cleveland Clinic, OH; **Benjamin J. Freda, DO**, Department of Internal Medicine, Cleveland Clinic Foundation, OH.

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Your Guide to Caring for Elderly Patients in the Emergency Department

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Volume 1, No. 1 April 2002

Lower Gastrointestinal Bleeding in the Elderly Population

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Peer Reviewer: **Will B. Ignatoff, MD,** Emergency Physician, Emergency Room Associates, Carondelet St. Joseph's and Carondelet St. Mary's Hospitals, Tucson, AZ.

As the population ages and more diseases of the elderly manifest themselves, colorectal diseases—and, in particular, lower gastrointestinal (GI) bleeding—present with increasing frequency to the emergency department (ED). The elderly often have co-existing illnesses that increase their morbidity and mortality. It is incumbent upon the emergency physician to be able to stratify these patients according to risk, recognize the presenting complaints of various diseases, and know the most common etiologies for GI bleeding in this population.

Although there are myriad potential causes for lower GI bleeding, the most common etiologies are diverticulosis, angiodysplasia, colorectal carcinoma, polyps, and radiation proctitis.[1] These will be explained in detail, highlighting the pathophysiology, incidence, clinical presentation, and management. Additionally, some of the less frequent causes will be discussed to broaden the differential diagnosis. The cause of lower intestinal bleeding can be identified by routine investigation in 95% of cases.[2]

There are definite changes in the elderly bowel that predispose these patients to GI bleeding. These changes, as well as the most common locations for bleeding sites, will be elucidated.

Diagnostic studies have changed in the past 10 years, enabling the emergency physician and the internist to diagnose the dilemma more accurately. Because most of the diagnostic challenges will take place in an inpatient setting, the emergency physician needs to know which of these patients will require admission and where they should be admitted for appropriate observation.

Pearls and pitfalls regarding the management of rectal bleeding also will be discussed.

— The Editor

Introduction

Lower GI bleeding is an infrequent presenting complaint to the ED physician. For the patient, the occurrence of rectal bleeding or blood in the stool is alarming, and often will prompt immediate consultation with a physician.

Although rectal bleeding or lower GI bleeding is by no means exclusively a disease of the elderly, the preponderance of patients with this complaint will be older adults. Factors contributing to this include natural changes in the colonic mucosa that predispose the patient to diverticula, hemorrhoids, ischemic colitis, and angiodysplasia. There are certain diseases that present with rectal bleeding that almost exclusively are found in the elderly population, such as ischemic colitis, angiodysplasia, and mesenteric ischemia. As with many presenting complaints that in a younger population are usually of a benign origin, the physician must be vigilant regarding the presenting complaint of rectal bleeding in a geriatric patient. Often the etiology can cause considerable morbidity. Because the etiologies are more likely to be vascular, malignant, or ischemic, the incidence of mortality is considerably higher as well. The elderly often have pre-existing, co-morbid conditions that must be factored into the equation, as they will not tolerate blood loss and hemodynamic instability as well as their younger counterparts.

Often, the diagnosis will not be reached in the ED, as it will require invasive procedures to diagnose definitively the cause of rectal bleeding. But, with careful inquiry, prudent diagnostic testing, and a careful consideration of the differential diagnosis pertinent to the elderly population, the emergency physician often will be able to exclude maladies that need immediate surgical correction or thorough evaluation. This enables the physician to decide the disposition of the patient to home, to a medical ward bed, or

to an intensive care unit (ICU) setting, and with confidence contact the appropriate consultant and jointly decide if the patient requires emergent or urgent diagnostic testing and further care.

Elderly patients often require hemodynamic stabilization, which can be tricky if there are other co-morbid illnesses that predispose the patient to fluid overload. Also, elderly patients often do not manifest volume loss as readily as their younger counterparts, so the physician must take extra caution when evaluating hemodynamics in these patients and err on the side of conservative care and admission. Almost all elderly patients with lower GI bleeding will require admission and evaluation of their disease.

There will be instances when the emergency physician will be able to make the definitive diagnosis of the cause of bleeding and will be able to send the patient home safely for follow-up care. Some pearls and pitfalls can assist the physician so that he or she is better able to make that decision. *(See Table 1.)*

As the population ages, we will continue to see an increase in the care of the elderly in the ED, and diagnoses that now are considered uncommon will be seen with increasing frequency. Therefore, it is incumbent upon emergency physicians to be as familiar with deadly, uncommon presentations as possible. The mortality in one series of patients with lower GI bleeding was 5%,[3] although in a more recent study, the mortality of patients presenting with lower intestinal bleeding was 3.6%.[1]

Several pieces of historical information must be sought when questioning patients about their bleeding. These include whether there is a large or small amount of bleeding; whether the blood is bright red or the stools are darker (melanotic or maroon). There may be concomitant abdominal pain. Based on these factors, the emergency physician can narrow the differential diagnosis, appropriately work up these patients, and arrive at a disposition.

By definition, lower GI bleeding occurs distal to the ligament of Treitz. The patient may state that his or her stools are black and tarry (melanotic), or maroon and bloody, or they may report bright red blood in the toilet bowl or on the tissue paper. There is a fair amount of confusion regarding the factors that determine how much blood has been lost and where the loss is occurring to produce certain types of stool. Although eliciting the type of stool from the patient may yield important information to relay to the gastroenterologist, it rarely will assist the emergency medicine physician caring for a patient unless it is bright red blood, which usually indicates a stable anorectal source. Suffice it to say that melanotic stool usually comes from upper GI bleeding, because it takes eight hours for melena to be produced from as little as 60 mL of blood in the bowel. Stools may stay tarry for several days after the bleeding has stopped. Bloody or maroon stools indicate a more brisk and distal bleed, requiring more than 1000 mL of blood and fewer than four hours transit time.[4] Bright red blood usually indicates an anorectal source, although if the bleeding is brisk from a distal site in the colon, the presentation also may be bright red.

Because of atherosclerosis, elderly patients may not manifest orthostatic changes like a younger adult with volume loss. Also, they may become dizzy for a variety of reasons, none of which may be related to their bleeding, so orthostatics may not be very helpful diagnostic tools.[5] However, it will be important to monitor vital signs, which usually will indicate the severity of the bleed and dictate the disposition. Remember also that patients usually grossly exaggerate the amount of blood in the toilet because it is unnerving, and it only takes 10 mL of blood to turn toilet water bloody. Up to 20% of reported lower GI bleeding results from a non-GI source.[4]

Table 1. Pitfalls

- Don't rely on the color of stool to determine the bleeding site. Colors change as transit times vary and blood products break down.
- All that bleeds bright red is not a hemorrhoid. Unless it's bleeding before your eyes, look for another diagnosis.
- Elderly patients may not manifest orthostatic changes from blood loss as readily as their younger counterparts.
- The initial hemoglobin may not be a reliable indicator of the volume of blood lost, as the volume may be contracted.
- Look for other systemic causes if your investigation of the abdominal structures turns up negative and the patient still has abnormal vitals, especially if the rectal bleeding has ceased.
- Drop a nasogastric tube (NGT) in the presence of bright red rectal bleeding.
- Resuscitate the patient aggressively with fluids for abnormal vitals and hypovolemia.
- Order typed blood products.
- Peritoneal signs may take up to 20 hours to manifest.
- Perform a digital exam and anoscopy on a patient with anorectal bleeding.

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Pathophysiology

There are slight changes in the anatomy and physiology of the epithelium of the digestive system due to aging. Connective tissue changes take place in midlife and increase as one ages. The tunica muscularis of the colon is protected by collagenous tissue, and as patients age, less of this fibrous tissue is available to prevent herniations of the intestinal mucosa, which results in pseudodiverticula.[6] Because the elderly have more chronic concomitant diseases and often have sustained a lifetime of environmental insults (i.e., alcohol use, poor diet, smoking, and polypharmacy), it can be difficult to tease apart which factors are most responsible for the changes that take place. Angiodysplasia is more common among the elderly and is thought to be due partly to chronic, intermittent, low-grade obstruction of the submucosal veins, which results in mucosal ischemia. This causes the arteriovenous malformation, whether congenital or not, to bleed more easily from friable mucosa.

The blood supply of the colon is from both the inferior and superior mesenteric arteries. There is contributing vasculature and blood supply from the iliac arteries as well. Because the rectum has a redundant blood supply, it is not as susceptible to ischemic events. Elderly patients have a greater predisposition to tortuosity among their blood vessels, as well as to thrombus and plaque formation. This reduces colonic blood supply. If the main blood supply is reduced by a thrombus, then a low-flow state, such as congestive heart failure (CHF), can result in ischemia. This sets into motion autonomic regulation and the renin-angiotensin system, which causes vasospasm of the arterioles, resulting in arteriovenous shunting in the vascular plexus supplying the mucosal villi. End arterioles that supply the vascular plexus in the submucosal layer are very sensitive to vasospasm. High colonic intraluminal pressures exacerbate this shunting. Ischemia and injury of the villi and mucosa of the intestine will cause sloughing and produce bloody diarrhea or bloody mucus.

The pathophysiology of individual entities will be discussed in more detail.

ED Evaluation

Obviously, careful attention to the patient's vital signs will dictate how aggressively to manage the patient and institute volume replacement. Do not withhold volume resuscitation just because the patient has concomitant diseases that may result in fluid overload. Because the colon can hold a large amount of blood, these patients often have been bleeding for some time before they present, and are more hypovolemic than is evidenced by their vital signs. Excess fluid always can be removed. Replenish bleeding patients with at least a liter of normal saline or lactated Ringer's solution and monitor vital signs for improvement. All patients need a complete blood count, chemistry panel, and coagulation studies. Remember that initial hemoglobin studies may not reflect the degree of blood loss due to volume contraction, and may fall significantly after hydration. The blood urea nitrogen (BUN) level may be elevated, without a concomitant rise in creatinine, due to the absorption of proteins from blood in the GI tract and dehydration.[7] Blood type and screen also should be ordered. If the patient is hemodynamically unstable even after attempts at fluid resuscitation, order four units of cross-matched blood in anticipation of transfusion. If the patient demonstrates resultant chest pain because of anemia or has a strong cardiac history, an electrocardiogram (ECG) should be obtained, as well. A rigid abdomen, inactive bowel sounds, rebound, or guarding indicate the possibility of perforation, so an upright chest x-ray (CXR) is in order, as this is the most sensitive test for elucidating a perforated viscus.[8]

The pertinent history should include such details as how much bleeding has occurred, the color of the stool, preceding weight loss, decreased appetite, fever, abdominal pain, vomiting, hematemesis, syncope or chest pain, prior GI bleeding episodes, prior episodes of diverticulitis or other GI disorders, prior abdominal surgeries, alcohol intake, previous GI tests, and medication use. The patient should be asked about the presence of peripheral vascular disease, atherosclerosis, and aneurysms, which are diseases more commonly found in the elderly.

In many instances, the physical examination of the elderly patient with lower GI bleeding will be relatively benign. Except for the obvious finding of blood on rectal exam, the abdominal exam could well be nondescript. This does not exclude serious illness, as several entities are hallmarked by a benign physical examination. Examine the patient for signs of peripheral vascular disease, such as decreased pulses, loss of hair on lower extremities, or the presence of bruits either on the abdomen or upon carotid exam. Abdominal tenderness to palpation will lead to specific diagnoses, which will be discussed later. Look for signs of liver disease, which could indicate colonic varices. Absence of bowel sounds or rigidity prompt evaluation for a perforation or obstruction. In the elderly population, it is well documented that signs of hypovolemia can be masked by arteriosclerotic disease, rendering the patient less able to exhibit tachycardia and hypotension. So, if these signs are present, the emergency physician should be even more vigilant to the presence of a large bleed or chronic bleed. Remember also that, due to changes in peripheral pain fibers that occur with age, elderly patients may not experience the same amount of tenderness to abdominal palpation as their younger counterparts. In fact, belly exams can be deceptively benign. Peritoneal signs in the elderly population can be delayed for up to 20 hours.[4]

Contrast-enhanced computed tomography (CT) scans of the abdomen have claimed a large role in the evaluation of GI bleeding. Sensitivity for detecting acute ischemic events in the mesenteric vasculature is upwards of 64-82%. Contrast infusion allows delineation of the bowel wall and highlights pneumatosis in the bowel wall and bowel wall thickening. Most thromboemboli in the superior mesenteric artery and superior mesenteric vein are detected easily on CT. CT also can help distinguish the presence of vasculitis. It has a 75% sensitivity for detecting portions of bowel with ischemic colitis secondary to an obstructing neoplasm.[8] Additionally, CT allows for the delineation of other disease processes that may be responsible for the bleeding. In one study, CT identified the pathology of 9% of lesions existing outside the colon. The sensitivity of unenhanced CT following oral contrast was found to be equal to or better than that of a barium enema. Six percent of the barium studies had to be abandoned because the patients were too frail to continue the study. The overall sensitivity was 75% for identifying the pathology associated with colonic complaints. The specificity was 96%, and the negative predictive value was 96%.[8]

Table 2. Most Common Causes of Major Lower GI Bleeding[3]

Diagnosis	%
Diverticulosis	23
Angiodysplasia	11
Undetermined	6
Radiation proctitis	3
Cancer	3
Polyps	2
Ischemic colitis	1
Anticoagulants	1

Table 3. Most Common Causes of Minor Lower GI Bleeding[3]

Diagnosis	%
Diverticulosis	16
Undetermined	5
Polyps	5
Cancer	4
Hemorrhoids	3
Fecal impaction	2
Anal stricture	2
Stercoral ulcer	2
Ischemic colitis	2
Fistula-in-ano	1
Inflammatory bowel disease	1
Radiation colitis	1

Remember that the cause of acute lower GI bleeding may be upper GI bleeding. *(See Tables 2 and 3.)* Although a negative aspirate from a nasogastric tube (NGT) is not definitive for ruling out an upper GI bleed, it is 98% sensitive. In one clinical series, 11% of patients presenting with hematochezia had an upper GI source. Unless the bleeding is minor and self-limited, an NGT should be placed to rule out an upper GI source. Also, the visualization of a potential source of bleeding (with anoscopy for instance) does not exclude the possibility of a more proximal site for bleeding.[7]

Disposition

The American College of Gastroenterology guidelines state that patients with the acute presentation of hematochezia coupled with anemia and unstable vital signs and/or the need for blood transfusion should be admitted. The gray area occurs in patients with a history of rectal bleeding that on exam have brown stool with a positive gastroccult card, chronic bleeding of obscure origin, or obvious self-limited bleeding where the likelihood of a change in vital signs or anemia is low.[7]

One study stratified patients with acute upper or lower GI bleeding into low risk and high risk for adverse outcomes during hospitalization. Patients with comorbid illnesses, a higher BUN, a lower albumin, and a higher prothrombin time fared worse than their cohorts. ICU admission is indicated for this group, as the in-hospital mortality rate was 15%[7].

Another study reviewed 219 admitted patients with acute lower GI hemorrhage, and found a very low mortality rate of 3.6% overall. Only one death was directly related to bleeding. The recurrence of hemorrhage was 9% at one year.[1]

The vast majority of elderly patients presenting with hematochezia will require admission and prompt evaluation. Only if the ED physician is able to concretely establish an anorectal source as a cause, or the bleeding is occult and self-limited in nature, will it be safe to send the patient home. Although mortality overall is low, these patients can mask hypovolemia and, because of comorbid illnesses, are more likely to require monitoring, stabilization, and further immediate care. They also are more prone to morbid complications. *(See Figure 1.)*

Etiologies of Lower GI Bleeding

Colonic Diverticulosis. Classified in the category of painless large bleeding, colonic diverticulosis is a disease of Western culture and our refined, low-fiber diet. Diverticula are rare in patients younger than age 30 and are present in two-thirds of patients 85 years or older.[9]

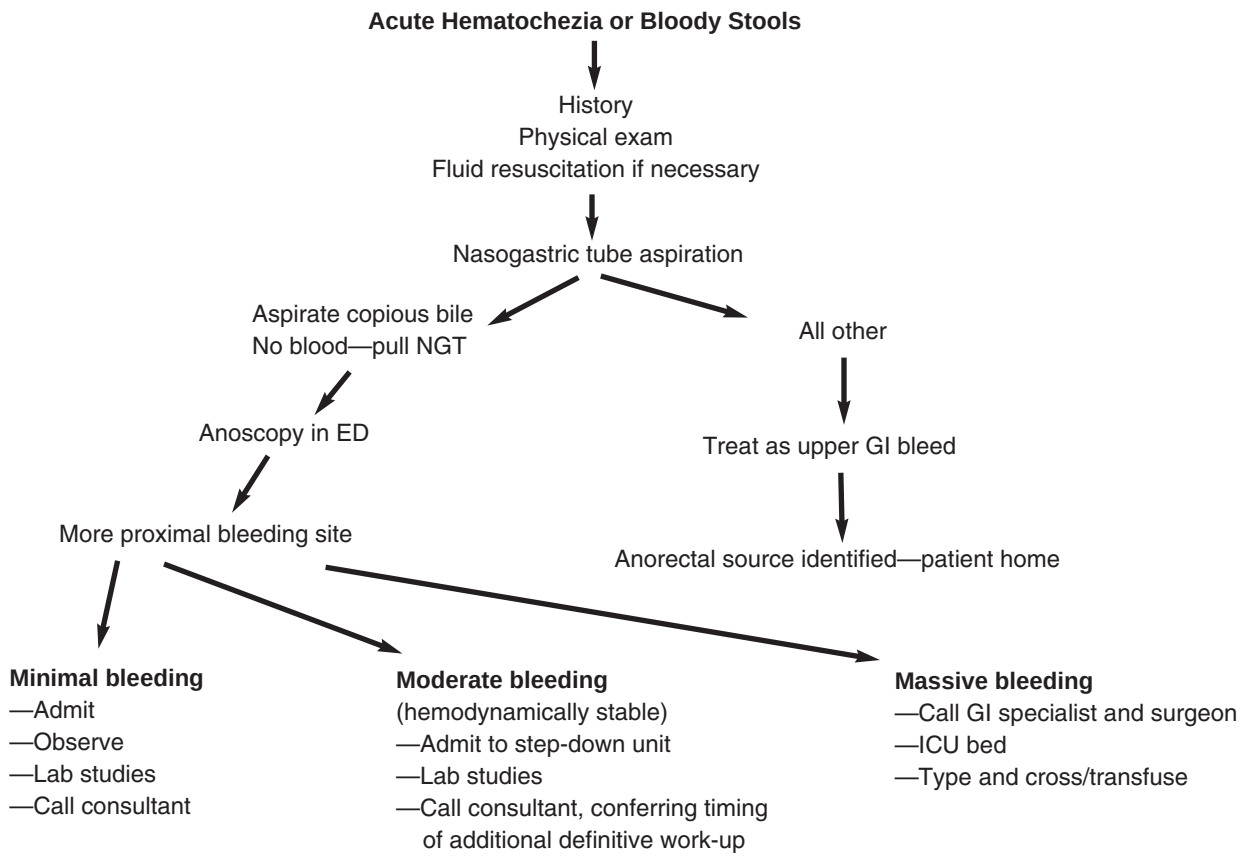
First described by Koch in 1903, diverticulosis originally was thought to be a rare cause of lower GI bleeding.[10] Fifteen percent of diverticula cause bleeding problems, with most bleeding diverticula originating from the right colon and most asymptomatic diverticula located in the sigmoid portion.[11] Significant hemorrhage occurs in 3-5% of those with diverticula. Diverticular disease in one study accounted for 9% of acute surgical admissions.[3] One study reported it to be the most common cause of bleeding in the elderly population, at a rate of 41.6%.[1] *(See Table 4.)* Another study found that out of 112 patients admitted for acute lower GI hemorrhage, two died following massive bleeding; none who underwent surgery died. The median age of those who died was 80 years. One-third of patients admitted with a complication of diverticular disease will be admitted again within five years.[12]

Diverticula are saccular outpockets of the colon, containing all layers of the bowel wall. Bleeding usually is caused by a fecalith within a diverticulum that erodes a branch of the colonic artery. Intimal thickening and medial thinning of the vasa recta as it courses over the dome of the diverticula predisposes a segmentally weakened artery to rupture.[9]

Because diverticula are arteriolar bleeds, they can be quite massive, requiring multiple units of blood for transfusion. Up to one-third of patients have severe hemorrhage with diverticular bleeding. In one study, 42% of 144 patients had massive bleeding, requiring more than 1500 mL of blood transfusion.[13]

Diverticular bleeding is characterized by the passage of voluminous red or maroon blood clots. Patients can present with perforation, obstruction, or fistula formation, in addition to hematochezia.[9] One group reported 42% of patients had only black, tarry stools. Most patients had experienced some GI symptoms prior to their bleeding episode, including constipation, diarrhea, or vague abdominal pain. Many have experi-

Figure 1. Stratification of Patients Presenting with Acute Upper or Lower GI Bleeding[7,14]



enced prior colonic bleeding or prior diverticulitis.[13] The signs of hypovolemia may be very mild in these patients. If perforation (which is present in 11% of patients with diverticulitis) is suspected, a CXR will confirm pneumoperitoneum.[9]

In one review, 76% of lower GI bleeding due to diverticular disease stopped spontaneously.[7] Diverticula rarely rebleed after the episode is finished completely, though a patient may experience rebleeding during the episode in a stuttering fashion. This may require emergent colonoscopy for definitive care in the form of cauterization. If the bleeding is massive or continuous and does not appear to be abating, call the gastroenterologist for an emergent consultation and probable colonoscopy.[14] Up to one-third of all patients with bleeding from diverticula were massive bleeders, defined as needing more than 1500 mL of transfused blood. Patients who needed fewer than four units of blood almost always stopped bleeding spontaneously. Patients who needed more than four units went to surgery.[13,15]

Primary resection was the former treatment for all diverticula bleeding.[10] The advancement of endoscopy and interventional radiology has enabled the physician to use less invasive means of controlling bleeding diverticula. Surgical consultation and resultant hemicolectomy remains the procedure of choice for patients who continue to bleed despite conservative therapy, or who are evidencing significant hemodynamic complications as a result of their massive bleeding.[8] Diverticulitis rarely bleeds.[7] *(See Table 5.)*

Angiodysplasia. One of the most common causes of bleeding in the elderly population, angiodysplasia falls into the category of painless, voluminous bleeding. One-quarter of the elderly population have mucosal vascular ectasias without any evidence of bleeding. They usually are right-sided, colonic lesions, and occur in multiples. A study of 183 patients attempted to differentiate between bleeding diverticula and vascular ectasias. Of the 20 patients angiographically proven to have arteriovenous malformations (AVMs), only two had demonstrable bleeding at the time of the event. More than 80% of the subjects had three or more recurrent episodes of bleeding. They received a mean of five units of blood during hospitalization. The author favored angiography as both a diagnostic tool and, with vasopressor agents infused into the mesenteric circulation at the site of bleeding, a curative tool. Proof of the cause of bleeding was established when the patients received hemicolectomies and no further bleeding was found. For example, if a vascular ectasia was identified angiographically on the right side of the colon but was not actively bleeding, as was usually the case, the information gathered from angiography was used to dictate which portion of the colon should be removed. The patients then were followed prospectively, and if there was no rebleeding episode, the author concluded that the diagnosis and location had been accurate.[3,16]

More recent studies have concluded that angiodysplasia was not nearly as prevalent a cause of GI bleeding as previously was thought, with reports of actual cause closer to 3%.[1] In 15% of

Table 4. Final Diagnosis in Patients Hospitalized for Acute Lower GI Bleed[1]

Diagnosis	N
Colonic diverticulosis	42%
Colorectal malignancy	9%
Ischemic colitis	9%
Acute colitis	5%
Hemorrhoids	5%
Angiodysplasia	3%
Crohn's disease	2%
Stercoral ulcer	3 patients
Vasculitis	2 patients
Infectious colitis	2 patients
Radiation proctitis	2 patients
Polyp	1 patient
Diverticulitis	1 patient
Meckels' diverticulum	1 patient
Unknown	1 patient

patients with angiodysplasia, massive lower GI bleeding is the presenting feature. Because the bleeding is venous and capillary in origin, it usually is less dramatic than diverticular bleeding, which is arterial in origin. Most bleeding stops spontaneously, and mortality is unusual.

As stated above, the elderly are at a higher risk for GI bleeding. Chronic intestinal mucosal changes from intracolonic pressure and low-grade obstruction of the submucosal veins, and consequently, the venous capillary system, cause a loss of patency of the arteriolar-capillary-venular valves, resulting in an arteriovenous malformation.[3] The bleeding site usually is located in the cecum or ascending colon. Patients with cardiovascular disease have an increased predisposition to angiodysplasia, so this historical information should alert the emergency physician to the possibility of angiodysplasia.[17]

One study of 131 patients with obscure GI bleeding for which a cause previously had not been found used visceral angiography and found that many of the patients had both diverticula and vascular ectasias. The culprit was chosen by an educated guess as to which was responsible for the presenting bleed. The author found that patients with colonic angiodysplasia presented more often with rectal bleeding, whereas those with vascular anomalies of the small bowel presented more often as melena. The study showed an overall 84% success rate for identifying all causes of lower intestinal bleeding. The author concluded from his methods that angiodysplasia was the most common cause, accounting for 40% of all patients. Eight percent of his patients had a second possible cause for hemorrhage associated with angiodysplasia. He also suspected angiodysplasias to be the cause of bleeding in 50% of patients presenting with chronic anemia.[2]

Colorectal Carcinoma. In the category of minimally painful, minor bleeding, colorectal carcinoma is more insidious. Colon cancer is the third most common cancer found, disproportionately affecting geriatric patients. One group evaluated 822 patients with colorectal carcinoma and found that 90% of colorectal cancers develop in patients older than 65.[18] Of patients with known tumors, two-thirds will bleed at some point in time from the tumor, and 5% of lower GI bleeding is due to colorectal cancer, according to most studies.

Patients complain of intermittent bright red bleeding, anemia, weight loss, and changes in stools or constipation over a prolonged period of time. There may be a report of vague abdominal discomfort and bloating. Complications include obstruction, intussusception, massive bleeding from an eroded arterial supply within the tumor, perforation, and fistula formation.[19]

An upright abdominal x-ray will help rule out an obstruction or perforation, both of which are not uncommon with colorectal cancer. Provided there are no acute complications present, these patients can be worked up as outpatients, although it must be stressed to the patient the importance of prompt follow-up.[18] If the diagnosis is not definitive, consider admitting these patients for further observation and care.

Although colonoscopy is the modality of choice for discovering these lesions, CT scan of the abdomen is very sensitive for delineating a tumor, particularly if the lesion is complicated by proximal ischemic changes or obstruction.[20]

Ischemic Colitis. Almost exclusively a disease of the elderly, more than 90% of the patients with ischemic colitis are older than 70 years. It is the most common form of GI ischemia and often mimics other inflammatory diseases of the colon, such as inflammatory bowel disease (IBD), infectious diarrhea, and neoplasms.

Classified into occlusive and nonocclusive types, the most common occlusive cause is iatrogenic interruption of the inferior mesenteric artery during aortic surgery. Thromboembolism is another occlusive cause of ischemic colitis. Low-flow states, such as CHF, renal disease and shock, and atherosclerosis, account for the nonocclusive causes. Colonic ischemia is the end result when blood flow is restricted to the colon for any reason. Therefore, the number of inciting agents producing colonic ischemia is quite extensive.[21] It encompasses a spectrum of severity. Reversible, transient, self-limited disease confined to the mucosa and submucosa is the most common ailment; fulminant ischemia, which is transmural and progresses to necrosis, is the most rare and confers the most dismal prognosis. Chronic ischemia, producing ulcerating colitis, strictures, and gangrene, is rare.[22] As opposed to mesenteric ischemia, which requires immediate surgical or aggressive intervention and affects the superior mesenteric artery, ischemic colitis usually affects the inferior mesenteric artery (IMA). Areas of the colon supplied by the IMA have a better collateral and redundant blood supplies, rendering them less sensitive to ischemic insult. Ischemic damage to the tissue is caused by hypoxia during the ischemic period and by reperfusion, which releases free radicals.[23]

Presentation falls into the category of pain with minimal bleeding, usually maroon or bloody stools.[10] Patients usually present with colicky abdominal pain, abdominal distension, and bloody diarrhea. Blood loss usually is minimal, and on physical exam, the patients are only mildly tender. If the bleed is massive enough to cause hemodynamic changes, look for another cause.

Table 5. Bleeding and Pain Associated with Sources of GI Bleeding

Presentation	Large amounts of bleeding/ Pain	Minimal bleeding/ No pain	Minimal bleeding/ Pain	Large amounts of bleeding/ No pain
Diverticulitis				✓
Angiodysplasia				✓
Radiation proctitis			✓	
Colorectal carcinoma		✓		
Colonic polyps		✓		
Ischemic colitis			✓	
Inflammatory bowel disease	✓			
Acute mesenteric ischemia			✓	
Hemorrhoids		✓		
Infectious diarrhea			✓	
Vasculitis		✓		

Thumbprinting, suggesting ulcerations of the mucosal wall, may be seen on abdominal x-ray, but this is rare.[23] A more common finding would be dilated colon, or a gasless abdomen. Late radiographic findings indicative of colic perforation and full mucosal thickness involvement would include free peritoneal air, air within the bowel wall, and air within the portal venous system.[24] A CT scan would be much more helpful in delineating the ulcerative regions and mucosal thickenings, although usually the diagnosis is made by endoscopy. CT allows distinction of an ischemic segment in 20% of cases. Barium enemas, with a sensitivity of 85%,[22] and colonoscopy are much more sensitive for this diagnosis, revealing the clear demarcation of ulceration and normal bowel wall.[25] A high WBC count may help establish the diagnosis of ischemic colitis, although this is nonspecific.

The treatment is conservative, with bowel rest, optimal hemodynamic status, and broad-spectrum antibiotics. Patients usually recover in 24-48 hours. If acute, irreversible ischemic changes have occurred, these can result in gangrene and necrosis of the bowel wall and will require immediate surgical intervention. These patients present with signs and symptoms consistent with perforation and peritonitis.[14] Few patients develop severe cases of ischemic colitis and progress to gangrene, necrotizing colitis, clostridial colitis, and colonic infarction.[21,24] Even fewer require immediate surgical resection, although some require blood transfusions. Mortality attributed to sequelae of peritonitis is high in this small group of sick patients with complications.

The differential diagnosis of colonic ischemia includes infectious diarrhea, IBD, pseudomembranous colitis, colon carcinoma, and acute mesenteric ischemia. All patients most likely will need admission for a complete GI work-up, since it will be difficult to differentiate ischemic colitis from mesenteric ischemia.[25] A stool culture also should be obtained for infectious causes.

Mesenteric Vascular Insufficiency. Ischemia and necrosis of the bowel wall can result from an acute loss of intestinal blood supply secondary to arterial embolus, venous or arterial thrombosis, or nonocclusive or low-flow states. Mesenteric ischemia causes minor bleeding with major pain. The average age of patients affected is 65 years; most patients have comorbid illnesses, such as arteriosclerotic heart disease, peripheral vascular disease, diabetes, and hypertension.[15] The mortality is as high as 90% in these patients, due to the combination of delayed diagnosis, co-existing illnesses, frail health, and resultant bowel necrosis.[26]

The highest risk population are those patients with CHF, cardiac arrhythmias, valvular disease, arteriosclerotic heart disease, hypovolemia or hypotension, recent myocardial infarction, or history of emboli in the extremities. Sixty-six percent have evidence of peripheral vascular disease.[22,27] The chronic mesenteric venous occlusion usually presents as weight loss, and post-prandial angina, and the pain resembles the squeezing pain of claudication. The pain is much more insidious at onset and more moderate in nature. The classic historical presentation of acute embolism or thrombosis is a patient in severe abdominal pain who looks sick, with a relatively benign physical exam.[28]

Acute embolic occlusion may present with bloody diarrhea and vomiting, and will include rapid onset of severe abdominal pain and a history of either prior embolic events or a cause such as atrial fibrillation, valvular prosthesis, or arrhythmia.[26] Because the pathology is one of sudden restriction of blood flow without collateral circulation, intense intestinal spasm results, manifesting as acute onset of violent unremitting abdominal pain with forceful vomiting and diarrhea without significant physical findings. In a patient with a high WBC count and a prior embolic event, this diagnosis should jump to the top of the physician's differential list. Arterial embolic events account for 75% of acute mesenteric ischemia.[25,28]

The physical exam on most of these patients is non-diagnostic with the complaint of pain far out of proportion to their abdominal physical findings. Occlusions usually don't present with rectal bleeding, although in one report, one-third of patients presented with grossly bloody stools.[25]

The mortality of mesenteric venous thrombosis hovers around 20%. The percentage of cases attributable to mesenteric venous occlusion is 5-15%. It is more likely to be reversible than arterial occlusion, accounting for its lower mortality.[29] The mortality of superior mesenteric arterial occlusion surpasses 50-80%.[28]

Acute thrombotic occlusions tend to occur in older patients with peripheral vascular disease. These patients usually present with severe cramping, abdominal pain, and often, bloody diarrhea. They generally have fewer physical findings, a higher WBC count, and more peripheral arterial occlusions than other patients with acute abdominal pain.[26]

Non-organic causes or low-flow states would be an abnormal blood flow from another vascular source that limits the blood flow to the mesentery. Examples of this would be CHF, renal failure, sepsis, and hypovolemia. This is the most lethal cause of mesenteric ischemia, with a mortality of 90%.[27] These patients often present with acute onset of pain without defecation or with no urge to defecate.

Diagnosis rests largely on maintaining a high level of suspicion, since definitive diagnostic studies are intensive and can be difficult to obtain, and physical exam and ordinary studies usually are non-specific and not helpful. Because of its non-specific complaints and rarity, it is a difficult diagnosis to make before the patient becomes moribund. The first 24 hours are critical, with a survival rate of 60% if discovered in this time period.[27] Once abdominal signs, such as peritoneal findings, become apparent, bowel necrosis already has taken place. The late occurrence of ileus, abdominal distension, shock, and sepsis is a bad prognostic indicator.

One researcher advocated highly aggressive management with early angiography to identify the pathology and use of local vasodilators to interrupt persistent splanchnic vasoconstriction. It is the persistent vasoconstriction of the splanchnic vasculature that is responsible for the majority of bowel necrosis. With this approach, he increased the survival rate to 54% vs. the usual 20-30% reported in other literature.[27] Although angiography is the gold standard for definitive testing and therapy, it often is not performed, either because the diagnosis is not suspected clinically or because the patient requires emergent surgical intervention. CT has appeared in the literature as a viable option for diagnosing thrombotic and occlusive events with good accuracy and sensitivity. In one series, CT had a 93% sensitivity for detecting superior mesenteric venous thrombosis.[22] CT with contrast often is much easier to obtain in the ED.[29] Unfortunately, often the bowel will be dying while studies are taking place and the physician is trying to figure out the etiology of the pain. Remember: Time is bowel. A normal, plain abdominal film in a high-risk patient is compatible with the diagnosis of ischemia, although 80% of plain films in one study revealed ileus or free abdominal fluid.[26,27] Unfortunately, by the time a plain film is diagnostic, with thumb-printing or dilated segments of colon or small bowel indicative of fluid collection, there already is bowel infarction and necrosis.[27] Contrast-enhanced CT scans, useful in the diagnosis of mesenteric venous thrombosis, reveal a high density mesenteric vein wall with a central mesenteric clot. In several studies, the use of CT scans and magnetic resonance imaging (MRI) enabled the early detection of clots, obviating the need for surgical resection.[25] The sensitivity of the CT scan for diagnosing a mesenteric arterial occlusion ranges from 37-80%. Conversely, almost all mesenteric venous thrombosis can be detected by CT.[30]

Once diagnosed, the patient requires emergent laparotomy, unless the cause is a low-flow state, which needs to be reversed systemically or locally with a vasodilator. If this diagnosis is suspected and there are risk factors present, and as diagnostic studies are done to corroborate the diagnosis, contact the gastroenterologist immediately for consultation, as well as the general surgeon.

Anorectal Causes. Anorectal causes of GI bleeding include: hemorrhoids, fissures, fistula, abscess, prolapse, proctitis, and impaction. These usually cause minor bleeding. Hemorrhoids are found in 70% of the geriatric population, and are the most painless common cause of minor GI bleeding.

Internal hemorrhoids occur above the pectinate line in the rectum and appear as varicosities of the hemorrhoidal venous capillary plexuses covered with mucosa. They usually present with painless, bright red bleeding from the rectum. Hemorrhage is possible, though rare, and usually can be treated with endoscopic intervention and cauterization.[31]

External hemorrhoids originate below the pectinate line. Covered in skin, they usually present with painful bleeding and often are visible on anoscopy. Although hemorrhoids can bleed profusely, usually the bleeding is self-limited and minor in nature, obviating the need for an extensive work-up beyond an anoscopy. The patient usually will complain of bright red, painful bleeding.

Anal fissures are a common cause of anorectal pain and bleeding. They can be caused by hard stools, diarrhea, infection, and idiopathic causes. Most fissures or ulcerations of the anal squamous epithelium occur in the posterior midline from the anal verge to the dentate line. Diagnosis usually is accomplished by careful inspection of the anal canal, which may require sedation because of concomitant pain. Medical management includes a high-fiber diet, bulk laxatives, and warm sitz baths. Follow-up care is provided by the primary care physician.

Anal tumors are rare, accounting only for 1-6% of all anorectal tumors. The mean age of patients with these cancers is 60-70 years. Presenting symptoms include painless rectal bleeding, painful defecation, anal pruritis, discharge, and a sensation of a rectal mass. Easily overlooked, the diagnosis often is missed initially, delaying appropriate treatment. In the elderly population, the examining clinician must perform a digital exam and anoscopy, looking for any suspicious lesions. A high index of suspicion must prevail in this population. If any anorectal masses or ulcerations are detected, these patients should be referred to a surgeon for further evaluation. Local surgical excision has an excellent survival rate.[32]

Rectal prolapse usually is mild and easily reducible or self-reducing, and treatment is on an outpatient basis with referral to a general surgeon. Rectal prolapse is more common in elderly women, as their pelvic musculature has been weakened by child-bearing. When a patient strains to defecate, the force pushes the rectal mucosa outside the anus, producing pain with defecation and mucoid, bloody discharge with stools.[33]

If the prolapse is not easily reduced by the emergency physician manually, or the tissue appears necrotic or blanched, consider an incarcerated prolapse, which requires surgical intervention to prevent mucosal necrosis.

Radiation proctitis, caused by radiation therapy weakening the mucosa and its supplying vasculature, can be the etiology of bloody rectal discharge. Commonly found in those who have received radiation therapy, the bleeding can occur during radiation therapy and for up to six months after therapy has concluded.

Upper Gastrointestinal Sites. In one clinical series, 11% of patients who presented with a lower GI bleed had an upper GI source. Therefore, placement of an NGT should be done in all patients with significant lower GI bleeds. Because blood from a duodenal source may not reflux into the stomach, an aspirate negative for blood doesn't positively exclude an upper bleed, although the test is 98% sensitive. The GI consultant most likely will perform upper endoscopy on patients with hematochezia.[7]

Idiopathic Inflammatory Bowel Disease. In the category of painful, minor rectal bleeding, 5-10% of all cases of inflammatory bowel disease in patients age 65 and older are caused by Crohn's disease or ulcerative colitis, both of which are long-standing conditions. The hallmark of presentation is bloody

diarrhea and weight loss, with abdominal cramps and, sometimes, fever. Occasionally, patients may present with constipation and rectal bleeding. Usually, the onset is insidious, with vague abdominal cramps and discomfort and gradual changes in the frequency and character of stools. Gross blood in the stool is a universal finding.

The proportion of elderly patients who develop Crohn's disease after age 60 is 16%. Seventy percent of patients with Crohn's disease ultimately will require surgical resection of the diseased bowel.[34]

Ulcerative colitis. Ulcerative colitis appears for the first time in elderly patients in 12% of cases.[35] In the case of ulcerative colitis in the elderly, the predilection for disease is proctitis and proctosigmoiditis.[35] Therefore, on anoscopy aphthous ulcers and rectal and anal inflammatory mucosal changes may be seen with ulcerative colitis.[10]

Crohn's Disease. A characteristic physical finding in Crohn's disease is right lower-quadrant abdominal pain, representing inflamed bowel and mesentery, and sometimes an abscess, although it has been found in elderly patients to have a predilection for the left lower quadrant.[35] If the presentation is one consistent with inflammatory changes, fever, marked tenderness, and leukocytosis, CT scan of the abdomen is an excellent tool to differentiate the etiology of the pain. The differential diagnosis would include radiation proctitis, infectious diarrhea, lymphocytic colitis, ischemic colitis, diverticulitis, and colon cancer.

In mild cases, outpatient therapy is warranted, and topical steroids, sulfasalazine, and broad spectrum antibiotics that include anaerobic coverage are acceptable forms of treatment. If the patient is otherwise stable and not evidencing marked lab abnormalities, marked tenderness, or toxicity, he or she may follow up as an outpatient with the gastroenterologist.[34] Consultation with a gastroenterologist is advisable before beginning empiric treatment on these patients. This also will ensure prompt outpatient referral.

Zebras. Unusual etiologies ("zebras") represent 5% of all causes of lower GI bleeding. They include the following conditions:

Rectal ulcer—A chronic and benign condition that causes rectal bleeding, stool with mucus, and tenesmus, patients with a rectal ulcer usually will complain of difficulty with defecation and straining, often utilizing digital disimpaction to assist defecation. Most bleeding is minor and probably will be mistaken for an internal hemorrhoid, which is fine in this instance, since the diagnosis is made by sigmoidoscopy and the patient in either case will be worked up as an outpatient.

Infectious diarrhea—Commonly found in the elderly, infectious diarrhea may be due to viruses, bacteria, or parasites. If the diarrhea is bloody or mucoid, obtain a stool culture and blood culture before empiric treatment begins. Patients usually present with crampy abdominal pain, fever, bloody diarrhea, and hematochezia.[14] Infection caused by *Clostridium difficile* can cause pseudomembranous colitis, and must be kept in mind if a patient has been on broad-spectrum antibiotics. It is of particular concern in nursing homes, as it spreads rapidly through sequestered populations. It is thought by some to be the most common cause of diarrhea in the geriatric population.[35,36]

Radiation proctitis—Under the category of minor painful bleeding, radiation proctitis can occur shortly after radiation therapy or months later. It is due to the vascular changes associated with radiation, as well as ischemia of the delicate mucosal tissue. Proctitis (characterized by rectal bleeding, crampy abdominal pain, and bowel disturbances) is the most common presentation. A careful history probably will deduce this entity. Patients may be worked up on an outpatient basis, provided they are stable.[25]

Colonic polyps—A common finding in the elderly population, colonic polyps may be asymptomatic in many cases. These will be discovered by colonoscopy and biopsied. From an ED standpoint, the bleeding usually is not severe, presents as hematochezia, generally requires admission and a work-up, but will not render the patient hemodynamically unstable or require transfusions.

Constipation—Common in the elderly population for a variety of reasons, chronic constipation can cause excessive pressure on the mucosal walls as well as mucosal irritation that causes GI bleeding.[37] Severe constipation can cause abdominal pain, fecal incontinence, infection, and toxic megacolon. Stercoral ulcer, which is a colonic ulcer secondary to inspissated fecal material eroding the colonic wall, is a secondary complication of constipation and accounts for a small number of bleeding episodes in various studies.

A careful history and an abdominal film revealing large amounts of stool will lead to the diagnosis. These patients need disimpaction, whole-gut irrigation with non-absorbable plyethylene glycol (GoLytely), and enemas (mineral oil is preferred) until the fecal impaction has been dissolved and evacuated.[38] Obviously, if the patient is unstable, has a volvulus from toxicity, or has a high fever, he or she will require admission and whole bowel evacuation, as well as antibiotic therapy.[39]

Colonic varices—Colonic varices are found in 0.07% of GI bleeds. The most common cause is portal hypertension due to liver disease.[25] In almost all cases, the bright red bleeding is intermittent, but often is massive. Obviously, seeing massive amounts of bright red blood pouring from the patient will prompt the emergency physician to admit, type and cross, and call the gastroenterologist. The giveaway to diagnosing this entity will be the history of liver disease.

Diversion colitis—Seen with colostomies and stomas 3-36 months after surgery, in diversion colitis the bowel wall distal to the anastamosis becomes inflamed and produces purulent and sometimes bloody discharge into the anus. The patient complains of abdominal pain, pelvic pain, low-grade fever, tenesmus, and bloody or mucoid discharge. It is seen in up to 50% of patients with a diverting colostomy. The pathogenesis is thought to be related to the diversion of the fecal stream, causing an imbalance in the colonic flora and starvation of the colorectal epithelial cells, which then necrose and bleed. The cure is reanastamosis: Call the surgeon. These patients almost always are clinically stable, making admission optional.[40]

Vasculitis—Found in the category of minor bleeding with pain, vasculitides are characterized by inflammation and necrosis of blood vessels and are classified by the size of the affected vessels. The GI tract is involved in 20% of patients with vasculitis.[25] Polyarteritis nodosa affects small vessels. GI symptoms are due to visceral ischemia and are marked by abdominal pain, nausea, anorexia, diarrhea, and, if ischemia ensues, GI hemorrhage. Churg-Strauss syndrome affects larger vessels, but the presenting symptomatology is the same. Henoch-Schonlein purpura

affects small vessels, causing abdominal pain in 20-69% of patients, 50% of whom present with melena. Systemic lupus erythematosus can cause inflammation in any organ system, the intestinal tract being no exception. Patients can develop ulcerations, hemorrhages, and infarctions. High morbidity and mortality are associated with bowel vasculitis.

Small intestinal ulceration—Small intestinal ulceration is uncommon, but causes considerable morbidity and mortality. A whole litany of etiologies is included, but anything that can cause an ulceration and subsequent abdominal pain, perforation, intestinal obstruction, and hemorrhage is fair game. The causes vary from celiac sprue to Crohn's disease to syphilis and typhoid fever. Although most of these lesions can be worked up on an outpatient basis, the patient obviously will require admission in the presence of obstruction, bleeding, or perforation. Most of these patients will present to their primary clinicians with insidious symptomatology and will not present to the ED unless they have a complication.[25]

Small bowel vascular anomalies—Thirty-eight percent of patients in one series had a lesion in the distal duodenum or jejunum, presenting as obscure bleeding. Vascular ectasias were the most common.[7]

Meckels' diverticulum—In the category of painless bleeding, Meckels' diverticulum is a diverticulum of the ileum located within 100 cm of the ileocecal valve and is the most common congenital intestinal abnormality, affecting 1-3% of the population. Most Meckels' diverticula remain asymptomatic throughout life, with the majority of complications and bleeding occurring in childhood. Bleeding and obstruction are extremely rare in the adult population. It presents with hematochezia and would be treated like other diverticula from an ED perspective, since it would be impossible, from our perspective, to differentiate one diverticular bleeding source from another.[25]

Gastric vascular anomalies—Painless, brisk bleeding characterizes gastric vascular anomalies. More than likely, these also would cause upper GI bleeding. Patients may present with hematochezia if the bleeding is brisk, which is another reason to insert an NGT with lower GI bleeding. GI vascular anomalies are responsible for 2-8% of all cases of bleeding.[41]

Diagnostics in the ED and Beyond

Colonoscopy. Endoscopy is the test of choice for the evaluation of lower GI bleeding, and the yield for positive results is more than of 80%.[7] One researcher evaluated 304 patients with rectal bleeding, and found that 45% of patients with normal barium studies had significant lesions found on colonoscopy. Cancer, telangiectasias, inflammatory bowel disease, and polyps were the most common findings. The overall incidence of finding significant lesions by colonoscopy is 41.5%.[42]

Barium Enema. Barium enemas are only 50% sensitive in identifying the source of bleeding, and no longer are advocated as really useful diagnostic tools. They will miss 20% of all cancers and up to 30% of polyps larger than 5 mm. They also are poorly tolerated by the elderly population, and often must be aborted before the tests are complete.[42]

Angiography. Although older literature stated that angiography was the procedure of choice both for identification of the lesion and therapeutic value, it clearly has fallen by the wayside in the GI literature, replaced by colonoscopy as a more definitive test. It now is advocated for patients with such massive bleeding that nothing can be seen with an endoscope, or when colonoscopy has not identified the source. The diagnostic yield is 40-70% and the complication rate is higher than with colonoscopy.

Sigmoidoscopy. Sigmoidoscopy can be used as the initial diagnostic tool for evaluation of hematochezia, which has a greater likelihood of an anorectal disorder as the etiology. Although some EDs have rigid sigmoidoscopy, the ability to utilize such a device is not the standard among ED physicians—leave it up to the GI consultant.

CT Scan. CT is an excellent test for the evaluation of abdominal complaints in the elderly. Some authors recommend CT as the diagnostic tool of choice for diverticulitis and diverticulosis. It is quite sensitive for detecting ischemic colitis; the most common finding is bowel wall thickening, although this is non-specific. It also can detect mesenteric vein thrombosis, mesenteric or portal venous gas, and other abnormalities.[30] The sensitivity of CT scans for this purpose is 64-82%. The sensitivity of detecting a strangulated obstruction ranged from 83-100%.[8] It reportedly also is useful for differentiating tumoral vs. ischemic segments of bowel in 75% of cases. When contrast is given overnight and CT is performed the next day, the sensitivity for detecting the etiology of colonic complaints was 75%. The negative predictive value was 96%. Although this may be more optimal than giving patients oral contrast in the ED and scanning them within two hours, immediate CT scanning still is relatively sensitive.[20] In addition, perhaps one of the greatest values of CT scanning is that it provides information on other possible etiologies for an abdominal complaint.

MRI. MRI is excellent for detection of bowel wall infarction and thickening, intramural pneumatosis, mesenteric or portal venous gas, or mesenteric occlusion.

Labeled RBCs. Usually, technetium scans are utilized. Scans in lower GI bleeds are positive 26-72% of the time. The literature is quite diverse on the opinion of whether a positive scan is the site of true anatomic bleeding. Therefore, the usefulness of the test, particularly in an acute setting, is questioned.

Anoscopy. Anoscopy is useful in the ED for identifying distal lesions, such as hemorrhoids and fissures. Never attribute the bleeding to a hemorrhoid unless it is bleeding during the procedure.

NGT. Drop an NGT with lower GI bleeding; 11% of lower GI bleeding will be caused by upper GI bleeding. NGT is 98% sensitive for detecting an upper GI source. If no blood or bile is aspirated, you cannot determine if the test is negative or positive. If the patient is passing bright red blood in front of you and the aspirate is bilious and the gastrocult is negative, it's not an upper GI bleed.

Plain Abdominal Films. Plain films do not offer much bang for the buck. They are best for detecting ileus, megacolon, small bowel obstruction, or constipation and fecal impaction, and are too insensitive to detect ischemia, edema of the bowel wall, source of bleeding, etc.

Conclusion

Acute lower GI bleeding in the elderly population may be associated with significant morbidity and mortality. Pay close attention to the patients' vital signs, comorbid illnesses, avail-

ability of follow-up care, toxicity, and duration of bleeding. These factors will guide admissions, as well as how intensively patients should be monitored if admitted.

Give volume generously to patients who appear hypovolemic, unless otherwise contraindicated. Once rehydrated, recheck the hemoglobin, as it may have been falsely elevated from volume contraction. A chemistry panel will alert you to chronic or large amounts of blood in the GI tract, as evidenced by an elevated BUN. Coagulation panels will direct anticoagulant therapy or reversing anticoagulant therapy. An elevated WBC count will alert you to the possibility of an infection, although there can be demargination.

Involve your consultants early, as they may want to plan for a colonoscopy sooner rather than later. They also may have a specific diagnostic tool in mind, such as angiography or contrast CT. Depending on the probable lesion, the first consultant most likely is going to be the gastroenterologist, who will want to endoscope the patient emergently or urgently, depending on the severity of the bleed. If you suspect diverticulosis with massive bleeding, these patients need stabilization and emergent surgical intervention. Likewise, if presented with peritoneal signs and symptoms, elevated WBC counts, or perforation, call for immediate surgical intervention. Severe abdominal pain in a patient with risk factors for an embolic event and an otherwise nonspecific exam and lab studies merits consultation with a surgeon and probable CT scanning to look for a mesenteric occlusion or ischemia.

Use anoscopy as an adjunct. If the hemorrhoidal bleeding is not apparent, don't attribute the GI bleed to a hemorrhoid. Remember that in the elderly, postural vital signs are pretty useless, and these patients can be delayed in how long it takes them to evidence volume loss with compensatory mechanisms.

In these days of managed care and decreasing admission rates, you may be asked to send some of the minimally symptomatic patients home. Most of the literature suggests that patients with lower GI bleeding with stable vital signs, who are nontoxic in appearance, and who have a normal hemoglobin not requiring transfusion, have a low risk of morbidity and mortality. An upper GI cause must be ruled out first. Additionally, it is imperative that the patient have close follow-up and a GI workup. Conservative treatment would dictate admission for the acute onset of hematochezia, as this is the most common presenting symptom for lower GI bleed. This is not the disposition for patients with chronic bleeding of obscure origin, self-limited rectal bleeding, or occult positive stool. Most of these patients can be sent home safely for an outpatient evaluation.

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Physician CME Questions

To earn CME credit for this issue of Geriatric Emergency Medicine Reports, *please refer to the enclosed Scantron form for directions on taking the test and submitting your answers.*

1. Bright red bleeding usually is due to:
   A. diverticulitis.
   B. diverticulosis.
   C. ischemic colitis.
   D. hemorrhoids.

2. Severe pain with a benign physical exam raises suspicion for:
   A. acute mesenteric ischemia.
   B. diverticulosis.
   C. ischemic colitis.
   D. Crohn's disease.

3. Crampy abdominal pain and bloody diarrhea is consistent with:
   A. ischemic colitis.
   B. idiopathic inflammatory bowel disease.
   C. infectious diarrhea.
   D. diverticulitis.
   E. All of the above

4. Painless rectal bleeding is consistent with:
   A. internal hemorrhoids.
   B. angiodysplasia.
   C. colon cancer.
   D. diverticulosis.
   E. All of the above

5. Which of the following is mainly a disease of the elderly?
   A. Acute mesenteric ischemia
   B. Diverticulosis
   C. Ischemic colitis
   D. All of the above

6. Which of the following is correct in initially assessing the elderly patient?
   A. The color of the stool does not always indicate where the bleed started.
   B. The initial hemoglobin may be elevated falsely due to volume contraction.
   C. An NGT should be dropped unless the bright red bleeding is self-limited and minor.
   D. All of the above

7. Common pitfalls in evaluating the elderly patient include:
   A. not resuscitating with fluids for fear of fluid overload.
   B. not performing a type and cross of blood products.
   C. attributing bright red bleeding to a hemorrhoid without visualizing the bleed.
   D. using orthostatic vital signs as an indicator of volume loss and status.
   E. All the above.

8. Massive painless bleeding is consistent with:
   A. ischemic colitis.
   B. diverticulosis.
   C. inflammatory bowel disease.
   D. stercoral ulcer.

9. The modality of choice for discovering cancerous lesions of the colon is:
   A. CT scan.
   B. colonoscopy.
   C. upright abdominal x-ray.
   D. barium enema.

10. An excellent initial diagnostic tool for evaluation of lower GI disorders is:
    A. MRI of the abdomen.
    B. CT scan of the abdomen.
    C. labeled RBCs technetium scan.
    D. angiography.

CME Objectives

Upon completing this program, participants will be able to:

- Quickly recognize or increase index of suspicion for specific conditions in the elderly patient;
- Understand the difference in treatment methods between the older adult and elderly patient and a younger adult patient;
- Understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- Perform necessary diagnostic tests correctly and take a meaningful patient history that will reveal the most important details about the particular medical problem discussed;
- Apply state-of-the-art therapeutic techniques (including the implications of the pharmaceutical therapy discussed) to patients with the particular medical problem discussed;
- Understand the differential diagnosis of the entity discussed, and likely and rare complications that may occur; and
- Provide patients with any necessary discharge instructions.

BIOTERRORISM WATCH

Preparing for and responding to biological, chemical and nuclear disasters

Building a bridge over the abyss: Will bioterrorism help bring disjointed health system together?

Getting in same boat as 'tsunami' of money builds

Diverse and disjointed, the nation's public health and clinical settings have education needs and communication gaps that must be bridged if the system is to improve its response to bioterrorism, a group of consultants recently told the Atlanta-based Centers for Disease Control and Prevention (CDC).

The CDC's national center for infectious diseases is holding a series of meetings to assess the lessons of last year's anthrax attacks and begin to close the long-standing breach between public health and clinical medicine.

The gap may stem from differences between the private and public health care systems, both of which are fragmented and highly variable by geography and urban vs. rural settings, according to a CDC draft summary of the Jan. 7, 2002, consultants' meeting, which was obtained by *Bioterrorism Watch.*

Seeking collaboration

"There was lot of [discussion] about the gap between public health, private practices, and hospitals and how to bridge that gap and make things more collaborative," said **William Scheckler**, MD, a consultant at the meeting and hospital epidemiologist at St. Mary's Hospital in Madison, WI. "[We need] to reduce some of the redundancies in the systems both in terms of preparing and education."

Scheckler also is a member of the CDC Healthcare Infection Control Practices Advisory Committee (HICPAC), which met Feb. 25-26, 2002, in Atlanta.

Scheckler gave a report on the consultants' meeting, telling HICPAC members that the CDC had input from a broad range of bioterrorism groups and clinical specialties. There is a wealth of information scattered among these groups and on numerous web sites, he noted. For example, a dermatology group at the meeting has photographs of skin lesions that could be a good resource in an investigation of cutaneous anthrax.

"When an outbreak occurs, the same questions [arise]: What do people need to know? What is the best way to get out the information?" he said. "There should be one best-practices web page that you can go to."

The CDC currently operates several different clearinghouses for information as well as different public inquiry numbers. The agency now is considering the possibility of centralizing its clearinghouses and public inquiry services, the CDC report states.

"During the anthrax crisis, the CDC public inquiry system was overwhelmed, and therefore the agency set up a new system during the outbreak," the CDC report continues.

In addition, the CDC found that "during the attacks, the amount of information on anthrax increased from virtually nothing to an overwhelming number of e-mails, web sites, printed

This supplement was written by Gary Evans, editor of *Hospital Infection Control*. Telephone: (706) 742-2515. E-mail: gary.evans@ahcpub.com.

documents, and other materials. Much of this information and work was duplicative."

The consultants suggested that the CDC devise a strategy to centralize information development activities and then distribute the product, rather than having so many individuals working independently. **(See CDC action items, below right.)**

Linking the data base

Regarding public health and clinical partnerships, a relatively simple system of linking health departments with hospital emergency departments (ED) was described by HICPAC member **Alfred DeMaria Jr.**, MD, state epidemiologist at the Massachusetts Department of Public Health in Jamaica Plain.

Under the program, participating hospitals in the Boston area report their daily number of ED visits to the health department. The numbers are compared against emergency visits a week earlier and on the same date a year prior to detect surges that might suggest a bioterrorism event, he said.

The information is easily obtainable by the hospitals and can be submitted electronically to the health department without extra work. That is important because bioterrorism surveillance systems that are labor-intensive will likely falter as vigilance inevitably wanes, DeMaria noted.

The system has provided the secondary gain of improving communication between public health and clinical sectors. The threshold for investigation occurs at two orders of magnitude above baseline, which thus far has occurred with influenza ED visits and those associated with a large trauma event such as a bus crash, he said.

Sometimes, the threshold will be reached simply out of random chance, as ED visits increase for no single reason. "The question is, we don't know how big an event has to happen [to be detected]," DeMaria said.

The CDC is interested in such bioterrorism surveillance systems, and also may seek to apply its existing hospital sentinel networks, including the National Nosocomial Infections Surveillance system, said **Steve Solomon**, MD, chief of special studies activity in the CDC division of healthcare quality promotion.

National concerns about patient safety and bioterrorism have created a "tsunami of money" to address such issues, Solomon told HICPAC members.

"We have a lot of concerns about the surveillance and response needs," he said. "We are seeking a small trickle of that tidal wave of funds."

Ultimately, the CDC may help shape a national system or contribute to a "mosaic" of systems that track surrogate markers such as severity of illness in "real time," he said.

The research and development needs for such a system are in the ballpark of $120 million to $180 million, which may be available in the current climate over the next four or five years, he said. There is considerable interest being expressed from health care-related industries in partnering with the CDC on such efforts.

"They are standing in line," Solomon told HICPAC members. "The phone is ringing off the hook. We are trying to figure out who is the best partner." ■

CDC gets plenty of advice for action

Clarify roles, make info user-friendly

A recent consultants' brainstorming session on education and communication needs for bioterrorism resulted in numerous suggestions to the Centers for Disease Control and Prevention (CDC) in Atlanta. Some of the points of information and recommended items for action included:

- ✔ Strengthen the CDC Health Alert Network e-mail notification system to ensure that all state and local health departments are involved.
- ✔ Make surveillance and reporting as automatic as possible, and do not depend on the clinician to initiate the report quickly.
- ✔ Because the CDC is recognized as an authoritative source for information provided through *Morbidity and Mortality Weekly Report* and press releases, the CDC web site should be changed to make it more user-friendly.
- ✔ Ruling out disease is the most important clinical issue, rather than identifying new cases of disease.
- ✔ Clarify roles when a criminal investigation is going to occur during a public health emergency.
- ✔ Develop a prototype disaster plan for use by communities and make it readily available.
- ✔ The cacophony of information is a problem. For clinicians, an appropriate tool would be a page of bulleted information necessary for the

clinical setting. This should be provided in addition to baseline information.

✔ The CDC smallpox plan is a good model for allowing outside review during the development phase.

✔ Identify additional ways for using communication technology, particularly e-mail, to link local resources together. ■

Was anthrax mailer a bioweapons researcher?

'This has military lab stamped all over it'

Given the difficulty of creating high-quality anthrax in a civilian research lab, the original source of the *Bacillus anthracis* that killed five people last year was likely a U.S. bioweapons facility, the president of the American Society of Microbiology (ASM) tells *Bioterrorism Watch*.

"Given the high quality of the preparation that was used, this has military laboratory stamped all over it," says **Abigail Salyers**, PhD, ASM president and a professor of microbiology at the University of Illinois in Urbana-Champaign.

The U.S. bioweapons program was formally disbanded as part of a global treaty in the early 1970s, but many military labs remained open for "biodefense" research to counter bioterrorism, she says. "These anthrax spore preparations last for decades," Salyers says.

Anthrax mailer is 'criminal, but not stupid'

The atmosphere of a university research lab is too open and freewheeling for someone to produce anthrax undetected, she says. Salyers' personal theory is that someone who worked in a military bioweapons laboratory stole the anthrax, possibly years ago.

"It's anybody's guess as to what is going on here, but I would be astounded if this came out of a university laboratory," she says. "[This person] is crazy, criminal, but not stupid. I can't imagine that anybody who was going to do that would take the trouble and risk of trying to do that in a university laboratory environment."

In a related matter — despite a published report to the contrary — the Federal Bureau of Investigation denies it has narrowed its anthrax investigation to a former scientist in a U.S. bioweapons lab.

A FBI spokeswoman at the agency's national office in Washington, DC, told *Bioterrorism Watch* that the agency has not identified "a prime suspect" in the hundreds of interviews it has conducted in the investigation.

A story that was published in the Feb. 25, 2002, *Washington Times* reported that the FBI's search was focusing on a former U.S. scientist who worked at a government bioweapons laboratory. The government's chief suspect, the article reported, is believed to have worked at the U.S. Army Medical Research Institute of Infectious Diseases at Fort Detrick, MD, which has maintained stores of weapons-grade anthrax. No charges had been filed as this issue of *Bioterrorism Watch* went to press.

Do you know this person?

Salyers described her theory on the case — before the newspaper report was published — when the FBI openly solicited help from the ASM in the investigation. In a message appealing for help from ASM members, **Van Harp**, assistant director of the FBI's Washington, DC, field office, said "a single person" is most likely responsible for the mailings. "It is very likely that one or more of you know this individual," he told ASM members.

A $2.5 million dollar award is offered to anyone providing information that leads to an arrest of the bioterrorist. The FBI profile describes a socially withdrawn person who has "a clear, rational thought process" and is very organized. "The perpetrator might be described as 'standoffish' and likely prefers to work in isolation as opposed to a group/team setting," Harp told the ASM. It is possible the mailer used off-hours in a laboratory or may have even established an improvised, concealed facility to produce the anthrax, the FBI profile noted.

"The person is experienced working in a laboratory," Harp told the ASM. "Based on his or her selection of the Ames strain of *Bacillus anthracis,* one would expect that this individual has or had legitimate access to select biological agents at some time. This person has the technical knowledge and/or expertise to produce a highly refined and deadly product."

Indeed, the Ames strain used in the attacks has been used in bioweapons research both in the United States and worldwide, Salyers says. In

addition, given the elaborate research protocol required, it is unlikely a university laboratorian creating anthrax would go undetected no matter how "standoffish" he or she was.

"I'm just telling you what you have to go through if you were crazy enough to be a bioterrorist," Salyers says. "If a deranged scientist tried to do this in a university laboratory, red flags would be going up all along the way."

Recipe for disaster

The first step — cultivating the bacteria and producing spores — is something that almost any microbiologist could do, she says.

"But you get this slush, and that is not going to hurt anybody," she says. "There are people who will tell you that you can do this the hard way with a mortar and pestle and grind it up in the laboratory. But it is clear that the powder that was in the letters was a much higher quality than that."

The anthrax "slush" must be ground into a fine powder to be capable of getting past human respiratory defenses. "The machinery for doing this is mostly in military research laboratories," Salyers says. In addition, sophisticated treatment of the spores must be done to defeat their general property of clumping and sticking together.

"You would want to treat the spores so that they don't stick together and also so that you get a preparation that is very volatile — goes into the air and stays in the air," she adds.

Regardless of whether the mailer worked in a military lab or other facility, there is growing consensus that the attacks were not the work of foreign terrorists.

"The current thinking among many people is that this is a domestic event that kind of occurred in the slipstream of 9/11," says **William Schaffner**, MD, ASM member and chairman of preventive medicine at the Vanderbilt University School of Medicine in Nashville, TN.

"The [FBI profile] characteristics don't seem terribly surprising. They seem akin to the kind of characteristics that were part of the picture of [the Unabomber] Ted Kaczynski — a disgruntled person who is very bright, and in this instance, has a substantial amount of professional and technological expertise in order to carry this off."

[Editor's note: Those who think they may have information relevant to the case can contact the FBI via telephone at (800) CRIME TV — (800) 274-6388 — or via e-mail: Amerithrax@FBI.gov.] ■

Bioterrorism forensics: The burden of proof

If bug does not fit, you must acquit?

Already asked by federal investigators to assist in finding the anthrax mailer, the American Society of Microbiology (ASM) is taking the next step and discussing the emerging science of bioterrorism forensics.

Despite an impressive array of scientific methods, primarily used in health care epidemiology and outbreak investigations, linking a pathogen to a terrorist will not be easy.

"You want to trace it back to the 'smoking gun,' says **Abigail Salyers**, PhD, ASM president and a professor of microbiology at the University of Illinois in Urbana-Champaign. "We know how to tell what bullet came from what particular gun. But when it is bacteria, viruses, or other microorganisms we really don't have established forensics for that."

To address the issue, the ASM will hold meetings later this year that may result in a booklet on how to use molecular epidemiology techniques to establish a chain of evidence rather than identify the source of an outbreak, she says.

The methods typically used by outbreak investigators include DNA fingerprinting and pulsed-field gel electrophoresis. But using such methods to link a bioterrorist to a biological weapon would be unprecedented, Salyers notes. "Suppose they find somebody [who] might have perpetrated the [anthrax attacks], and they find some spores on that person or the immediate environment."

"Trying to prove that that is the [exact strain] will be unprecedented. It is not just a question of finding the person. It is a question of what are going to be the legally binding types of evidence," Salyers explains.

Another problem in the anthrax attacks is the separation of act and outcome, she says. As opposed to a bomb exploding and leaving an immediate impact, the anthrax mailer had time to dispose of evidence after the mailings.

"You have a perpetration of an act and the consequences of the act separated by nearly a month," she says. "There has been a lot of time for the perpetrator to cover up tracks. This is very different from putting nerve gas into a subway system, where the cause and effect are very close together," Salyers adds. ■