

Cardiology**Dermatology****Endocrinology****Gastroenterology****General Internal Medicine****Geriatrics****Hematology****Infectious Diseases****Nephrology****Neurology****Oncology and Palliative Care****Pharmacology and Toxicology****Pulmonary Medicine****Rheumatology**

William Osler writing Principles and Practice of Medicine ca 1896

This collection of notes addresses some of the topics listed in the Internal Medicine Core knowledge and Clinical Skills Outline, and is an attempt to provide clinical perspective as well as pearls and pitfalls. It is NOT an exhaustive collection of core information. It is an ongoing initiative, and will be expanded, updated and revised over time. Like any information source, it will benefit from feedback and contributions by its users.

The outline is based on core knowledge and skills objectives identified by the Medical Council of Canada and as well as by Internists and Family Physicians in Region 10. The clinical practice guideline summaries have been provided by permission from the Alberta Medical Association Clinical Practice Guidelines Program.

Acute coronary syndromes

- Etiology
- Stable and unstable angina
- Basic management

Diagnosis and Management of Acute Myocardial Infarction

Cardiovascular Risk Reduction

Congestive Heart Failure and pulmonary edema

- **Diagnosis and clinical presentation of right, left or bi-ventricular failure**
- Differential diagnosis of pulmonary edema and shortness of breath
- **Etiology and precipitating causes (determining etiology for more rational and effective management)**
- **Therapy and Prevention: drugs prolonging survival**
- **Prognosis**
- **Laboratory utilization: Chest X-ray, Echocardiography**

Approach to Leg Edema

- Etiology/differential diagnoses
- List and interpret basic investigations

Heart sounds Murmurs and Valvular Heart Disease

- Clinical presentation and cardinal physical findings

Palpitations and arrhythmias

- Distinguish / benign palpitations and those associated with disease
- **Atrial fibrillation: Clinical presentation, ECG recognition, stroke and embolic risk, Therapy Prevention and Harm Other complications (worsening heart failure)**
- **Stroke prophylaxis; Coumadin versus ASA**

Clinical Skills (see Clinical Skills Section)

- **Assessment of chest pain**
- **Assessment of Congestive heart failure**
- **Inspection, palpation and auscultation of the Precordium**
- **Examination of the venous pulses**
- **Blood pressure measurement and assessment of hypertension including secondary causes and target organ damage**
- **Examination for chronic peripheral arterial insufficiency**
- **Electrocardiography (see ECG Powerpoint tutorial and quiz)**

Acute coronary syndromes include **unstable angina and non-Q myocardial infarction**. Thrombus formation is the main pathogenesis. Plaque rupture in the coronaries cause platelet adherence to exposed sub-endothelium with ensuing platelet activation. Plaques with high potential to produce acute ischemic syndromes generally have thin fibrinous caps, a large, soft, lipid rich pool, less collagen support, and more lipid laden macrophages (foam cells). Plaque rupture almost always occurs at the “shoulder”- the junction of the plaque and surrounding normal endothelium.

Acute coronary syndromes are associated with serious outcomes. Recent large trials among patients with unstable angina or non-Q-wave MI have reported rates of nonfatal MI and death between 8 and 12%, and there is a high risk of subsequent arrhythmias as well.

Diagnosis

Recognize typical features of angina and differentiate it from other causes of chest pain (see Chest pain history module).

Although the diagnosis of unstable angina does not require the presence of ECG abnormalities, the presence of ST segment and T-wave abnormalities increases the specificity of the diagnosis of acute myocardial ischemia and indicates a worse prognosis. The clinical diagnosis of unstable angina is in most settings based on anginal pain with the following features:

Clinical Presentation of Unstable Angina		
I.	New onset angina	Onset within past 4-8 weeks, at least Canadian Cardiovascular Society (CCS) grade III (see chest pain module)
II.	Crescendo angina	Previously stable angina that is now distinctly more frequent, easily induced, severe, or prolonged, or less responsive to nitroglycerin
III.	Rest angina	Angina occurring at rest and lasting longer than 15-20 min

Encompassed within this spectrum of symptomatic manifestations of ischemic heart disease are variant or Prinzmetal’s angina and angina in the early post-MI period (>24 hr). Non-Q-wave myocardial infarction generally cannot be differentiated from unstable angina on initial clinical presentation and the initial management is not different. ST- and T-wave abnormalities are common. The development of new Q-waves or the elevation of cardiac enzymes to more than twice normal defines the occurrence of myocardial infarction.
 Reproduced from Can J Cardiol 1996;12:1279-92

Identify high-risk patients in need of more intensive therapy

The risk for progressing from unstable angina to acute MI in near future is highest in patients with:

- Angina at rest or prolonged episodes (> 20 minutes)
- Myocardial infarction within last 14 days
- Need for intravenous Nitroglycerin to achieve pain relief
- Baseline ST segment depression occurring with episodes of pain
- Recurrent chest pain post-MI or while on intensive medical therapy
- Diabetes
- Older age
- Hemodynamic instability (e.g.hypotension), or evidence of left ventricular dysfunction (mitral regurgitation or presence of a third heart sound), occurring during episodes of pain
- Positive Troponin I

This is a marker unique to cardiac muscle that is not elevated by exercise, skeletal muscle injury, rhabdomyolysis, or non-cardiac surgery. After an MI, peak levels are reached at 12 hours and detectable for 7-14 days. It is positive in 35% of patients with unstable angina. If positive, it denotes the highest mortality risk patients with unstable angina and may be an independent risk factor for significant cardiac disease (1)(2)

Exercise stress testing (EST)

EST is contraindicated during the acute presentation of acute coronary syndromes. Once the patient is stabilized, it gives valuable prognostic information. If the patient has a normal ECG, is pain free on arrival to ER and has normal cardiac enzymes, an early EST can help rule out unstable angina. A positive EST, especially at low workloads or with a hypotensive response, can identify particular high-risk groups that often have 3-vessel or left-main disease, and who should undergo coronary angiography. A negative EST does not rule out recent plaque activity where the thrombus has resolved, or pain from dissecting aneurysm.

Management

Principles

- Block platelet adherence, platelet activation, and thrombus formation
- Relieve pain and ischemia
- Decrease risk factors for MI
- Treat potential complications such as arrhythmias and congestive heart failure/pulmonary edema

General Management

The patient may present in a non-medical setting or by telephone, in the office or in the hospital emergency room or ward. Those with the simple new onset of angina or mild exacerbation of previous stable angina, with no angina at rest, and with no ECG changes or hemodynamic abnormalities, should be carefully assessed, but they may generally be managed and followed-up as outpatients.

However, high-risk patients require admission to the coronary care unit (CCU), generally to remain there until about 24 hours after the last episode of rest pain. Patients at intermediate risk might go to the CCU, an intermediate care unit or even to a regular ward depending on the availability of facilities and the specific level of risk. The development of emergency room chest pain units following diagnostic protocols based on risk predictors including measurement of troponin is likely to allow safer and more rigorous selection of optimal management settings.

ASA and other anti-platelet agents

ASA should be given to all patients with acute coronary syndromes—the only contraindication is a true allergy to it. ASA provides a 10% absolute risk reduction (31-50% relative risk reduction) in the rate of progression to MI. One MI is prevented for every 10 patients treated (NNT= 10). The acute dose is 160 mg chewed slowly and swallowed, followed by 81-325 mg/day orally for an indefinite period.

Clopidogrel is an effective inhibitor of ADP-mediated platelet aggregation, and may be substituted for ASA in patients with ASA hypersensitivity.

Heparins

Heparin is likely of greatest benefit in the highest risk patients. Use in combination with low dose ASA. The maximum duration of use in patients without symptoms is 48 hours. If symptoms persist, the infusion is continued until an invasive intervention can be performed. Low molecular weight heparins (LMWHs) plus ASA are more effective than unfractionated heparin (UFH) plus ASA in reducing the incidence of ischemic events, recurrent angina or death in patients with unstable angina or non-Q-wave myocardial infarction in the early phase. They also have less bleeding risk, do not require coagulation test monitoring, and have a lower incidence of thrombocytopenia than unfractionated heparin (7,8-9).

Nitrates

Nitrates are standard medication in the management of acute coronary syndromes. Although there are no convincing data demonstrating reductions in mortality or rate of new myocardial infarction, or the superior efficacy with intravenous nitroglycerin, nitroglycerin is widely used, and the IV route is generally chosen for high-risk patients because of greater ease of titration.

Start with 0.3 mg sublingual and topical paste. If this is ineffective, IV nitroglycerine can be titrated to pain resolution or if hypotension (SBP < 90) is encountered. Contraindications to use include a potential interaction (hypotension) if sildenafil (Viagra) has been used in last 24 hours.

Beta-blockers

B-blockers are indicated in situations of severe chest pain, recurrent or prolonged episodes of pain, ECG abnormalities, hemodynamic instability associated with chest pain, or evidence of sympathetic nervous system hyperactivity.

Patients at low or intermediate risk may benefit from gradual initiation of oral therapy, whereas those at high risk in the CCU setting may benefit from intravenous beta-blocker or rapid escalation of oral dosage. Atenolol or metoprolol may be given as 5 mg IV boluses q 5 minutes until a target heart rate of 50-60 bpm is achieved or to a maximum of 3 doses. Contraindications to BB use include severe asthma, acute congestive heart failure, respiratory failure, systolic BP < 90 or 2nd or 3rd degree heart block. Mild to moderate COPD, diabetes, age greater than 80, and left ventricular ejection fractions less than 20% are *not* absolute contraindications. (6)

Calcium channel blockers

Short-acting nifedipine increases mortality and is not indicated. Diltiazem appears to be as effective as B-Blockers, but is contraindicated in the presence of hypotension or 2nd or 3rd degree heart block.

Thrombolytics and direct thrombin inhibitors are not indicated

Use of thrombolytics (like streptokinase and rt-PA) and direct inhibitors of fibrin bound thrombin (like hirudin) appear to worsen outcomes and are not indicated in the emergency management of acute coronary syndromes.

Early Intervention with angiography and revascularization where appropriate

Patients at low risk who are not hospitalized may generally be managed medically, reserving angiography and consideration for revascularization for those who fail optimal medical control as outpatients or who have a poor prognosis on noninvasive testing. (see above)

Optimal *medical* therapy of the patient with unstable angina of *intermediate* risk includes CCU care with continuous ECG monitoring, bed rest or minimal exertion, aspirin and heparin, and a combination of nitrates, beta-blockers and calcium antagonists sufficient to prevent tachycardia and hypotension while avoiding major side effect. If there are recurrences of ischemic pain or silent ischemia at rest or with attempts at mobilization, optimal medical therapy may be considered to have failed. Such patients have a high incidence of subsequent MI and death. The general approach has been to proceed to cardiac catheterization with a view to revascularization. Case series support the use of the intraaortic balloon pump for the particularly unstable patient until an operating room is available for a revascularization procedure. The choice of coronary angioplasty versus CABG is generally governed by expert evaluation of case series and clinical experience.

The recent Fast Revascularization during Instability in Coronary artery disease (FRISC II) study (5) showed that early angiography and directed revascularization (within 7 days), when combined with optimal medical pretreatment with dalteparin sodium, aspirin, and appropriate anti-anginal medication should be the preferred strategy for patients with an acute coronary syndrome *who present with signs of ischemia on the electrocardiogram or raised biochemical markers of myocardial damage at admission.*

References

1. Antman EM et al . Cardiac specific Troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. N Eng J Med 1996;335: 1342-9
2. Hamm,J et al Emergency room triage of patients with acute chest pain by means of rapid testing for cardiac troponin T or troponin I. N Eng J Med 1997;337: 1648
3. Heeschen C et al Lancet 1999;354:1757-1762
4. N Engl J Med 1997;337:447-52
5. FRISC II Lancet. 1999;354:701-07
6. Roe MT et al J Emerg Med 1999; 17: 581-588
7. Cairns J, Theroux P, Armstrong P et al .ACC Current Journal Review July/August 1998 p43-48
8. SS et al. NEJM 1998;339:489-97
9. Marc Cohen, Christine Demers, Enrique P. Gurfinkel, Alexander G.G. Turpie, Gregg J. Fromell, Shaun Goodman, Anatoly Langer, Robert M. Califf, Keith A.A. Fox, Jerome Premmereur, Frederique Bigonzi, Jim Stephens, Beth Weatherley, for the Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-Wave Coronary Events Study Group . A Comparison of Low-Molecular-Weight Heparin with Unfractionated Heparin for Unstable Coronary Artery Disease N Engl J Med 1997;337:447-52.
10. Topol E et al PURSUIT N Eng J Med 1998;339:436-43
11. Fuster V N Eng J Med 1993;329:723-24

Diagnosis and Initial Management of Acute Myocardial Infarction

Revised BF Aug 2003

Half of the deaths due to AMI occur in less than one hour after onset of symptoms. **The most important contributing mechanism is ventricular fibrillation.**

Importance of subgroups

Elderly AMI patients are more likely to develop important clinical complications such as congestive heart failure, cardiogenic shock, atrial fibrillation, and death.

Diagnosis

World Health Organization Criteria require at least two of three:

- Characteristic chest pain
- Elevated CPK levels
- Diagnostic EKG changes

Note that the sensitivity of the initial EKG is only about 50-75%. Although the CK-MB mass can be elevated with skeletal muscle damage or renal failure, a fraction of > 5% strongly suggests infarction.

Various Markers

Marker	SNout	SPin	Peak (hrs)	Normalize (hrs)
CK	38%	80%	10-36	72-96
CKMB	34%*	88%	9-30	48-72
Troponin I	6-44	93-99	14-20	5-7 days

*rises to 100% at 12-16 hours

SNout = sensitivity "rules diagnosis out"

SPin = specificity "rules diagnosis in"

Management of Myocardial infarction

Primary angioplasty (PCI)

Several modest-sized trials have indicated that primary angioplasty for acute ST-segment-elevation myocardial infarction is associated with lower mortality, fewer re-infarctions, less congestive heart failure, and fewer revascularization procedures and is (only slightly) less costly than treatment with IV streptokinase (4,5). The addition of coronary artery stenting also results in less target revascularization and angina at 6 months than does treatment with angioplasty alone. (2) However, this is only true if provided by experienced hospitals or operators in a timely fashion. Thrombolytic therapy is much more readily available outside of such health centers. The CAPTIM trial assessing primary angioplasty versus pre-hospital fibrinolysis, showed no differences other than increased numbers of unplanned revascularization in the fibrinolysis group, but unfortunately did not assess the use of GPIIb-IIIa inhibitors in the PCI group. (6) Perhaps shifting patients toward PCI by adapting a care strategy analogous to trauma networks could help ensure that patients with acute MI are rapidly and appropriately triaged to a facility with a range of reperfusion options. RCTs in acute MI will soon compare primary PCI with facilitated PCI (i.e., combinations of fibrinolysis, antithrombotic therapies, and immediate PCI). If facilitated PCI proves superior to primary PCI by providing more rapid reperfusion, it may diminish some of the pressures associated with a transfer strategy and allow a smoother transition to a regional system of MI care.

Thrombolytic therapy

Thrombolytic use may salvage ischemic myocardium, reopen occluded arteries, prevent infarct expansion and promote healing. Earlier thrombolysis results in greater mortality reduction, although benefits continue for delayed (> 6 hour) thrombolytic therapy. Thrombolytic therapy has unequivocal benefit in anterior infarctions, the benefit for inferior infarcts is more modest, but still significant. Combinations of thrombolytics and ASA are significantly better in reducing mortality than either agent alone.

Indications include:

- At least 1 mm ST segment elevation in at least 2 adjacent *limb* leads
- At least 1-2 mm ST segment elevation in at least 2 adjacent *precordial* leads
- New LBBB

Absolute contraindications include:

- Previous hemorrhagic stroke (ever)
- Other stroke within 6 months
- Neurosurgery or head trauma within 6 months
- Intracranial neoplasm
- Significant dementia (increased risk of bleeding?)
- Aortic dissection
- Gastrointestinal, urologic, or other internal bleeding within the 6 weeks
- Any active bleeding or known bleeding disorder
- Major surgery or trauma within 6 weeks
- Traumatic cardiopulmonary resuscitation within 3 weeks
- Use of SK in the last year *with possibility of neutralizing antibodies, or past history of allergic reaction*
- Acute pericarditis

Relative contraindications include:

- TIA within the last 6 months
- Uncontrolled hypertension SBP > 180, DBP > 110
- Known intracardiac thrombus
- Oral anticoagulant Rx
- Active peptic ulceration
- Acute pancreatitis
- Infective endocarditis
- Puncture of non-compressible blood vessel within 2 weeks
- Pregnancy or < 1 week post-partum
- Advanced liver disease
- Previous SK therapy (if planning SK therapy)

Heparin

Heparin is used *in combination with tPA* (for 48 hrs post t-PA infusion) to maintain patency. It is given in a dose to maintain the PTT in the range of 1.5-2 times normal. It is not required to maintain patency if SK is being used, and may actually increase hemorrhagic stroke or major bleeding. Heparins may also be used for DVT prophylaxis or therapy.

ASA

Although independently helpful, benefits of ASA administration are greatest when combined with thrombolytic therapy. Give aspirin immediately if an acute infarction or acute coronary syndrome is suspected-the only contraindication is known hypersensitivity. Ask the patient to chew before swallowing. If there is known hypersensitivity to ASA, use clopidogrel.

Beta blockers

A great deal of evidence indicates that mortality is reduced in acute infarction if B-blockers are used. The mortality benefit is greatest in the first 48 hours, and mortality rates are lower in every subgroup of treated population. Early IV therapy should be followed by long-term oral therapy in all patients without contraindications. Patients with COPD, diabetes age > 80, or LV ejection fractions < 20% have the greatest absolute risk reductions, likely because these groups are at the highest baseline risk. Therefore the presence of these co morbidities is not a contraindication to B-blocker use. **Contraindications or cautions in use of B-blockers do include:** Bradycardia of < 50 bpm, AV block (2nd or 3rd degree), significant hypotension, cardiogenic shock, active bronchospasm or history of severe asthma, or clinical evidence of CHF (crackles in > 1/3 of lung fields).

ACE inhibitors (ACEI)

Large trials support using ACEI in patients with AMI and Systolic Blood pressure > 100 mm Hg. ACEIs appear to be most effective when given early in all patients without contraindications and stopped after 4-6 weeks in those patients with normal LV function. Patients most likely to benefit are those with repeat MI, anterior MI, or clinical LV dysfunction.

Nitrates

Nitrates decrease preload and after load, and are important for symptomatic relief, but have not been shown to reduce mortality in AMI patients. Present recommendations are to use IV nitrates for the first 24-48 hours in patients with large anterior infarcts, acute CHF, persistent ischemia, or hypertension. **Use with caution in the presence of aortic stenosis or right ventricular infarction.**

Calcium Channel blockers

Numerous studies have investigated the efficacy of calcium channel blockers after acute MI. The recent ACC/AHA guidelines for the treatment of acute MI emphasized that no calcium channel blocker has been shown to reduce mortality in acute MI, and that in certain patients they may be harmful. The excess early mortality with *short-acting dihydropyridines* (such as nifedipine) in patients with acute MI suggests that these agents should be avoided. Verapamil or diltiazem are recommended as adjunctive therapy only in patients unable to take beta-blockers in whom there is no congestive heart failure, left ventricular dysfunction, or atrioventricular block. Diltiazem is recommended only in non-ST-elevation infarcts in patients without congestive heart failure or left ventricular dysfunction. When used in this setting, diltiazem should be started after 24 hours and continued for one year.

Intravenous magnesium

The ISIS-4 and MAGIC trials (3) have shown that early administration of magnesium in high-risk patients with STEMI has no effect on 30-day mortality. There is no indication for the routine administration of intravenous magnesium in patients with STEMI. Magnesium may be indicated if there is digoxin toxicity, and or in the treatment of Torsades de pointes (polymorphic ventricular tachycardia).

Oxygen therapy

Although widely used, there have been no trials to examine the effectiveness or value of supplemental oxygen!

References

1. Zijlstra F, Hoorntje JCA, et al: N Engl J Med 1999; 341 (November 4): 1413-1419
2. Grines CL, Cox DA, et al: N Engl J Med 1999; 341 (December 23): 1949-1956
3. Magnesium in Coronaries (MAGIC) Trial Investigators. Lancet. 2002 Oct 19;360(9341):1189-96
4. Aversano Tet al., for (C-PORT). JAMA. 2002 Apr 17;287:1943-51.
5. Moon JC et al. Int J Cardiol 2002 Oct;85(2-3):199-201
6. Bonnefoy E, Lapostolle F, Leizorovicz A, et al. Lancet. 2002;360:825-9

Summary of Management of Acute Myocardial Infarction

Grade of Recommendation	Action	Contraindications
	Obtain vital signs, a 12-lead ECG and do a targeted history.	
	If diagnose AMI describe: Acute (type (ST-segment elevation or non-ST segment elevation, Q wave versus non-Q wave)(location) MI	
	Admit to CCU for continuous ECG monitoring	
	IV access orders	
	O2 via nasal prongs at	
A	ASA 160-325 mg chewed (STAT), then ECASA 325 mg od	Hypersensitivity: may substitute clopidogrel
	Morphine IV for pain relief	Hypersensitivity
A	Intravenous B-blocker	Bradycardia, systolic BP < 100 mmHg, moderate to severe CHF, severe asthma or COPD, heart block
C	For persistent or recurrent ischemia: Nitroglycerin IV or paste increasing dose until either effective or BP systolic < 90 mmHg or MAP < 80 mmHg. (May also consider using if hypertensive or CHF)	Hypotension
A	<p>Indications for thrombolysis therapy met:</p> <ol style="list-style-type: none"> 30 or more minutes of ischemic cardiac chest pain Any one of: <ul style="list-style-type: none"> 1 mm ST segment elevation in > 2 adjacent limb leads or > 1 mm ST segment elevation in 2 or more adjacent precordial leads or Complete bundle branch block <p>Current trials indicate that only patients with ST segment elevation benefit from early reperfusion.</p> Patient has presented within 12 hours of onset of symptoms <p>Give ASAP: Streptokinase IV or rTpa IV</p>	<p>Absolute:</p> <ul style="list-style-type: none"> Aortic dissection Acute pericarditis Active bleeding <p>Relative</p> <ul style="list-style-type: none"> Pregnancy Increased risk of bleeding Prolonged or traumatic CPR Major trauma or surgery in prior 2 weeks Active peptic ulcer disease Significant liver dysfunction Current use of anticoagulants or known bleeding diatheses Hypertension > 200/120 Diabetic proliferative retinopathy CVA in last 6 months <p>Specific: Streptokinase or APSAC allergy or resistance</p>
A	Primary angioplasty in the setting of AMI provides equivalent if not superior clinical benefits compared to thrombolysis. It is an alternative when patients have important contraindications to thrombolysis and is the preferred option in patients presenting with cardiogenic shock. Primary bypass surgery is occasionally another option in the context of severe left main disease or failed angioplasty	
C	Heparin IV to keep PTT 1.5-2 times control if Using rtPA or High risk for systemic or venous thromboembolism (CHF, anterior MI, atrial fibrillation, prior embolus)	
B	Otherwise, unfractionated Heparin 7500 U s/c q12h until ambulatory	

Dyslipidemia

Hypercholesterolemia is common and an important modifiable risk factor for cardiovascular and cerebrovascular disease. A high HDL is a predictor of lower risk. Therefore patients at high risk for these conditions should be screened with fasting lipid profiles. The relationship of elevated triglycerides is less clear.

Primary causes of hypercholesterolemia

- Polygenic (common)
- Familial Hypercholesterolemia (rare)

Secondary causes include

- Diabetes mellitus
- Hypothyroidism
- Nephrotic syndrome
- Obstructive liver disease
- Drugs (cyclosporin)

Low HDL is associated with obesity, smoking, and inactivity.

Primary causes of hypertriglyceridemia include dietary, and familial. Secondary causes include obesity, diabetes, chronic renal failure, and excess ethanol use. Severe hypertriglyceridemia may be associated with pancreatitis.

The complete lipid profile includes total cholesterol, LDL, HDL and triglyceride. Total cholesterol is made of both LDL-C and HDL-C, and LDL-C is calculated from a formula that uses the triglyceride level. Triglyceride levels are only loosely associated to cholesterol levels and cannot be inferred from total cholesterol. The tests are preferably performed after a 12-hour fasting to avoid perturbation from elevated triglyceride levels. One cannot tell from perusal of the total cholesterol level, what the component levels will be. The combination of elevated LDL, and low HDL confers substantially different risk than a low LDL and elevated HDL. Measurement of apolipoprotein a levels is very specialized, often available only on a research basis, and should not be ordered on routine blood work.

References and suggested reading material:

Rational for and outline of the recommendations for the Working Group on Hypercholesterolemia and Other Dyslipidemias: Interim Report. Can J. Cardiol 14:17A-21A 1998
Modifiable Risk Factors in Adults at High Risk for Cardiovascular Events: CQIN Guidelines of the Alberta Medical Association



Modifiable Risk Factors in Adults at High Risk for Cardiovascular Events

This Guideline replaces the “Guideline for the Management of Modifiable Risk Factors in Adults at High Risk for Cardiovascular Events.”

GOALS

- ◆ To increase rates of investigation and treatment of modifiable risk factors in patients at high or very high risk for cardiovascular events, which will, in turn, reduce mortality and morbidity from cardiovascular disease
- ◆ To provide a simple, practical, and cost-effective multidisciplinary approach to risk factor modification
- ◆ To assist and empower patients to identify their risk for cardiovascular events and take responsibility for reducing this risk

The focus of this guideline will be on patients at high to very high risk for cardiovascular events. However, cardiovascular risk is a continuum, and risk factor modification should be considered in all patients, regardless of their current level of risk.

RECOMMENDATIONS

Target Patients At High to Very High Risk:

- ◆ Adult patients with atherosclerotic vascular disease:
 - clinical or angiographic evidence of coronary artery disease
 - peripheral vascular disease
 - cerebrovascular disease
- ◆ All patients with diabetes mellitus >30 years of age
- ◆ Patients with an estimated 10 year risk of coronary artery disease of >20% (Framingham Risk, see Appendix)

Practice Point

An active (rather than passive) identification of patients at risk is recommended. Patients may also be referred by other health professionals such as pharmacists or public health workers.

Identify and Manage Modifiable Risk Factors

- ◆ Smoking:
 - Target complete cessation (regular counselling by physicians is very important and effective. Nicotine replacement and bupropion may be effective short-term adjuncts)
- ◆ Excess Weight:
 - Aim for healthy body weight (prescribe a low-fat, heart-healthy diet. Refer patient to a dietician for advice)
- ◆ Sedentary Lifestyle:
 - Recommend at least 30 minutes of physical activity per day, most days of the week (encouragement by physicians is important)
- ◆ Hypertension:
 - Target: systolic <140 and diastolic <90 mmHg (in diabetics, systolic <130 and diastolic <80 mmHg)
 - In addition to diet and exercise, medications (diuretics, beta blockers, ACE inhibitors, or calcium channel blockers) are often necessary.
- ◆ Dyslipidemias
 - Targets and thresholds for treatment depend upon risk level
 - Initiate drug therapy immediately in high or very high risk patients (see Tables 1, 2 and 3). Drug therapy may be initiated in moderate and low risk patients after a 3 month trial of lifestyle changes.

The above recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making.

Table 1

Risk Level	Definition	Target		
		LDL-C (mmol/L)	TC/HDL	TG (mmol/L)
VERY HIGH	Established CVD, diabetes, or 10y risk >30%	<2.5	<4	<2
HIGH	10y risk of 20 to 30%	<3.0	<5	<2
MODERATE	10y risk of 10 to 20%	<4.0	<6	<2
LOW	10y risk <10%	<5.0	<7	<3

Table 2: Drugs of Choice For Management

Lipid Profile	1 st Choice	2 nd Choice
↑↑ LDL	statin	resin
↑↑ LDL, ↑ TG	statin	fibrate or niacin
↑ LDL, ↓ HDL	fibrate or statin	combination therapy
↑ LDL, ↑↑ TG	fibrate or niacin	combination therapy
↓ HDL, ↑ TG	fibrate or niacin	combination therapy

- Consider:
 - ASA (80-325 mg daily or every other day)
 - Angiotensin Converting Enzyme (ACE) inhibitors such as ramipril (10mg daily), enalapril (10mg BID), lisinopril (20mg daily), or quinapril (40mg daily)

Monitor and Follow-up

- ◆ Regular follow-up visits are necessary to:
 - Titrate/change of medications to ensure patients reach their targets for cholesterol and blood pressure
 - Reinforce adherence to lifestyle modifications (smoking cessation, diet and exercise) and medications
 - Recheck lipid panel and blood pressure 6 to 12 weeks if not at target values, after medication changes, and yearly once targets achieved.

BACKGROUND

Atherosclerotic vascular disease, particularly coronary heart disease (CHD), continues to be the leading cause of death and disability for Canadian men and women¹. Substantial advances have been made in the treatment of myocardial infarction and other acute ischemic syndromes, and this has contributed to improved survival following an acute event. However, these survivors, along with others who have documented atherosclerotic vascular disease (e.g., cerebrovascular or peripheral vascular disease), remain at very high risk for subsequent ischemic vascular events and/or death. The risk of these individuals is considerably higher than that of the general population. However, this risk can be substantially lowered through stringent control of known modifiable cardiovascular risk factors, notably smoking, dyslipidemia, hypertension, diabetes, and a sedentary lifestyle. Moreover, risk factor

Table 3: Lipid Lowering Agents

DRUGS	INITIAL DOSE	MAINTENANCE DOSE	MAXIMUM DOSE	POTENTIAL INTERACTIONS	REQUIRED LABORATORY	SIDE-EFFECTS	COMMENTS
Resins Cholestyramine	4 g qd - bid	8-16 g/day (qid or bid)	24 g/day	<ul style="list-style-type: none"> Decreased absorption of digoxin, warfarin, thyroid, oral hypoglycemics, statins, folic acid, gemfibrozil, thiazides, tetracycline, vitamins A,D,K 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> GI upset, constipation Esophageal spasms or respiratory distress (if ingested in dry form) 	<ul style="list-style-type: none"> Space administration of other agents 1h before or 2h after resin Increase fluid and fiber intake to help relieve side effects
Colestipol		15-30 g/day (qid or bid)	30 g/day				
Fibrates Gemfibrozil Bezafibrate Fenofibrate - regular - micronized (lipidil micro) - macrocoated (lipidil supra)	300 mg bid 200 mg 100 mg tid 200 mg/day 160 mg/day	600 mg bid 200 mg tid 200 mg/day 160 mg/day	1500 mg/day 600 mg/day 400 mg/day 200 mg/day 200 mg/day	<ul style="list-style-type: none"> Displacement of warfarin or oral hypoglycemics Increased risk of myopathies with statins, niacin, or cyclosporine 	<ul style="list-style-type: none"> LFTs at baseline, 6 months, and 6 months to 1 year thereafter CK at first sign of muscle pain (d/c drug if CKs 10x upper limit of normal) 	<ul style="list-style-type: none"> GI upset, hepatotoxicity, rash, pruritis, headaches, insomnia, myopathies 	<ul style="list-style-type: none"> Take with food (except gemfibrozil which should be taken 30 min. prior to meals)
Niacin (nicotinic acid)	125 mg/bid	1.5 to 2.0 g/day (500mg tid or qid)	2 g tid	<ul style="list-style-type: none"> Decreased effects of insulin or oral hypoglycemics Increased risk of myopathies with statins or fibrates 	<ul style="list-style-type: none"> LFTs at baseline, every 6 to 12 weeks for first year then every 6 months thereafter Uric acid and glucose at baseline and as necessary thereafter 	<ul style="list-style-type: none"> Flushing, headache, pruritis, GI upset, hyperuricemia and gout, hyperglycemia, hepatotoxicity 	<ul style="list-style-type: none"> Always take with food Tolerance often develops to flushing 325mg ASA 30 min. prior to niacin may help to alleviate flushing Avoid hot beverages
Statins Atorvastatin Fluvastatin Lovastatin Pravastatin Simvastatin	10 mg 20 mg 20 mg 10-20 mg 5-10 mg	10-60 mg qd 20-60 mg qd or bid 20-60 mg qd 20-40 mg qd 10-40 mg qd	80 mg qd 40 mg bid 40 mg bid 40 mg qd 80 mg qd	<ul style="list-style-type: none"> Increased risk of myopathies with niacin, erythromycin, gemfibrozil, ketoconazole, itraconazole, or cyclosporine Increased digoxin with atorvastatin or fluvastatin Increased warfarin levels with fluvastatin 	<ul style="list-style-type: none"> LFTs at baseline, 6 months, and 6 months to 1 year thereafter CK at first sign of muscle pain (d/c drug if CKs 3-4x upper limit of normal) 	<ul style="list-style-type: none"> GI upset, myopathies, hepatotoxicity 	<ul style="list-style-type: none"> All statins should be taken with evening meal or at bedtime Taking with food helps to alleviate side-effects

modification in this high-risk population has been shown to be cost effective.²

Despite the compelling scientific evidence for the efficacy of aggressive risk factor modification in patients at high risk, the application of risk reduction strategies is often inconsistent and incomplete.³⁻⁵ A multidisciplinary, systematic approach to the identification of such individuals, and consistent and aggressive attention to risk factor assessment and modification in the population at highest risk is will result in reduced clinical event rates and enhanced patient outcomes. Recommendations and targets for risk factor modification are outlined here.

Research Findings

Accumulated scientific data clearly demonstrate that risk factor interventions, when effectively applied to population groups at high or very high risk (>5% cardiovascular event rate per year) for future atherosclerotic vascular events reduce morbidity, as well as total and cardiovascular disease (CVD) mortality.⁶⁻⁸

Risk Stratification

A simple scheme for risk stratification of patients will help to guide treatment decisions and set targets for risk factors:

- ◆ All patients with evidence of atherosclerotic vascular disease (coronary artery disease, including stable or unstable angina, myocardial infarction, or revascularization, peripheral vascular disease, or cerebrovascular disease) are *automatically considered at very high risk for cardiovascular events*.⁶
- ◆ All patients with diabetes mellitus (> 30 years of age) are also *automatically considered at very high risk for cardiovascular events*.⁶
- ◆ All other patients should have a risk estimation performed using the Framingham Risk Calculator (see Appendix). Those with 10 year risk estimates of >30% or 20-30% are considered at very high or high risk, respectively.⁶

Smoking Cessation

Successful smoking cessation in patients with CVD substantially reduces mortality risk.⁹⁻¹¹ A decrease in total mortality up to 50% has been shown for individuals who discontinue smoking after a first myocardial infarction.⁹ Similar findings have been documented in the Coronary Artery Surgery Study.¹⁰ In this study, smokers also spent more days in hospital than non-smokers, with a substantial concomitant excess in hospital costs.¹⁰

Studies have shown that interventions delivered by physicians can have a significant impact on patients' smoking behaviour.¹² Advice to stop smoking is associated with a cessation rate of 3%. Advice given in a 3 to 5 minute counselling session, with follow up visits at 1, 3, and 6 months, can increase the cessation rate to 23% or more.^{12,13}

Control of Hypertension

Extensive clinical and epidemiologic investigations have clearly demonstrated that hypertension is associated with accelerated coronary atherosclerosis, development of congestive failure, and up to a six-fold increase in stroke risk.¹⁴⁻¹⁶ Treatment of mild-to-moderate hypertension is associated with significant decreases, approaching 40%, in risk for stroke, with reductions of 8 to 12% in CHD risk.¹⁵ Among high risk subjects, including those with established CHD or multiple risk factors, even minor decreases in blood pressure can result in marked benefits in terms of prevention of premature death or disabling vascular event.¹⁷

Blood pressure targets have been defined by various hypertension working groups⁸⁻¹⁶:

Patient Group	Target Blood Pressure (mmHg)
Systolic and/or Diastolic Hypertension	<140/90
Isolated Systolic Hypertension	<140
Diabetes	<130/80

Unfortunately, many patients do not reach their target blood pressure, highlighting the importance of close follow-up.

Management: Initial Drugs of Choice¹⁶

Age <60y	Low-dose thiazide diuretics, beta blockers, ACE inhibitors, or long-acting dihydropyridine calcium channel blockers
Age >60y	Low-dose thiazide diuretics, ACE inhibitors, or long-acting dihydropyridine calcium channel blockers

The recommendations for initial drugs of choice are for patients with uncomplicated hypertension. For patients with concurrent disease states, please refer to the guidelines for treatment recommendations. If monotherapy is insufficient after dosage increases, consider use of combination therapy. The reader is referred to recent Canadian and U.S. guidelines for the diagnosis and treatment of hypertension.^{8,16}

Management of Diabetes Mellitus

There is a well-documented excess of mortality in persons with diabetes mellitus compared to the general population, and estimates indicate 75 to 80% of adults with diabetes die from coronary, peripheral or cerebrovascular disease.^{18,19} Recent epidemiologic studies have indicated that patients with diabetes (and ‘no evidence of heart disease) have an equal risk of myocardial infarction to those patients with a previous myocardial infarction but without diabetes.²⁰ This has led to the recommendation that **all patients with diabetes mellitus >30 years of age be automatically considered at very high risk for cardiovascular events**, regardless of clinical history.⁶

Although optimization of glucose control is central to the management of diabetes, smoking cessation and aggressive control of cholesterol and blood pressure are critical to improve patient outcomes. At any given level of risk, individuals with diabetes have a 4 to 5 fold increase in risk for CVD and its attendant complications. While macrovascular complications are

not tightly linked to glycemic control, clinical and laboratory studies do indicate that lipoprotein particles undergo glycation and oxidation with increased frequency in the presence of hyperglycemia. Such altered lipoprotein particles are believed to stimulate atherogenesis, underscoring the importance of optimizing both glycemic control, and serum lipid levels, in persons with diabetes.

Similarly, blood pressure control is of particular importance in patients with diabetes, and lower target values of <130/80 reflect this.

Modification of Activity

Physical activity has beneficial effects on several risk factors, including serum lipids, blood pressure, glucose/insulin utilization, and body weight.²¹ Recent studies suggest a 34% population-attributable risk of CHD death related to physical inactivity.²¹ Conversely, numerous epidemiologic studies have demonstrated that regular physical activity is associated with reductions in CHD incidence and mortality.²¹ Randomized trials of exercise have suggested reductions of about 25% in cardiovascular mortality for men with CHD.²²

Recommendations for the appropriate types, intensity, and duration of physical activity should be routinely, provided to high risk patients. Many patients will begin from a low fitness level, and a mild activity that is convenient and safe if preferable in the initial phase. This can be increased gradually to achieve 30 minutes of accumulated moderate-intensity activity on most, preferably all, days.²³

Modification of Serum Cholesterol

Compelling scientific evidence, including data from large scale randomized clinical trials, have demonstrated that a lipid lowering diet and/or drug therapies result in improved arteriographic measurements, reductions in clinical events, and decreased CVD and all-cause mortality, even in patients with average cholesterol levels.²⁴⁻²⁸

Summary of Major Cholesterol Trials:

	Primary Prevention	Secondary Prevention
“High” Cholesterol	WOSCOPS ²⁷ 30% ↓ in cardiovascular events	4S ²⁴ 30% ↓ all-cause mortality
“Low” Cholesterol	AFCAPS/ TexCAPS ²⁸ 36% ↓ in coronary events	LIPID ²⁶ 23% ↓ coronary events CARE ²⁵ 23% ↓ cardiovascular death

Thus, the research evidence is clear for the benefit of aggressive treatment of cholesterol risk in moderate to very high risk.

Treatment Targets

Treatment targets are based upon LDL cholesterol levels, and are determined by the level of risk of the individual patient.⁶ (See Table 1)

* For information on how to calculate the 10 year Framingham Risk (for subsequent development of cardiovascular disease), please consult Appendix 1).

Initiate drug therapy immediately in high or very high risk patients. Drug therapy may be initiated in moderate and low risk patients after a 3 month trial of lifestyle changes. For management drugs of choice see Table 2.

Despite the unequivocal scientific evidence supporting the need for assessment and treatment of dyslipidemia in patients at high risk for atherosclerotic vascular events, recent studies indicate that risk factor assessment and modification is inconsistent and often incomplete. A study by the Clinical Quality Improvement Network in 4 Western Canadian hospitals has shown that, among 3,304 patient with documented atherosclerotic vascular disease recently discharged from hospital, only 28% had a serum cholesterol

measurement documented in the medical record. Overall, only 7% of patients were prescribed lipid-lowering medication. Evaluation and treatment of other risk factors were at even lower levels. These findings have been duplicated by numerous other investigators. Moreover, based upon a review of the literature describing practice patterns in lipid management, as few as 8% of patients do not reach their LDL cholesterol targets, highlighting the need for close follow-up and medication adjustment where necessary.

Summary

Extensive clinical and observational research has established that CVD risk factor control in patients at high risk for atherosclerotic vascular events is associated with improved survival and a reduced need for revascularization and hospitalization. Despite wide dissemination of the scientific evidence, application of risk assessment and intervention strategies in the high risk population appears inconsistent and suboptimal. A comprehensive, patient-centred multidisciplinary approach to risk factor modification will improve outcomes for the entire population at risk, and can be expected to reduce the economic and societal burden of atherosclerotic vascular disease.

NOTES ON THE APPLICABILITY OF THIS GUIDELINE

The recommendations in this Guideline are based on scientific evidence that aggressive risk factor modification in patients at high risk for atherosclerotic vascular events will improve or delay the need for hospitalization and invasive interventional procedures. It is acknowledged that major lifestyle modification requires cooperation between patients, physicians and other health care professionals. Additionally, the preferences of individual patients with regard to lifestyle changes must be taken into account in selecting risk modification strategies. Patient education is an integral component of optimal risk factor management.

This Guideline reflects current knowledge of cardiovascular risk factors and efficacious risk factor modification strategies. Guidelines may be subject to changes in the event of the following:

- ◆ Identification of additional risk factors which are amenable to modification.

- ◆ Development of new strategies for risk factor modification.
- ◆ Improved ability to predict the benefits to individual patients of aggressive risk factor modification.
- ◆ Target lipid levels were derived from published recommendations from the Canadian Working Group on Hypercholesterolemia and Other Dyslipidemias,⁶ the National Cholesterol Education Program (NCEP III),⁷ the Canadian Hypertension Recommendation Working Group,¹⁶ and the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure⁸, and may change as new evidence is published.

REFERENCES

1. Heart and Stroke Foundation of Canada. The Changing Face of Heart Disease and Stroke in Canada 2000.
2. Superko, HR. Sophisticated primary and secondary atherosclerosis prevention is cost effective. *Can J Cardiol* 1995;11 (Suppl C):35C-40C.
3. The Clinical Quality Improvement Network (CQIN) Investigators. Low incidence of assessment and modification of risk factors in acute care patients at high risk for cardiovascular events, particularly among females and the elderly. *Am J Cardiol* 1995;76:570-573.
4. Northridge DB, Shandall AM, Rees A, Buchalter MB. Inadequate management of hyperlipidaemia after coronary bypass surgery shown by medical audit. *Br Heart J* 1994;72:46-67.
5. Olson KL, Bungard TJ, Tsuyuki RT. Cholesterol Risk Management: A Systematic Examination of the Gap From Evidence to Practice. *Pharmacotherapy* 2001; 21: 807-817.
6. Fodor J, Frolich J, Genest J, et al. Recommendations for the management and treatment of dyslipidemia. *CMAJ*, 2000; 162(10): 1441-1447.
7. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; 285: 2486-2497.
8. Joint National Committee. The Sixth Report of the Joint National Committee of Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 1997; 157: 2413-2446.
9. Salonen JT. Stopping smoking and long-term mortality after acute myocardial infarction. *Br Heart J* 1980;43:463-9.
10. Cavender JB, Rogers WJ, Fisher LD, Gersh BJ, Coggin CJ, Myers WO. Effects of smoking on long-term survival and morbidity in patients randomized to medical or surgical therapy in the Coronary Artery Surgery Study (CASS). *J Am. Coll Cardiol* 1992;20:287-92.
11. Mulcahy R, Hickey N, Graham IM, MacAirt J. Factors affecting the 5 year survival rate of men following acute coronary heart disease. *Am Heart J* 1977;93:556-9.
12. Okene J. The influence of medical care on smoking cessation: treatment of smoking to prevent coronary heart disease. In: Higgins MW, Luepker RV (eds). *Trends in Coronary Heart Disease Mortality. The Influence of Medical Care*. New York: Oxford University Press, 1988:131-42.
13. Wilson D, Best A, Lindsay-McIntyre E, et al. Can training family practice physicians improve compliance with nicotine gum use? In: Okene JK (eds): *Proceedings of the Congress on the Pharmacologic Treatment of Tobacco Dependence*, Cambridge Mass., Nov 3-5, 1985. Cambridge, MS: Institute for the Study of Smoking Behavior and Policy, 1986.
14. McMahan S, Peto R, Cuttler J, et al. Blood pressure, stroke and coronary heart disease. Part I. Prolonged differences in blood pressure: prospective observational studies correction for the regression dilution bias. *Lancet* 1990;335:765-74.
15. Collins R, Peto R, MacMahon S, et al. Blood pressure, stroke, and coronary heart disease. Part 2, Short-term reductions in blood pressure: overview of randomized drug trials in their epidemiological context. *Lancet* 1990;335:827-38.
16. McAlister FA, Levine M, Zarnke KB, et al. The 2000 Canadian recommendations for the management of hypertension: Part 1 – Therapy. *Can J Cardiol* 2001; 17: 543-559.
17. Hennekens CH, Satterfield S, Hebert PR. Treatment of elevated blood pressure to prevent coronary heart disease. In Higgins MW, Luepker RV (eds). *Trends in Coronary Heart Disease Mortality. The Influence of Medical Care*. New York: Oxford University Press, 1988:103-09.

18. Morrish NJ, Stevens LK, Fuller JH, Keen H, Jarrett RJ. Incidence of macrovascular disease in diabetes mellitus: the London cohort of the WHO Multinational Study of Vascular Disease in Diabetes. *Diabetologia* 1991;34:584-89.
19. Grundy SM, Benjamin IJ, Burke GL, et al. Diabetes and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. *Circulation* 1000; 100: 1134-1146.
20. Haffner SM, Lehto S, Ronnema T, Pyorala K, Laakso M. *N Engl J Med* 1998;339:229-234.
21. Pate RR, Pratt M, Blair SN, et al. Physical activity and public health: A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA* 1995;273:402-07.
22. Oldridge NB, Guyatt GH, Fischer ME, Rimm AA. Cardiac rehabilitation after myocardial infarction: Combined experience of randomized clinical trials. *JAMA* 1988;260:945-50.
23. Fletcher GF, Balady GJ, Amsterdam EA, et al. Exercise Standards for Testing and Training. A Statement for Healthcare Professionals From the American Heart Association. *Circulation* 2001; 104: 1694-1740.
24. Scandinavian Simvastatin Survival Study Group. Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study. *Lancet* 1994;344:1383-9.
25. Sacks FM, Pfeffer MA, Moyer LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. *N Engl J Med* 1996;334:1001-9
26. The Long Term Intervention with Pravastatin in Ischaemic Disease (LIPID) study group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. *N Engl J Med* 1998;339:1349-57.
27. Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *N Engl J Med* 1995;333: 1301-7.
28. Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels. *JAMA* 1998;279:1615

THE ALBERTA CLINICAL PRACTICE GUIDELINES PROGRAM

The Alberta Clinical Practice Guidelines Program promotes appropriate, effective and quality medical care in Alberta by supporting the use of clinical practice guidelines. The program is administered by the Alberta Medical Association under the direction of a multi-stakeholder steering committee.

This guideline update was prepared by the Alberta CPG Program and the Epicore Centre, Division of Cardiology, University of Alberta.

TO PROVIDE FEEDBACK

The Alberta CPG Program encourages your feedback. If you need more information on this guideline or if you have difficulty applying this guideline, please contact:

The Alberta Clinical Practice Guidelines Program
 12230 - 106 Avenue NW
 EDMONTON, AB T5N 3Z1
 (780) 482-2626
 or toll free 1-800-272-9680
 Fax: (780) 482-5445
 Email: cpg@albertadoctors.org
 Website: <http://www.albertadoctors.org>

APPENDIX 1: Determine Risk Points^{36,37}

Risk Factor		Men	Women
Age	30-34	-1	-9
	35-39	0	-4
	40-44	1	0
	45-49	2	3
	50-54	3	6
	55-59	4	7
	60-64	5	8
	65-69	6	8
	70-74	7	8
Total Cholesterol	<4.14	-3	-2
	4.15-5.17	0	0
	5.18-6.21	1	1
	6.22-7.24	2	2
	≥7.25	3	3
HDL Cholesterol	<0.9	2	5
	0.91-1.16	1	2
	1.17-1.29	0	1
	1.30-1.55	0	0
	≥1.56	-2	-3
Systolic BP (mmHg)	<120	0	-3
	120-129	0	0
	130-139	1	1
	140-159	2	2
	≥160	3	3
Smoker (Yes)		2	2
Add Points			
Calculate 10 year risk (%)			
Total Points		Men	Women
1		3	2
2		4	3
3		5	3
4		7	4
5		8	4
6		10	5
7		13	6
8		16	7
9		20	8
10		25	10
11		31	11
12		37	13
13		45	15
14		≥53	18
15			20
16			24
17			≥27

Guidelines for the Management of Modifiable Risk Factors in Adults at High Risk for Cardiovascular Events

Summary of the Alberta Clinical Practice Guideline, March 2002

Identify patients at high to very high risk

- ◆ Adult patients with atherosclerotic vascular disease:
 - Clinical or angiographic evidence of coronary artery disease
 - Peripheral vascular disease
 - Cerebrovascular disease
- ◆ All patients with diabetes >30 years of age
- ◆ Patients with an estimated 10 year risk of coronary artery disease (see below)

Determine Risk Points

RISK FACTOR		MEN	WOMEN
Age	30-34	-1	-9
	35-39	0	-4
	40-44	1	0
	45-49	2	3
	50-54	3	6
	55-59	4	7
	60-64	5	8
65-69		6	8
		7	8
Total Cholesterol	<4.14	-3	-2
	4.15-5.17	0	0
	5.18-6.21	1	1
	6.22-7.24	2	2
	≥7.25	3	3
HDL Cholesterol	<0.9	2	5
	0.91-1.16	1	2
	1.17-1.29	0	1
	1.30-1.55	0	0
	≥1.56	-2	-3
Systolic BP (mmHg)	<120	0	-3
	120-129	0	0
	130-139	1	1
	140-159	2	2
	≥160	3	3
Smoker (Yes)		2	2
Add Points			

Calculate 10-year risk (%)

Total Points	Men	Women
1	3	2
2	4	3
3	5	3
4	7	4
5	8	4
6	10	5
7	13	6
8	16	7
9	20	8
10	25	10
11	31	11
12	37	13
13	45	15
14	≥ 53	18
15		20
16		24
17		≥ 27

Identify and Manage Modifiable Risk Factors

- ◆ Smoking:
 - Target complete cessation (counselling by physician. Nicotine replacement and bupropion may be effective short term adjuncts)
- ◆ Excess weight:
 - Target healthy body weight (prescribe low fat, heart healthy diet. Refer to dietician)
- ◆ Sedentary lifestyle:
 - Target at least 30 minutes physical activity per day
- ◆ Hypertension:
 - Target systolic <140 and diastolic <90mmHg (in diabetics, systolic <130 and diastolic, 80 mmHg). In addition to diet plus exercise, diuretics, beta blockers, ACE inhibitors or calcium channel blockers are often necessary
- ◆ Dyslipidemias:
 - Initiate drug therapy immediately in high or very high risk patients
 - Also consider the following to further reduce cardiovascular risk:
 - ASA (80-325mg daily or every other day)
 - Angiotensin Converting Enzyme (ACE)
 - Drug therapy may be initiated in moderate and low risk patients after 3 month trial of lifestyle changes if target lipid values not achieved

Target Lipid Levels

Risk Level	Definition	Target LDL-C (mmol/L)	Target TC/HDL	Target TG (mmol/L)
Very High	Established CVD, diabetes, or 10y risk >30%	<2.5	<4	<2
High	10y risk of 20 to 30%	<3.0	<5	<2
Moderate	10y risk of 10 to 20%	<4.0	<6	<2
Low	10y risk of <10%	<5.0	<7	<3



Administered by the
Alberta Medical Association

For complete guideline refer to the Alberta Medical Association Website: www.albertadoctors.org
Revised March 2002

Management: Drugs of Choice Based on Lipid Profile

Lipid Profile	1 st Choice	2 nd Choice
↑↑ LDL	Statin	Resin
↑↑ LDL, ↑ TG	Statin	Fibrate or niacin
↑ LDL, ↓ HDL	Fibrate or statin	Combination therapy
↑ LDL, ↑↑ TG	Fibrate or niacin	Combination therapy
↓ HDL, ↑ TG	Fibrate or niacin	Combination therapy

Relative Effects of Lipid-lowering Agents

Drug	LDL	HDL	TG
Resins			
- Cholestyramine	↓↓	↑	↑
- Colestipol	↓↓	↑	↑
Fibrates			
- Gemfibrozil	↓	↑↑	↓↓↓↓
- Bezafibrate	↓↓	↑↑	↓↓↓↓
- Fenofibrate	↓↓	↑↑	↓↓↓↓
Niacin	↓↓	↑↑	↓↓↓↓
Statins	↓↓↓	↑	↓↓

Dosing of Lipid-Lowering Agents

Drug	Initial Dose	Maintenance Dose	Maximum Dose
Resins			
Cholestyramine	4 g qd-bid	8-16g/day (given bid or qid)	24 g/day
Colestipol		15-30g/day (given bid or qid)	30g/day
Fibrates			
Gemfibrozil	300mg bid	600mg bid	1500mg/day
Bezafibrate	200mg	200mg tid	600mg
Fenofibrate	200mg	200mg qd	200mg qd
Niacin	125mg bid	1.5g –2.0g daily (tid)	2g tid
Statins			
Atorvastatin	10mg	10-60mg qd	80mg qd
Fluvastatin	20mg	20-60mg qd-bid	40mg bid
Lovastatin	20mg	20-60mg qd	40mg bid
Pravastatin	10-20mg	20-40mg qd	40mg qd
Simvastatin	5-10mg	10-40mg qd	80mg qd

Comments on Lipid Lowering Agents

Drug	Side effects	Comments
Resins	GI upset Esophageal spasms or respiratory distress (if ingested in dry form)	Space administration of other agents 1 hr before or 2 hrs after resin. Increase fluid and fiber intake to help relieve side-effects.
Fibrates	GI upset, hepatotoxicity, rash pruritis, headaches, insomnia, myopathies	Take with food (except gemfibrozil which should be taken 30 min. prior to meals)
Niacin	Headache, flushing, pruritis, GI upset, hyperuricemia, and gout, hyperglycemia, hepatotoxicity	Tolerance often develops to flushing. 325mg ASA 30 mins prior to niacin may help alleviate flushing. Avoid hot beverages. Take with food.
Statins	GI upset, myopathies, hepatotoxicity	Taking with food helps to alleviate side-effects (lovastatin should always be taken with evening meals)

Potential Drug Interactions and Laboratory Monitoring

Drug	Potential Interactions	Required Lab Monitoring
Resins	Decreased absorption of digoxin, warfarin, thyroid, oral hypoglycemics, statins, folic acid, gemfibrozil, thiazides, tetracycline, vitamins A,D,K	None
Fibrates	Displacement of warfarin or oral hypoglycemics. Increased risk of myopathies with statins, niacin, or cyclosporine	LFTs at baseline, 6 mths, and 6 mths to 1 yr thereafter. CK at first sign of muscle pain (d/c drug if CKs 10x upper limit of normal)
Niacin	Decreased effects of insulin or oral hypoglycemics. Increased risk of myopathies with statins or fibrates	LFTs at baseline, every 6 to 12 weeks for 1st yr, every 6 mths thereafter. Uric acid and glucose at baseline and as necessary thereafter
Statins	Increased risk of myopathies with niacin, erythromycin, gemfibrozil, ketoconazole, itraconazole, or cyclosporine. Increased digoxin with atorvastatin or fluvastatin. Increased warfarin levels with fluvastatin	LFTs at baseline, 6 mths, and 6 mths to 1 yr thereafter. CK at first sign of muscle pain (d/c drug if CKs 10x upper limit of normal)

Monitoring and Follow-up

- ◆ Regular follow-up visits are necessary to:
 - Titrate/change medications to ensure patients reach their targets for lipids and blood pressure
 - Recheck cholesterol and blood pressure every 6 to 12 weeks if not at target values after medication changes, yearly otherwise
 - Reinforce adherence to lifestyle modifications (smoking, diet, exercise) and medications

Congestive heart failure is common. Its high mortality rate can be reduced with proper therapy

The short-term mortality rates associated with CHF are comparable with those associated with several types of cancer.

Pathophysiology and Etiology: CHD and hypertension are the commonest causes.

The Framingham study of 5209 patients followed over 35 years shows hypertension (HTN) and Coronary heart disease are the most common causes of heart failure (accounting for 60-70% of cases). Diabetes increases the risk 2-7 times, especially in females.

Other (less common) causes include:

- Valvular heart disease
- Alcohol
- Idiopathic (up to 20% of cases)
- Toxicities (Adriamycin, doxorubicin, radiation, uremia, cocaine)
- Infectious (Chagas' disease, Coxsackie virus, HIV)
- Endocrine (Hyperthyroidism, acromegaly, diabetes)
- Infiltrative (Sarcoid, amyloid, hemochromatosis, neoplasia)
- Genetic (HOCM)
- Metabolic (Thiamine, selenium deficiencies)
- Arrhythmia-induced (Atrial fibrillation with rapid VR, incessant SVT)
- Peripartum cardiomyopathies

Clinical presentation: See Clinical Examination for heart failure module

Always ask:

- Is the failure systolic, diastolic or both?
- How severe is the heart failure?
- Are there any precipitating factors for the CHF

In about one third of patients with CHF diastolic dysfunction predominates and is characterized by pulmonary or systemic venous congestion in the presence of normal or near normal systolic function. Diastolic dysfunction results from impaired LV filling, in turn secondary to decreased LV compliance from myocardial ischemia, hypertrophy or fibrosis. Clinical characteristics that may help determine the kind and severity of CHF include:

Characteristic	Systolic Dysfunction	Diastolic dysfunction
Peripheral edema	Present	Minimal if present
S3	Present	-
S4	-	Present
Cardiomegaly	Present	-

Severity Class	NYHA classification of Functional limitation
1	No limitation in ordinary activity
2	Slight limitation by dyspnea and or fatigue during moderate exertion or stress
3	Symptoms with minimal exertion that interfere with normal daily activity
4	Inability to carry out any physical activity without symptoms

Severity Class	Killip Classification of Left ventricular function in Acute Myocardial Infarction	Hospital Death Rate (%)
I	No crackles, no S3	low
IIa	Crackles < 50% of lungs, no S3	low
IIb	Crackles < 50% of lung fields, S3 present	moderate
III	Crackles > 50% of lung fields, pulmonary edema	high
IV	Cardiogenic shock	Very high

Useful Laboratory tests

- CBC (anemia and polycythemia with pulmonary disease)
- Serum Sodium: hyponatremia, a marker for excess neurohormonal activation, is a indicator of worse prognosis
- 12 lead ECG
- CXR (PA and lateral)
- The Canadian cardiovascular society strongly recommends either echocardiography or radionuclide scanning to determine type and degree (and sometimes etiology) of CHF
- Brain Natriuretic peptide (BNP) is released in response to LV mechanical stretching, may be a useful discriminator between lung disease and CHF as a case of dyspnea, and higher values may be a prognostic sign for increased risk of mortality (6)

Treatment of congestive heart failure is directed towards reducing neurohormonal activation

Neurohormonal activation involving the renin-angiotensin-aldosterone, and adrenergic systems is deleterious, and reduction of such action is a mechanism by which ACE inhibitors, ARBs, spironolactone, and B-blockers have positive therapeutic effects on CHF.

Management is most successful if patients are actively involved.

The main cause of decompensation and re-hospitalization is poor therapeutic adherence. Educating the patient and his or her family is crucial to helping stabilize the condition of patients with CHF. Fluid restriction may be advised, to 1-1.5 liters/day and sodium restriction to 1.5-2 gm/day. Daily weights are a valuable surveillance tool. Advise your patients to look for an increase in weight of more than 2 kg in 2-3 days. This may be the first indication of worsening failure, and may precede obvious worsening of peripheral edema. Prompt adjustment in anti-failure therapy may pre-empt an exacerbation of CHF or admission into hospital.

Pharmacologic Therapy for systolic dysfunction.

It is not clear which agents are best for diastolic dysfunction.

ACE inhibitors (ACEI) improve survival in patients with systolic dysfunction and remain the first choice for treatment in heart failure. Angiotension receptor blockers (ARBs) may be used as an alternative to ACEIs in those patients unable to tolerate these agents. ARBs may have a negative impact if used with B-blockers.

ACEI should be given to all symptomatic patients, all patients with LVEF \leq 35% regardless of symptoms, and all patients with recent MI and EF < 40%. Survival studies have shown that the following therapeutic doses must be attained to improve survival:

- Enalapril 15-20 mg/day
- Captopril 150/mg day

The V-HeFT II study used a combination of hydralazine and isosorbide dinitrate, and showed improved hemodynamics, but no improvement in prognosis. However, if a patient cannot tolerate ACE inhibitors due to symptomatic hypotension, azotemia, hyperkalemia, cough, rash or angioneurotic edema, then hydralazine and isosorbide nitrate can be utilized.

To date, the two largest trials to date Elite-II and Val-Heft (using valsartan), as well as a meta-analysis (5) of 17 trials looking at ARBs vs placebo [7 trials], ARBs vs ACEIs [6 trials], ARBs and ACEIs in combination vs ACEIs alone [6 trials] have failed to show that ARBs are superior to ACEIs in prevention of death or cardiovascular events in patients with symptomatic heart failure. The combination of ARBs and ACEIs appears to be beneficial for reducing the hospitalization rate over ACEIs alone. There is a worrying suggestion of a negative interaction when ARBs are added to beta-blocker and ACE combinations, which is a reason for *caution in using the ARBs*, NOT a reason to avoid using beta-blockers. **ACEIs should remain the standard of care, with an ARB in those patients unable to tolerate an ACE (cough etc).**

Example ACEI and ARB dosing in CHF:

Enalapril	2.5-10 mg twice daily
Ramipril	2.5-10 mg daily
Lisinopril	2.5 mg daily up to 20-40 mg daily
Valsartan	80-160 mg daily
Losartan	25-50 mg daily
Candesartan	4-16 mg daily

Gradually increase the dose of the agent, every 2-4 weeks, aiming for maximum recommended doses, (or maximum dose tolerated). Repeat serum electrolytes, creatinine and blood pressure assessment before each increment.

B-blockers are safe and effective in the treatment of heart failure.

Beta-blockers work by modifying increased neuroendocrine excitation, myocardial ischemia and ventricular arrhythmias.

Results from recent studies using of carvedilol, bisoprolol, and metoprolol (CR/XL) demonstrate total mortality reductions by 34%. The MERIT-HF study, which included patients with NYHA class 2-4 heart failure, demonstrated decreased hospitalizations due to worsening heart failure (RR 31%), and improved functional class and patient well-being. Metoprolol was started after symptomatic heart failure had been stabilized, at 12.5 mg daily for patients with class 3-4 and 25 mg a day for class 2 and titrated up over 6 weeks to a target of 200 mg/day (1)

Start *after* the patient has recovered from any acute decompensation. Start low and double the dose every 2-4 weeks until the patient is either unable to tolerate higher doses or the target dose is reached.

Bisoprolol	Start 1.25 mg, titrated to 5-10 mg/day
Metoprolol	Start 6.25 –12.5 mg, titrated to 75 mg daily
Carvedilol	Start 3.25-6.5 mg, titrated to 25 mg twice daily

To avoid transiently worsening heart failure, do not start B-blockers in patients who are acutely decompensated, or have severe symptoms at rest (NYHA IV), or who are severely volume overloaded, or who are very hypotensive (BP sys < 85 mm HG). Avoid B-blocker use in patients with *severe* bronchospastic disease.

Spironolactone is safe and effective adjunctive therapy in patients with SEVERE heart failure.

The RALES (randomized aldactone evaluation study) showed that the addition of spironolactone (25-50 mg/day) to standard therapy (ACE Inhibitors and loop diuretics) significantly reduced the risk of both morbidity and death from progressive heart disease among patients *with severe (NYHA class III and IV)* heart failure. The incidence of serious hyperkalemia appears to be minimal. (2). Spironolactone should

NOT be started on patients with creatinine values > 220 $\mu\text{mol/L}$ or a serum K > 5.2 mmol/L . After starting, check electrolytes and creatinine one week later, then at one month, and then periodically thereafter.

Digoxin may reduce rate of hospitalization, *but not mortality*, if used with ACEI and diuretics.

Digoxin use has little effect on mortality. If a patient is in atrial fibrillation and has LV dysfunction, it may be beneficial for rate control. If a patient with CHF is already on digoxin and ACEI, evidence suggests there is a risk of deterioration if the digoxin is stopped.

Calcium Channel Blockers do not appear to improve survival in patients with heart failure

In the PRAISE trial, amlodipine did not have a negative impact on mortality. In the subgroup of patients with non-ischemic dilated cardiomyopathy it was associated with an ARR of 5%. However many of these patients were also receiving ACEIs.

Continuous Positive Airway Pressure (CPAP) may be beneficial in management of CHF

Continuous positive airway pressure (CPAP) is a mechanical means of reducing transmural wall tension and allows the heart to remodel. Patients with heart failure often have enlarged hearts and concomitant respiratory or sleep disorders, such as sleep apnea or Cheyne-Stokes respiration. CPAP reduces LV volume, decreases the amount of mitral regurgitation, improves EF, and reduces neurohumoral activation. In addition, patients report improved sleep patterns and less fatigue.

Nocturnal Continuous positive airway pressure therapy (CPAP) is helpful for patients who have co-existing CHF and sleep apnea, but may also be useful in the failing heart even in the absence of clinically significant sleep apnea. (3) Cheyne-Stokes respiration with central sleep apnea is commonly observed in patients with congestive heart failure, and is an independent risk factor for death. An ongoing multicenter trial is currently evaluating CPAP in patients with heart failure and sleep apnea (4).

Surgical and Future Therapies for Heart Failure

There are multiple surgical options that may enhance the medical treatment of heart failure. These include myocardial replacement therapies, such as mechanical circulatory support systems, allo-transplantation or xeno-transplantation and myocardial enhancement therapies such as cardiomyoplasty, ventricular reduction therapy, and transmyocardial revascularization. Newer modalities for the treatment of heart failure include gene therapy in the form of vascular or myocardial growth factors, growth hormones or cell transplantation.

References

1. Hajlmarson A Goldstein S et al JAMA 2000;283:1295-1302
2. Pitt, B et al. NEJM 1999;341:709-17)
3. Leung, R and Bradley TD. Can J Cardiol 1999;15: 1009-1012
4. Bradley TD for CANPAP investigators. Can J Cardiol 2001;17:677-684
5. Jong P, Demers C, McKelvie RS, Liu PP. Angiotensin receptor blockers in heart failure: meta-analysis of randomized controlled trials. J Am Coll Cardiol. 2002; Feb 6;39:463-70
6. Ezekowitz J Armstrong PW. Can J Cardiol 2004; 20: 684-5

Always differentiate generalized from local edema, and consider causes during history taking. These may include:

- Cardiac (CHF, valvular heart disease, pericarditis, pulmonary hypertension)
- Renal (failure or nephrotic syndrome)
- Gastrointestinal (Protein losing enteropathy, liver Failure)
- Venous insufficiency or obstruction (including venous thromboembolism or extrinsic compression)
- Lymphatic obstruction
- Drugs (NSAIDS, dihydropyridine calcium channel blockers), or intravascular volume expansion from IV fluids or “idiopathic”.

Localized edema

This is often due to increased capillary pressure. If confined to the lower limbs, determine whether it is unilateral or bilateral. Unilateral edema more strongly favors obstruction or compression of venous or lymphatic outflow.

Generalized edema

Measure the CVP by determining the JVP.

Normal JVP?

- Measure the serum albumin and urinary protein.
- If the serum albumin is decreased and there is protein on urinalysis, quantify it with a 24-hour collection. More than 3.5 grams of protein per day suggests nephritic syndrome. If there is no renal loss of protein check liver function including transaminases and PTINR. If normal check prealbumin and cholesterol to evaluate for malnutrition.
- If serum albumin is normal, check urine for sediment, and BUN/ CR for renal pathology.
- If urinalysis is normal order a TSH to rule out myxedema. If al of this is normal consider drug induced or idiopathic edema

Elevated JVP

- Look for clinical and x-ray signs of cardiomegaly. If cardiomegaly is present do an echocardiogram to look for pericardial effusion or evidence of constrictive pericarditis, ventricular size, function and wall motion, and valvular disease.
- If there is no cardiomegaly, look for signs of pulmonary hypertension (e.g. cor pulmonale). Clear lung fields, an elevated JVP, small heart and unexplained generalized edema are also consistent with constrictive pericarditis.

Heart Sounds

First heart sound

Loud (mitral stenosis, short PR interval from any cause, hypertension)

Soft (Mitral regurgitation, prolonged PR interval from any cause)

Second heart sound

The S2 may be soft in Left heart failure, aortic valve stenosis, or loud in hypertension.

“Normal” splitting occurs with inspiration, and is maximal at end inspiration-early expiration. The second heart sound is single in many elderly patients without important heart disease. The S2 may have pronounced “normal” splitting in Pulmonary hypertension, embolism or stenosis, RBBB, or fixed splitting (ASD), or have paradoxical splitting that occurs in mid-end expiration with LV outflow obstruction, or LBBB.

A Third heart sound (S3) may be found with a dilated ventricle with volume overload.

A fourth heart sound (S4) can be a normal finding-the true prevalence of a "normal" S4 in the healthy population is controversial, and it may be more common than originally thought. The presence of an S4 is not a specific sign. Left sided S4s may be heard with a stiff ventricle from hypertension, CHD, diabetes, aortic stenosis, or IHSS.

Early systolic clicks may be heard with hypertension, aortic and pulmonary stenosis.

Early to mid systolic clicks may be heard with mitral valve prolapse.

Innocent (Functional) Systolic Murmurs

These **systolic** murmurs are common in children and young adults, as well as in persons in states of increased cardiac output (fever, pregnancy, thyrotoxicosis, anemia). They are also commonly heard in persons with straight backs, pectus carinatum deformities, or narrow chest AP diameters.

Characteristics of an innocent (functional) systolic murmur include:

- Normal position and quality of point of maximal impulse
- Normal splitting of S2
- No S3 or S4 or other diastolic sounds
- II/VI or less in grade murmur that peaks early in systole
- Best heard in pulmonary area or lower left sternal border
- Poor radiation
- Normal ECG and CXR

Pulmonary systolic flow murmurs are greatly influenced by cardiac output and may be heard in the setting of anemia or hyperthyroidism. Differential diagnosis includes mild pulmonary stenosis (PS). Mild PS is almost always associated with an ejection click; this is an important discriminator.

Aortic sclerosis and Aortic stenosis

Aortic sclerosis is common in the elderly and most often represents sclerosis and calcification of a tricuspid aortic valve. Typically the calcification and sclerosis occur all along the edges of the valve leaflets, creating a “Mercedes Benz logo” narrowing. This in turn creates a turbulent complex jet that is diffusely directed along the ascending arch of the aorta. The vibrations of the aortic arch cause the murmur to be radiated down along the left sternal border (Gallavorden phenomenon), rather than up the carotids. If severe enough, the sclerosis and calcification can lead to significant aortic stenosis.

Rheumatic heart disease can lead to aortic stenosis (or regurgitation) but this is less common in North America, and it is unusual to have aortic valve involvement without mitral valve involvement as well. The narrowing of rheumatic heart disease occurs preferentially at the outer edges of the cusps and over time works its way inwards. With severe aortic stenosis, the aortic orifice may be limited to a narrow opening in the center of the valve.

Although differentiation between aortic sclerosis or mild aortic stenosis from significant aortic stenosis may be difficult on the clinical examination, the following criteria suggest significant aortic stenosis:

- Symptoms of syncope or near syncope, angina on exertion or CHF or signs thereof
- Delayed and diminished (Pulsus parvus and tardus) carotid upstroke (best predictor of significant AS)
- Low systolic BP (above 160 systolic makes critical aortic stenosis unlikely)
- LV heave
- Systolic crescendo decrescendo murmur that peaks at or beyond mid-systole
- The second heart sound is characteristically diminished due to poor excursion of thickened aortic leaflets
- Echocardiographic aortic valvular gradient of more than 50 mm Hg across the aortic valve or an aortic valve area of less than 0.8 cm²

Mitral regurgitation

Mitral regurgitation may be secondary to intrinsic valvular disease, papillary or chordae tendinae dysfunction, or dilation of the mitral annulus (as seen in congestive cardiomyopathy). Long standing mitral regurgitation is characterized by a blowing, relatively high-pitched murmur in the lower left sternal and apical areas with radiation towards the left axilla. The murmur may extend significantly into systole because the left atrium has enlarged and is quite compliant. The radiation pattern results from a regurgitant jet of blood baffling off the anterior leaflet, and causing vibration of the posterior wall of the left atrium. This directs sound towards the left axilla. In contrast, acute mitral regurgitation from a ruptured posterior papillary muscle (a complication of myocardial infarction) causes a regurgitant jet to bounce off the posterior (prolapsing) leaflet and hit the shared wall between the left atrium and the aortic root. In addition, the left atrium has had little time to enlarge and has little compliance for this regurgitating blood. The consequent murmur is quite different: a short systolic murmur heard best at the lower left sternal border.

Aortic insufficiency

Aortic regurgitation may be secondary to leaflet abnormalities (rheumatic heart disease, endocarditis, deteriorate bicuspid aortic valve, rheumatoid nodules, or ankylosing spondylitis) or abnormalities of the aortic root and ascending aorta (systemic hypertension, syphilitic aortitis, Reiter's syndrome, ankylosing spondylitis, or dissecting aneurysm).

The high-pitched quiet diastolic rumble of aortic insufficiency can be difficult to detect. Consider the possibility in any patient with a wide pulse pressure for no other discernable reason. The murmur is best heard in a quiet room, auscultating with the diaphragm along the left sternal border, with the patient sitting and leaning forward, and in held expiration. To prevent the patient from making noises or turning blue on you while you listen, get them oxygenated by asking them to breathe in and out and then say "stop breathing" at the end of the third expiration. You then listen while holding **YOUR** breath too. It is pointless to try to detect this murmur in a noisy environment.

Mitral stenosis

Although mitral stenosis is much less commonly encountered than in prior eras, it is still a problem to keep in mind, especially when seeing new patients from areas where rheumatic heart disease is still common (such as the Indian subcontinent). Mitral stenosis is really the only valvular lesion that presents with

significant dyspnea without clinical cardiomegaly. This is because the left ventricle is under loaded but the lungs are constantly congested, especially with exertion. Dyspnea may continue for many years in untreated patients.

Mitral stenosis is a low-pitched rumbling diastolic murmur heard best in a quiet room, with the patient positioned in the left lateral decubitus position, and with the bell of the stethoscope lightly pressed on the point of maximal impulse in the chest. The murmur can be extremely localized and may be only audible within the space of several centimeters. Classically the murmur follows an opening snap, (in turn following the S2), and has early and late accentuations. Generally, the closer the opening snap is to the S2, the more severe the mitral stenosis. Until the mitral stenosis is very severe, the S1 tends to be abnormally loud (i.e. louder than the S2 when listening in the base of the heart). This is a good screening test for mitral stenosis, as it is relatively easy to detect a loud S1 in a noisy emergency room. In contrast, you would be unable to hear most mitral stenosis murmurs in such circumstances. Therefore, earmark these patients for auscultation later in a quiet environment.

A very similar rumbling sound may be heard in patients with aortic regurgitation if the regurgitant jet hits the anterior leaflet of the mitral valve, as this jet inhibits the valve leaflet from opening and causes a relative stenosis. This “Austin Flint” murmur, lacks the opening snap and pre-systolic accentuation of intrinsic mitral stenosis.

Tricuspid regurgitation

Tricuspid regurgitation represents a relatively low-pressure jet of regurgitant blood directed posterior. Therefore it is not surprising that it is frequently missed on auscultation. A more sensitive approach to detection is to suspect it if the JVP is elevated and the “v” component is prominent. The murmur is often heard best along the lower sternum. A right ventricular heave, subxiphoid impulse, or a tender and/or palpable liver is other stigmata that may be detected.

Mitral Valve Prolapse (MVP)

This condition is common, and especially in young thin women. As end-diastolic volume increases with age, the slack chordae tendinae tighten, and regurgitation from MVP often remits. The significance of the condition is in the associated regurgitation. Classically high pitched single or multiple early systolic clicks are heard in the supine position, and these move closer to S1 with standing (reduced ventricular filling allows the leaflets more slack to prolapse earlier). Any associated regurgitation murmur following the clicks is prolonged by the same maneuver.

Suggested Reading

Bates, B A guide to the Physical Examination and History Taking. Lippencott
Constant, J Bedside cardiology. Lippicott, Williams and Wilkins 5th edition 1999

Palpitations are a common symptom and may indicate the presence of serious underlying disease. Attempts to diagnose the cause should be more aggressive if the palpitations persist and are poorly tolerated, or if the patient is at high risk for a serious arrhythmia.

General Investigation of Palpitations

The history should include how long the patient has been experiencing episodes, when do episodes stop and start, any precipitation factors such as exercise or emotion, whether they are of sudden or gradual onset, episode duration, whether the rate is slow or fast, and whether the rhythm is regular or irregular. For example, a patient who has had rapid palpitations since childhood is most likely to have a supraventricular tachycardia, particularly one that uses a bypass tract. On the other hand the onset atrial fibrillation is less likely until patients are older. It may help to ask the patient to tap out rhythms with their finger when describing their palpitations, in order to illustrate rate and rhythm. You can also give examples by the same method.

Patients are at higher risk for a serious arrhythmia if they have underlying organic heart diseases such as scar formation from previous MI, idiopathic dilated cardiomyopathy, hypertrophic cardiomyopathy, clinically significant valvular lesions, prolonged QT interval, known accelerated AV conduction syndromes (such as WPW), or a family history of arrhythmia, syncope, or sudden death from suspected cardiomyopathies or prolonged QT syndromes.

Premature atrial (PAC) and ventricular contractions (PVC) tend to occur spontaneously and often at night. Patients often describe PVCs as an intermittent pause followed by a strong beat in an otherwise regular rhythm. ("The heart seems to stop and then start again, producing a pounding or flipping sensation.") PACs are more common in the young and PVCs are more common in older persons.

Paroxysmal supraventricular tachycardia (AV nodal re-entry tachycardia or AVNRT) is characterized by sudden onset, variable duration, frequently a feeling of fast (160-180 bpm), regular, and forceful heartbeats, and sudden offset. A sensation of pounding in the neck, which suggests AV dissociation with atria contracting against closed tricuspid and mitral valves, is most typical of AVNRT. If patients report that vagal maneuvers (such as squatting or bearing down against a closed glottis to produce a Valsalva effect) abort the attacks, you should strongly suspect supraventricular tachycardias, and in particular AVNRT or those using a bypass tract.

The rhythm of atrial fibrillation is akin to that of popcorn popping. On examination the pulse is irregularly irregular with a **pulse deficit** (apex versus radial pulse rate > 10 bpm)

Episodes of Ventricular tachycardia are usually much shorter than atrial flutter or fibrillation. In about 75% of cases AV dissociation may be detected on the clinical examination (cannon or variable a waves, variable S1, variable systolic BP).

The physical examination is occasionally helpful for detecting episodes of palpitations (most often in atrial fibrillation) and may demonstrate causes, such as congestive or dilated cardiomyopathies, mitral valve prolapse or hypertrophic cardiomyopathy.

A 12-lead electrocardiogram may detect clues to causes, such as a short PR interval and delta wave (WPW), marked left ventricular hypertrophy (HOCM), evidence of prior myocardial infarction (increases likelihood of ventricular tachycardias), prolonged QT interval (polymorphic ventricular tachycardia) or atrial fibrillation. Should the history, physical examination, and ECG prove unrevealing, other investigations may include 24 hour Holter monitoring, loop recorders, and exercise stress testing, especially if the patient's symptoms come on with exercise. Finally if palpitations remain undiagnosed and especially if they are persistent and poorly tolerated, electrophysiologic studies can be done.

Atrial fibrillation

Atrial fibrillation (AF) is the most frequent form of serious cardiac arrhythmia, occurring in 5-10% of population over 65 with a male: female ratio of 2:1. It reduces exercise tolerance and heart function, and through the loss of atrial kick reduces cardiac output by 15-25%. The presence of AF doubles overall mortality rate, and incurs on average a 5% risk of stroke per year (versus 1% in general population baseline risk).

Clinical Risk factors for stroke in patients with AF include:

- Advancing age
- Diabetes
- Prior stroke or TIAs
- Hypertension
- Rheumatic heart valve disease (mitral stenosis increases risk 17-18 times above baseline)

Echocardiographic risk factors for stroke in patients with AF include:

- Enlarged left atrium, left ventricular dysfunction, presence of a left atrial thrombus or spontaneous echo contrast

Annual stroke Risk

- Less than 75 years old and no risk factors = 0.5%-1%
- 1-2 risk factors = 6%
- ≥ 3 = 18.6%

Pathophysiology

AF is due to irregular wavelets of electrical excitation propagating and interacting within the atria causing fibrilliform impulses at 400-700/min. The single commonest cause is coronary heart disease. Other etiologies include hypertension, diabetes, hyperthyroidism (9-20% in thyrotoxicosis), valvular heart disease, pericarditis, cardiomyopathies, high alcohol intake, acute systemic disease, or pulmonary embolism. Lone AF exists if no identifiable etiology can be found in a person less than 60-65 years old.

Clinical detection

Symptoms

AF may be paroxysmal or chronic, and many patients with atrial fibrillation are unaware of palpitations. AF may present with palpitations, dyspnea, or fatigue.

Physical findings

These include an irregularly irregular pulse-this may be missed with radial pulse palpation. Although it is not specific for AF, a pulse deficit may be detected. That is, one can hear more beats than one can feel by palpation of the pulse. There is also a loss of the "a" wave on JVP, and varying Korotokof sounds when taking the blood pressure. On precordial auscultation, there is a varying intensity of heart sounds, especially the S1. A particularly useful sign is the random occurrence of 2 sequential long pauses separated by only one beat. This is unlike the long pause heard with a PVC where the pause is preceded by a second beat close to the first.

Laboratory findings

Useful tests include an EKG, CBC, electrolytes serum creatinine, TSH, cardiac enzymes, chest X-ray, and 2-D echocardiogram. The ECG typically shows an irregularly irregular rhythm. Fibrillatory waves may be gross, mimicking flutter waves, or so fine as to be undetectable. Occasionally, a long R-R interval, followed by a very short R-R interval may cause stimulation of the bundle branch conduction system before it is completely repolarized. This in turn creates a wide-complex QRS (a bundle branch block pattern) which looks like a premature ventricular beat. This is called Ashman's phenomenon.

Management Goals

- Seek and correct causative or exacerbating factors
- Prevent thromboembolism
- Control ventricular response rate
- Restore and maintain normal sinus rhythm

Prevention of thromboembolism

Age (yrs)	< 65	65-75	> 75
No Risk factors*	ASA	ASA or Warfarin	Warfarin
Risk factors present	Warfarin	Warfarin	Warfarin

*Risk factors include: Advancing age, Diabetes, Prior stroke or TIAs, Hypertension, Rheumatic heart valve disease, echocardiographic risk factors (enlarged left atrium, left ventricular dysfunction, presence of a left atrial thrombus or spontaneous echo contrast). (ACCP recommendations)

Warfarin, used to maintain an INR (at 2-3), decreases embolism rate by 68%; ASA decreases rate by about 20%. Therefore, warfarin is superior except in situations where baseline risk of stroke is very low (such as lone atrial fibrillation). The most effective intensity of therapy appears to be an INR range of 2.0-3.0. INR values above 4-5 cause risk of hemorrhage to rapidly increase, and the risk of stroke rises rapidly at INR values less than 2.0 (1)

Factors increasing bleeding risk from warfarin include:

Advanced age (3-4% risk of significant bleeding per year if > 80)
Recent hemorrhage
Alcohol binge drinking or Liver disease
Renal insufficiency
Cancer
Low platelets
Uncontrolled hypertension
ASA, NSAID (includes COX2) use

High bleeding risks may overcome the benefits of decreased stroke risk. Bleeding risk is reduced by frequent monitoring, and avoidance of ultratherapeutic INRs.

Age, and in particular, fall risk in the elderly is not automatic contraindication to anticoagulation. Many physicians assume that a combination of warfarin therapy and head trauma due to falls leads to an excessively high risk of subdural hematomas, and choose not to prescribe warfarin for elderly persons with AF whom they deem at increased risk of falling. However a well-done decision analysis shows that warfarin fall-related subdurals are extremely infrequent, and pose a risk that is only a fraction of the average risk of stroke in elderly people with AF (0.0013% versus 6%/year). Therefore warfarin should remain the preferred therapy, even in patients with increased fall risk. (2)

Monitoring

After reaching a therapeutic range, check the INR 2-4 times during week 1, then 2 times in week 2, and if stable values are observed, increase to a maximal interval between measurements of about 4 weeks.

Control of ventricular response

Target for a ventricular response rate of 60-100 bpm at rest and less than 120 with moderate exercise. Digoxin is useful if left ventricular dysfunction is present but is not much value in the context of increased

sympathetic activation. It also takes about 20 minutes to have effect. Other agents include calcium channel blockers (CCB), B-blockers, and amiodarone. CCB and B-blockers are good for patients with hypertension or CHD, but may be contraindicated if the patient has significant heart failure or hypotension.

Restoration and maintenance of sinus rhythm

Immediate cardioversion is indicated in patients whose AF is causing serious hemodynamic instability. Otherwise, in stable patients, the rationale for attempted restoration of normal sinus rhythm has been to improve symptom, increase exercise tolerance and cardiac output by enabling atrial kick, prevent left atrial dilation, and prevent LV function deterioration (cardiomyopathy). However, the recent AFFIRM trial demonstrated no survival advantage of rhythm-control strategy over the rate-control strategy, and there may be potential advantages, such as a lower risk of adverse drug effects, with the rate-control strategy. (3)

Electric or chemical cardioversion unlikely to be successful if AF is of more than 6 month duration, the Left Atrial size > 45-60 mm (echocardiography), or mitral valve disease present.

Management Strategy (American College of Chest Physicians)

If AF duration is for < 48 hours

There is a 50% rate of spontaneous conversion from AF to sinus rhythm within the 8 hrs of onset of AF. However, chemical or electrical cardioversion can be performed immediately after institution of heparin anticoagulation. Thereafter, therapeutic crossover with subsequent 4 weeks of coumadin is recommended.

If AF duration is for > 48 hours or unknown duration

If possible, first perform *trans-esophageal* echocardiography (TEE), which has about 95% sensitivity in detecting atrial thrombus. If there is no detectable thrombus or spontaneous contrast (indicating slow flow), cardioversion can be done immediately after starting intravenous heparin and covering with warfarin for 4 weeks post-cardioversion.

If left atrial thrombus is detected on TEE the risk of post-cardioversion embolism is about 15%. If a TEE shows thrombus or no TEE available, give warfarin for 3 weeks pre and 4 weeks post-cardioversion. This reduces the risk of post-cardioversion embolism from 5-7% to 1.2%.

Electrical cardioversion:

Synchronized cardioversion with 100-200 J is successful in 85% of cases. Digoxin toxicity is one of the important contraindications for elective cardioversion, since digoxin can produce unstable arrhythmias that necessitate cardioversion. In these circumstances the cardioversion should proceed with low energies and utilizing lidocaine prophylaxis.

Chemical cardioversion:

Useful agents include Procainamide, Amiodarone, Sotalol, and Propafenone. Digoxin, Beta-blockers, calcium channel blockers, and Type 1b agents such as lidocaine and phenytoin *are ineffective*.

After electrical or chemical cardioversion, there is a 70% recurrence rate within 1 year if anti-arrhythmics are not used to maintain sinus rhythm (and a 55% recurrence with their use). Maintenance medications include Procainamide, Amiodarone, Sotalol, and Propafenone.

Invasive or surgical interventions for AF

Radio frequency ablation of AV node may be considered if medical management failed. It requires insertion of a permanent pacemaker and long term anticoagulation. Surgical treatments, including the Corridor and Maze procedures involve incisions of atrium to create scars to impede progression of wavelets and reduce atrial size, require open-heart surgery, and are rarely indicated.

Atrial Flutter

Atrial flutter is one of the easiest dysrhythmias to convert to normal sinus rhythm. The use of low energy discharges such as 50 joules usually converts flutter into fibrillation.

References

1. Hylek EM et al NEJM 1996;335:540-6
2. Man-Son-Hing M et al. Arch Intern Med 1999;159:677-684
3. Wyse DG et al NEJM 2002 Dec 5;347(23):1825-33.

Aging and the skin

Aging can produce a variety of skin disorders in the elderly. Physiologic changes occurring in the skin include flattening of the dermal-epidermal junction, dermal and subcutaneous loss of mass, and decrease in melanocytes. Dry skin and pruritis are common, as are skin tags (acrochordon), keratoses, lentiginos ("liver spots"), and senile purpura. Dry skin is the commonest cause of generalized pruritis in adults in the Edmonton area.

Erythema Multiforme

Most cases of recurrent erythema multiforme are due to herpes simplex virus. Penicillin is a common cause of erythema multiforme major (Stevens-Johnson syndrome), with systemic features, atypical target lesions, and mucosal lesions. Recurrent bouts are unusual. *Mycoplasma pneumoniae* produces erythema multiforme major in kids, but recurrent bouts are unusual.

Malignant melanoma

Melanoma incidence is increasing in Canada. This increase is likely real rather than due to lead time bias because if it were the latter one would expect the incidence to ultimately flatten or fall, the percentage of "earlier" lesions to increase, and the mortality rates to decrease. None of these have been observed. Females seem to be more prone to leg lesions, and men, to back lesions. Head lesions are more common in older men and in rural people.

Clinical Skills : See Dermatology in SDL section for slide show and Quiz of common skin conditions.

Diabetes Mellitus

- **Prevalence of the condition (type 1 and type 2)**
- **Compare and contrast type 1 and type 2**
- **Criteria for diagnosis**
- **Criteria for good glycemc control**
- **Gestational diabetes**
- Major diabetic complications: how to detect them and prevent or retard their development
- Insulin and Oral hypoglycemic use and adjustments to glucose levels
- **Diabetic ketoacidosis diagnosis and management**
- Hyperosmolar non-ketosis state diagnosis and management
- List factors that can lead to loss of glycemc control

Approach to hypoglycemia

Thyroid Disease

- Hypothyroidism diagnosis
- **Hyperthyroid diagnosis**
- Basic interpretation of thyroid function tests (TSH, T4, T3)
- **Thyroid nodules and Risks for thyroid cancer**

Adrenal Disease

- **Adrenal Insufficiency symptoms and signs**
- **Screening for adrenal insufficiency**
- Withdrawal from steroid use
- **Adrenal Masses**

Hypercalcemia

- Clinical presentation
- **Causes**
- Immediate management

Increased body weight

1. List serious diseases for which obesity is a significant risk factor
2. Calculate approximate ideal weight
3. Discuss safe weight-reduction strategies

Clinical Skills (See Clinical Skills section)

- History taking for long-standing Type 1 diabetes

Diabetes Mellitus

Contributors : P. Hardin, E. Ryan, R. Lewanczuk, B. Fisher

More than 5% of Canadians have the diagnosis of diabetes (with the recent increased sensitivity of the diagnostic criteria this percentage will increase). Diabetes is classified into Type 1 and 2, as well as more rare “other specific types (mainly specific genetically defined forms of diabetes or diabetes associated with other diseases or drug use).

Type 1 diabetes encompasses diabetes that is primarily the result of pancreatic beta-cell destruction and that is prone to ketoacidosis. It includes cases due to an autoimmune process and those for which the etiology of beta-cell destruction is unknown. It accounts for about 10% of diabetes cases.

Type 2 diabetes may range from predominant insulin resistance with relative insulin deficiency to a predominant secretory defect with insulin resistance. Ketoacidosis is rarely seen in type II diabetes. Type 2 diabetes accounts for 90% of cases of diabetes, and most Type 2 diabetics are of middle-aged or older, in contrast to the generally earlier onset in Type 1 diabetes. When Type 2 diabetes occurs in younger age groups it is termed “Maturity onset diabetes of the Young” or MODY. There is clearly genetic predisposition to Type 2 diabetes and penetrance may be very high in certain racial groups (e.g. Pima Native Americans). Both forms of diabetes, if poorly controlled, may lead to serum glucose levels above 16 mmol/L. Type 2 diabetes may pre-date its actual diagnosis by many years, and diabetic retinopathy is already present in about 20% of T2 diabetics at the time of diagnosis. Diabetic nephropathy (and therefore T2 diabetes) is the number one cause of end stage renal disease in Canada and elsewhere.

A recent re-evaluation of population studies suggests that a fasting plasma glucose “cutoff” level of 7.0 mmol/L correlates more closely with a 2 hour sample of the oral glucose tolerance test than did the prior 7.8 value, and best predicts development of micro vascular disease. The revised Canadian Guidelines (CMAJ 1998;159: S6) are as follows:

Diabetes is present if ANY ONE of the following criteria are met:

- Symptoms of diabetes* plus a random plasma glucose value ≥ 11.1 mmol/L
- A fasting plasma glucose value ≥ 7.0 mmol/L on two or more occasions**
- A plasma glucose value in the 2 hour sample of the oral glucose tolerance test ≥ 11.1 mmol/L (using 75 gm glucose load)

*The classic symptoms of diabetes include fatigue, polyuria, polydipsia and unexplained weight loss.

A confirmatory test must be done on another day in all cases **unless there is unequivocal hyperglycemia accompanied by acute metabolic decompensation

Patients with fasting levels between 6.1 and 7.0 mmol/L are considered to have “**impaired fasting glucose**” and have a higher risk of subsequently developing diabetes and cardiovascular disease than does the general population.

The following values can be used for assessing the degree of glycemic control.

	Fasting glucose	1-2 pc glucose	HbA1c
Non-diabetic	3.8-6.1	4.4-7	0.04-0.06
Optimal diabetic target	4-7	5-11	<0.07
Sub optimal	7.1- 10	11.1-14	0.07-0.084
Inadequate	>10	>14	> 0.084







Inadequate control is associated with markedly increased long-term complication rates. Because of lack of standardization of the HbA1c test it is not recommended for the diagnosis of DM but is useful in assessing control.

Diabetes Care Flow Sheet for Patients with Diabetes

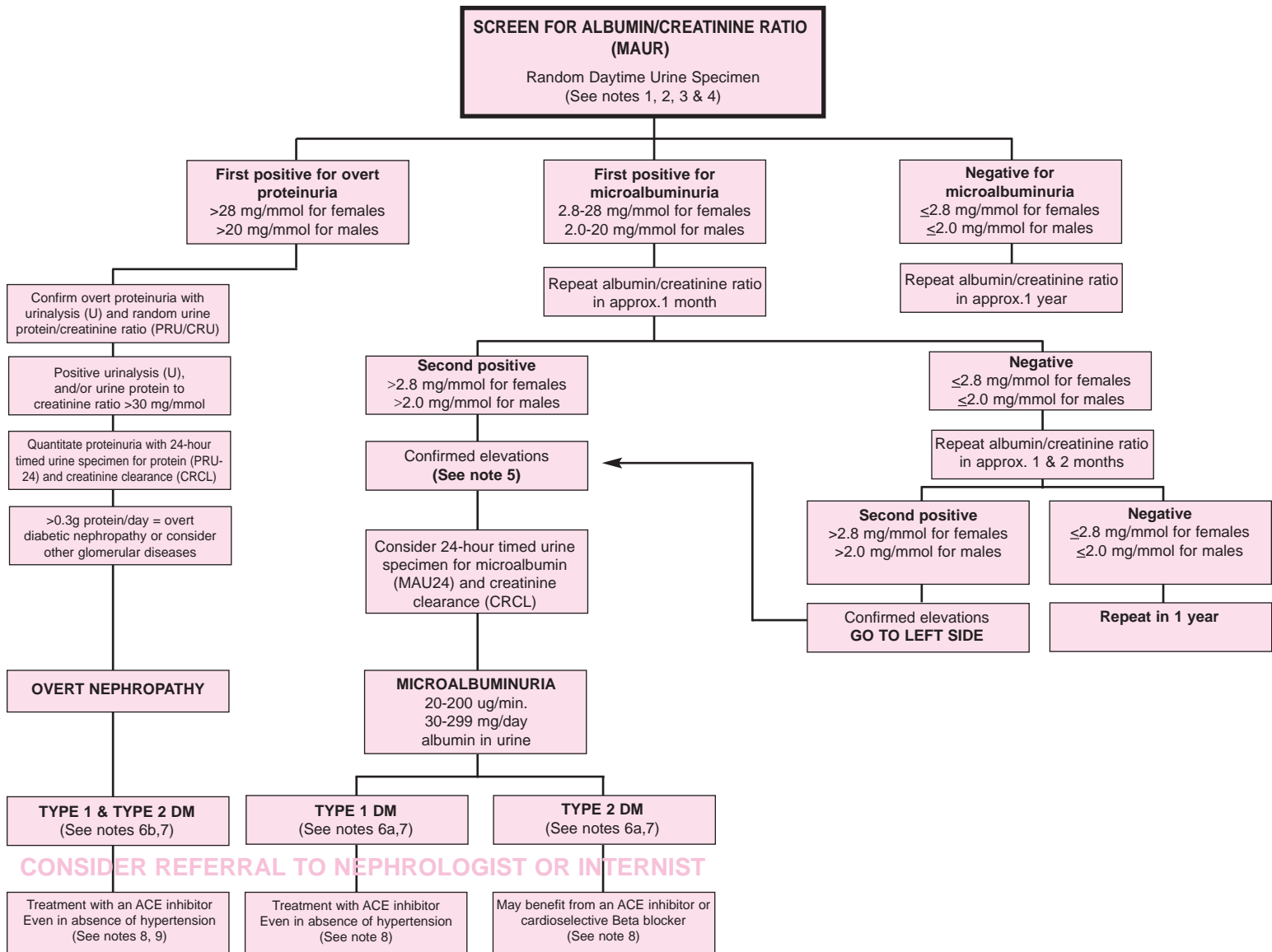
Date of Diagnosis: _____

Pre-existing Complications: _____

Diabetes Medications:	Date:	_____	_____	_____	_____	_____	_____
	Record Med Changes						

		GUIDELINES	PROCEDURE						
3 TO 6 MONTHS	Glycemic Control	Fasting or pre-meal glucose level 4-7 (mmol/L); 1-2 hrs after meal 5-11 (mmol/L)	Review Blood Glucose Records (✓ when done)						
		Every 3-6 months: Target <0.070 (<115% of upper limit of normal)	HgbA1c <i>value</i>						
			Hypoglycemia (indicate frequency)						
	Hypertension	Goal ≤130/80 Goal for pt's with overt nephropathy ≤125/75	BP <i>value</i>						
			BP medications <i>record meds</i>						
	Other	Goal body mass index (BMI) <25	Weight/BMI <i>value</i>						
Foot care		Lower extremity exam (✓ when done)							
Reinforce lifestyle counseling		Smoking, activity, diet, stress (✓ when done)							
ANNUALLY AND/OR AS INDICATED	Lipids	Fasting Lipid Profile (goal <4.0)	Total Chol <i>value</i>						
		For pt's ≥ 30 years of age (goal <2.5)	LDL <i>value</i>						
		(goal >1.0)	HDL <i>value</i>						
		(goal <2.0)	Triglycerides <i>value</i>						
		Total Chol/HDL Ratio (goal <4.0)	Ratio <i>value</i>						
			Lipid lowering Meds. <i>record meds</i>						
	Renal	Meter within 15% of simultaneous Lab value	Fasting Glucose Meter/Lab Comparison						
		Screen for Nephropathy • Type 1 Annually >15 yrs old & 5 yr hx of DM • Type 2 At diagnosis then annually *See reverse for screening protocol for diabetic Nephropathy	Microalbumin screen (albumin: creatinine ratio) (MAUR) <i>value</i> 24-hr Microalbumin as indicated <i>value</i>						
	Eyes	Dilated eye exam: Type 1 Annually >15 yrs old & 5 yr hx of DM Type 2 At diagnosis then as indicated, min. q 2 yrs.	Ophthalmologist/ Optometrist for dilated eye exam						
	Neuropathy	Test for loss of sensation with 10g monofilament on circled areas. Indicate + if positive response - if negative response	Sensory testing						
	Education	People with diabetes need the support of an interdisciplinary team of health and other professionals.	Diabetes/Lipids Education						
		• Annual Influenza vaccine • Once lifetime Pneumococcal vaccine <input type="checkbox"/>	Record Date	See clinical progress notes <input type="checkbox"/>	See clinical progress notes <input type="checkbox"/>	See clinical progress notes <input type="checkbox"/>	See clinical progress notes <input type="checkbox"/>	See clinical progress notes <input type="checkbox"/>	See clinical progress notes <input type="checkbox"/>

Screening Protocol for Diabetic Nephropathy



1. Type 1 DM - screening initiated in individuals ≥ 15 years of age with a 5-year history of Type 1 DM.
2. Type 2 DM - screening initiated upon diagnosis and annually.
3. Avoid screening if patient acutely ill, febrile or engaging in strenuous activity.
4. Option - may use urine dipstick in clinic for proteinuria - if positive ($>$ trace proteinuria) proceed directly to 24-hour timed urine specimen.
5. Confirmation required elevation in 2 out of 3 albumin/creatinine ratio measurements performed over 3 months. If uncertainty about elevation exists, consider a timed urine collection to measure the rate of microalbuminuria.
- 6a. Blood pressure goal $\leq 130/80$
- 6b. With overt nephropathy BP goal $\leq 125/75$
7. Other considerations:
 - Elimination of all CV risk factors (discontinue smoking, treat dyslipidemia)
 - Intensive glucose control
 - Protein as per recommended nutrient intake (consult dietitian)
 - Measure serum potassium and serum creatinine
 - If serum creatinine >130 $\mu\text{mol/L}$ discontinue Metformin
 - **$> 50\%$ decrease in creatinine clearance rate requires a referral to a nephrologist or internist**
8. ACE inhibitor use assumes no contraindications. Serum potassium and creatinine levels should be monitored 1-2 weeks after initiation of therapy or after each dosage change.
9. Monitor serum creatinine, serum potassium, 24-hour urine creatinine clearance and rate of proteinuria at least 2x/year.

*Adapted from the *1998 clinical practice guidelines for the management of diabetes in Canada*, CMAJ 1998;159(8 suppl) and also *Recommendations for the management and treatment of dyslipidemia*, CMAJ 2000;162(10)1441-7

Gestational Diabetes

Gestational diabetes refers to glucose intolerance with onset during pregnancy. It occurs in 2-4% of all pregnancies and its diagnosis has implications for both the baby and the mother. Established morbidity for the baby includes macrosomia and neonatal hypoglycemia. Screening should be done on **All** pregnant women over the age of 25, and all pregnant women of any age who are obese, belong to an ethnic group predisposed to diabetes, or have family history or previous history of diabetes, or who have a history of giving birth to babies with a birth weight over 4 kilograms. Screening should be done between 24-28 wks gestation. Preferred screening involves measurement of plasma glucose level 1 hour after a 50 gm oral load of glucose given at any time of the day.

If the glucose level at 1 hour is ≥ 7.8 mmol/L, a 75 gm 1 and 2 hour glucose tolerance test should be done. If the glucose level at 1 hour is ≥ 10.3 , then gestational diabetes may be diagnosed.

Reference: 1998 clinical practice guideline for the management of diabetes in Canada. CMAJ 1998 159 (8 suppl)

Diabetic Ketoacidosis

Revised 2003

Decreased insulin action decreases removal of glucose from blood and increases output from the liver. Osmotic diuresis causes loss of sodium and water into the urine, producing a vicious cycle of intravascular volume depletion, and reduced renal clearance of glucose. Decreased insulin action also causes lipolysis to produce ketones, with ensuing acidemia and impaired cellular function.

Thirst and weight loss commonly accompany the profound hyperglycemia of DKA. Dyspnea and associated Kussmaul respirations accompany the metabolic acidosis. Abdominal pain is common, and does not usually indicate abdominal pathology. Elevated amylase is also common in DKA, (usually non-pancreatic sources), and does not suggest pancreatitis. DKA can primarily elevate the WBC to as high as 25. Sodium levels can be factitiously depressed by elevated glucose (Na lowered by 3 meq/L for every 10 mmol/L rise in glucose above 5). Potassium may be high or low.

Common Errors in DKA management

Intravascular fluid replacement is too slow

Volume depletions, as great as 8-10 liters, are common and may require 2-4 liters to be given quickly (over 1-2 hours). Urine output should be assessed-significant increases after fluid administration suggests improving volume status.

Wrong fluid or insulin cut back inappropriately

Initially, use normal saline, until about half of the volume repletion has been done (1-4 liters), and/or the plasma glucose drops to about 12- 15 mmol/L. Glucose should be lowered by 3-5 mmol/L/hr to avoid osmotic shifts. If the glucose is not falling, increase the dose of the insulin drip significantly. When glucose has fallen to 12-15 mmol/L, switch the IV to a glucose-containing solution. (If still correcting intravascular volume use D5Saline.) **Do NOT decrease the insulin rate at the same time. The continuation of an insulin infusion is needed to treat the acidosis: the addition of glucose will prevent hypoglycemia.** Changing to a more hypotonic solution after fluid correction will also avoid excessive NaCl administration, which could cause a secondary non-anion gap metabolic acidosis.

Switching to SC insulin too soon

In significant DKA the ketosis can take a long time to resolve. An insulin drip may be needed for more than 24 hours. Following subcutaneous injection of short acting insulin, IV insulin should only be stopped after adequate "overlap" time has elapsed for the sc insulin to take effect (2 hours)

Inadequate potassium replacement

Serum potassium may be elevated by decreased cell uptake by insulin lack, shift from cells by acidosis, and catabolism, even if total body potassium is depleted. Serum potassium can fall very fast with institution of insulin and acidosis correction. Suggested initial rates of K⁺ administration:

K ⁺ meq/L]	Rate
>5.0	hold K and follow
4.1- 5.0	Ensure urine Output is OK and then give 20 meq/hour
3.0- 4.0	Give 40 meq/hr without waiting to check urine output
< 3.0	Give 60 meq/hr (need central line access) and slow down glucose correction

Failure to look for precipitating cause

Although lack of adherence to insulin is a common precipitant, always look for other causes including infection, asymptomatic UTI, pregnancy, silent MI etc.

Inadequate monitoring

Even if wrong choices are made in management, if you monitor frequently, (q1h for 2-4 hours, then q2h for 4-8 hours...), they can be corrected before they produce serious consequences.

Diabetic Ketoacidosis Management

	Hours of Therapy				
	Hour 1	Hour 2	Hours 3-4	Hours 5-8	Hours 8-24
Hydration	1 L NaCl (N) if corrected Na to > 145 use ½ N. NaCl	500 ml/hr NaCl (N)		250 ml/hr NaCl(N) When glucose < 15, use 5% dextrose/ ½ N. NaCl	Continue with 0.45% saline/ 5% \pm glucose at 125-250/hr
Insulin	10 units of IV insulin stat (5-10 units/hour) Hold for 2 hours if hypotensive or K < 3.5 Target glucose: 10-15 mM	Continue IV insulin Expect a fall of 5mM/hour Double dose if poor response	When glucose < 15 mM, decrease IV to 2-4 U/hr but continue IV until ketosis cleared. Use following scale: Glucose (mMol/L) < 5 stop & recheck in 1 hour 5.1 – 10 decrease by 1 U/hr 10.1-15 no change 15.1-20 increase by 1 U/hr 20-24 increase by 2 U/hr > 24 increase by 3 U/hr & call resident If glucose drops by more than 5 mM in 2 hrs, decrease insulin to 0.5 U/hr and call resident	Insulin drip stop & recheck in 1 hour decrease by 1 U/hr no change increase by 1 U/hr increase by 2 U/hr increase by 3 U/hr & call resident	After ketoacidosis has cleared, switch to s.c. insulin and then stop IV insulin
Potassium Replacement	Serum potassium < 3 mEq/L give	3-4 mEq/L give	4-5 mEq/L give	5-6 mEq/L give	
	Potassium replacement 40 mEq/hr	30 mEq/hr	20 mEq/hr	10 mEq/hr	
Laboratory	Baseline: Glucose, β -OH Butyrate, ABGs, urinalysis, CBC, 'lytes, PO ₄ , Cr., amylase if abd. Pain	Glucose, 'lytes, ABGs if H ⁺ > 100	Glucose, 'lytes, ABGs if H ⁺ > 100	Glucose hourly, 'lytes, PO ₄	Glucose q. 1-2 hr, 'lytes q. 4-8 hrs
Alkaline Replacement	<ul style="list-style-type: none"> - Rarely indicated unless severe acidosis (pH < 7, H⁺ > 100) with incipient circulatory collapse - Dose: 50-100 mEq, NaHCO₃ – in 0.45% saline over 30-60 minutes - Extra potassium may be needed with bicarbonate therapy 				
Phosphate Replacement	<ul style="list-style-type: none"> - Consider if serum phosphorus is < 0.65 mM and give if the serum phosphorus is < 0.35mM - 2.5-8 mM/hour (1 mM of phosphate = 31 mg of elemental phosphorus). Eg. 10 ml of KPO₄ in 1 L NaCl/6 hrs (30 mM PO₄, 44 mEq K) 				
General Measures	Make flow sheet, O ₂ if PO ₂ < 80	NG tube if unconscious, Antibiotics if ? infection	Catheter if no urine for 4 hrs SC heparin if elderly, unconscious or severely hyperosmolar		

NOTE: These guidelines are to assist, not replace good clinical judgment.

Approach to Hypoglycemia

See Alberta Medical Association Practice Guideline

In the short term, hypoglycemia is much more common than hyperglycemia. Hypoglycemia may be differentiated on the basis of whether it occurs in the fasting or postprandial state.

Postprandial hypoglycemia

Alimentary hyperinsulinemia (previous gastrectomy, gastrojeunostomy)
Idiopathic

Fasting hypoglycemia

Secondary overutilization of glucose With high insulin levels
 Exogenous insulin sulphonylureas
 Insulinoma and other insulin-like producing tumors
 Miscellaneous (pentamidine, quinine)

Secondary overutilization of glucose With normal insulin levels
 Large extrapancreatic tumors

Secondary to Impaired glucose production
 Hormone deficiencies (adrenal insufficiency and hypopituitarism)
 Substrate deficiencies (severe malnutrition, muscle wasting)
 Drugs (alcohol, ASA)
 Enzyme defects (Glucose-6-phosphatase deficiency)
 Critical illness (severe hepatic failure, cardiac disease, sepsis)
 Autoimmune hypoglycemia

Thyrotoxicosis

Signs of thyrotoxicosis include nervous, agitated or labile affect, weight loss, warm, flushed, moist skin, onycholysis, increased pulse pressure (major difference between systolic and diastolic BP), tachycardia, systolic outflow tract murmurs, tremor and hyperreflexia, proximal muscle weakness, pretibial myxedema, rarely (mild) splenomegaly, and eye signs. Lid lag, stare with decreased blink, and widened palpebral fissures are eye signs shared by all causes of thyrotoxicosis. Proptosis, chemosis, EOM dysfunction, corneal ulcerations and optic nerve entrapment are stigmata seen in Grave's disease with ophthalmopathy.

Goiters and nodules (especially multinodular goiter in the older patient) may be present. Auscultating for thyroid bruits is not of much use unless there are other symptoms or signs to suggest thyrotoxicosis.

Thyroid nodules J Ginsberg 1999

It is difficult to overstate the benefits of fine-needle aspiration biopsy (FNAB) on thyroid nodule management. A substantial reduction in thyroid surgery, increase in malignancy yield at thyroidectomy, and cost recovery have occurred since its inception. It has replaced other modalities in the initial investigation of the thyroid nodule in the euthyroid patient. The results of the FNAB agree with the surgical outcome 85-90% of the time.

References and suggested reading material:

1. Endocrin Metab Clin NA 1995;24:663-710
2. Ann Intern Med 1993;118:282-289
3. N Eng J Med 1993;328:553-565.

HYPOGLYCEMIA

GUIDELINE GOALS

- ◆ To assist the practitioner in the initial laboratory investigation in patients with suspected Hypoglycemia
- ◆ To optimize the use of diagnostic laboratory tests

RECOMMENDATIONS

Hypoglycemia Clinical Features

- Adrenergic excess:
 - sweating
 - palpitations
 - anxiety
 - tremor
- Neuroglycopenic (e.g., altered consciousness and seizures, behavioural changes)

- ◆ Hypoglycemia is defined as a serum glucose level below 2.5 mmol/L concurrent with the patient's symptoms. The symptoms should be rapidly reversible with the oral intake of glucose
- ◆ Glucose tolerance testing is of **NO** value in investigating patients with hypoglycemia and **SHOULD NOT BE ORDERED**
- ◆ The presence of hypoglycemia cannot be established by capillary reagent strip testing
- ◆ Fasting hypoglycemia should prompt a simultaneous fasting serum insulin and glucose measurement, i.e., occurring > 5 hours after a meal. Consultation is recommended in patients with fasting hypoglycemia

- ◆ Post-prandial hypoglycemia (< 5 hours after a meal) is usually not associated with any serious disorders. Reagent strip testing may be sufficient to guide appropriate dietary recommendations

BACKGROUND

Hypoglycemia is a clinical syndrome which should only be considered if the clinical features are met. Typical symptoms occur at a time when the serum glucose is demonstrated to be equal to or less than 2.5 mmol/L and symptoms are relieved by treatment which increases serum glucose. The diagnosis cannot be established using capillary glucose measurement because of inaccuracy of the technology in the Hypoglycemic range.

Fasting hypoglycemia has greater pathogenic significance. If the patient appears well in other respects, consideration should be given to drug induced hypoglycemia (including sulphonylureas and ethanol) or an insulinoma. Patients with other medical disorders may also experience hypoglycemia and investigation of adrenal or pituitary insufficiency, liver failure or renal impairment may be indicated.⁸⁴⁻⁸⁶

NOTES ON THE APPLICABILITY OF THESE GUIDELINES

1. These guidelines were developed after a detailed scientific review of the literature. In areas where evidence was inconclusive, the guidelines were based on expert opinion in consultation with the Divisions of Endocrinology at the University of Alberta and the University of Calgary.
2. Reference ranges are based on 95% of the population. Therefore, results for 5% of normal individuals will fall outside the reference range.
3. Reference ranges are specific to each laboratory.
4. The diagnosis of endocrine disorders relies heavily on appropriate clinical assessment and interpretation of laboratory results.
5. These guidelines are strictly for laboratory testing not clinical practice and management.

THE ALBERTA CLINICAL PRACTICE GUIDELINES PROGRAM

The Alberta Clinical Practice Guidelines Program promotes appropriate, effective and quality medical care in Alberta by supporting the use of clinical practice guidelines. The program is administered by the Alberta Medical Association under the direction of a multi-stakeholder steering committee.

Alberta Clinical Practice Guidelines Steering Committee

Alberta Health and Wellness
Alberta Medical Association
College of Family Physicians of Canada,
Alberta Chapter
College of Physicians and Surgeons of Alberta
Physicians at Large
Public Representative
Regional Health Authorities
University of Alberta
University of Calgary
Alberta Association of Registered Nurses
Alberta College of Pharmacists

TO PROVIDE FEEDBACK

The Alberta CPG Working Group for Endocrine Testing is a multi-discipline team composed of general practitioners, pathologists, endocrinologists, clinical biochemists, laboratory technologists and a member of public. The team encourages your feedback. If you have difficulty applying this guideline, if you find the recommendations problematic, or if you need more information on this guideline, please contact:

The Alberta Clinical Practice Guidelines Program:
12230 - 106 Avenue NW
EDMONTON, AB T5N 3Z1
(780) 482-2626
or toll free 1-800-272-9680
Fax: (780) 482-5445
E-mail: cpg@albertadoctors.org
Website: <http://www.albertadoctors.org>

*Reviewed and Revised, June 2001
Endocrine Guidelines, April 1998
Publication Mail Agreement #1630008*

Only 4% of thyroid nodules are cancerous. There are multiple risk factors for thyroid cancer including male gender, extremes of age (<20 or > 60), family history of thyroid cancer and previous head and neck irradiation. Mantle irradiation for Hodgkin's disease includes the thyroid in the field and constitutes as such a risk factor. Stigmata on physical examination suggestive of malignancy include nodule diameter > 4 cm, rapid nodule growth, regional lymphadenopathy, stony hard nodule consistency, fixation to adjacent structures, and vocal cord paralysis. Nodule consistency may be misleading, as hemorrhagic or calcified adenomas may feel hard. In one study, benign disease was found in 50% of patients with hard nodules. Unfortunately, findings on physical examination lack sensitivity and specificity, and surgery provides the only truly foolproof diagnosis.

Recommended approach for assessing palpable thyroid nodules in euthyroid patients:

1. Use above mentioned clinical risk factors to initially identify which nodules require surgical resection. Incidentally found "low clinical risk" thyroid nodules < 1 cm in diameter can be safely followed clinically
2. The Fine Needle aspiration Biopsy (FNAB) is the mainstay of investigation (Sensitivity 92%, Specificity 69%, Negative predictive value of 98%). Performance is only marginally improved with ultrasound-guided biopsies. Routine initial Radionuclide thyroid scans and ultrasounds are not specific in predicting malignancy and are NOT justified.

References and suggested reading material:

1. Endocrin Metab Clin NA 1995;24:663-710
2. Arch Int Med 1990;150:113-116
3. N Eng J Med 1991;325:599-605.

Adrenal insufficiency

[See Alberta Medical Association Practice Guideline](#)

Fatigue, weight loss, vague abdominal pains, orthostatic hypotension, hyponatremia, and a mild metabolic acidosis are most consistent with the presentation of adrenal insufficiency. The best screening test would be an AM serum cortisol, followed by a ACTH stimulation test

Adrenal mass

Adrenal masses are common (3.5% and almost 10% at autopsy) and may be found incidentally after CT MRI or ultrasound examination done for unrelated reasons. It is important to use efficient focused data gathering to differentiate functioning from nonfunctioning and benign from malignant tumors

Hypercalcemia

[See Alberta Medical Association Practice Guideline](#)

Hypercalcemia can cause severe anatomic injury to the kidneys, and if severe, may be fatal.

In the outpatient setting the commonest cause for hypercalcemia in adults is primary hyperparathyroidism. In hospitalized patients, malignancy is a more common cause. A more complete differential diagnosis includes:

Increased intestinal absorption (milk alkali syndrome, vitamin D mediated including granulomatous diseases), increased bone resorption (malignancy, primary hyperparathyroidism, secondary or tertiary hyperparathyroidism, hyperthyroidism, immobilization, Paget's disease), or diminished excretion (familial hypocalcuric hypercalcemia, drugs).

The prognosis of hypercalcemia associated with solid tumor malignancy is poor.

Obesity

The body mass index is calculated as the weight (kg) / (height in m)². The normal range for BMI is 20-25. "Overweight" is defined as a BMI of 25-30, whereas the term "obese" refers to a BMI > 30. North Americans are among the fattest people in the world, and obesity continues to increase in prevalence, with about 15% of the population having a BMI > 30 kg/m². Although obesity is associated with medical complications, it is only occasionally caused by disease, and costly investigations are not indicated to rule out hypothyroidism, Cushings, or hypothalamic disorders unless there are other signs of these conditions present.

ADDISON'S DISEASE

GUIDELINE GOALS

- ◆ To assist the practitioner in the initial laboratory investigation in patients with suspected Addison's disease
- ◆ To optimize the use of diagnostic laboratory tests

RECOMMENDATIONS

Addison's Disease Clinical Features

- Loss of appetite and weight loss
 - Chronic worsening fatigue and muscle weakness
 - Low blood pressure which falls further when standing, causing dizziness or fainting
 - Darkening of the skin in exposed and non-exposed parts of the body, particularly on skin creases and scars
 - Nausea, vomiting, and diarrhea occur in about 50% of cases
 - Hypoglycemia (more severe in children than in adults)
- ◆ URGENT CONSULTATION IS RECOMMENDED. As soon as the stimulation test is completed, glucocorticoids can be administered as a life saving measure
 - ◆ Synthetic ACTH stimulation testing is required for diagnosis
 - ◆ Low random serum cortisol levels have a poor predictive value and are not recommended. A serum cortisol with or without ACTH stimulation which exceeds 550 nmol/L excludes adrenal insufficiency⁷⁶
 - ◆ A normal response in the short ACTH stimulation test does not exclude secondary (pituitary) insufficiency as a cause

PRACTICE POINT

If the diagnosis of Addison's Disease is strongly suspected, treatment should be instituted immediately.

BACKGROUND

Addison's disease is a rare endocrine disorder that affects about 1 in 100,000 people. Addison's disease occurs in all age groups and afflicts men and women equally. Disease occurs more frequently in families predisposed to autoimmune endocrinopathies, e.g., thyroid, Type 1 Diabetes Mellitus. Additionally, a normal response in the short ACTH stimulation tests does not exclude secondary (pituitary) insufficiency as a cause. Addisonian crisis is a catastrophic complication of adrenocortical insufficiency, which can develop rapidly. The patient usually develops adrenocortical insufficiency symptoms followed by profound hypotension. The patient may remain alert. Because this crisis is life threatening, urgent consultation **cannot** await laboratory results.⁷⁶⁻⁷⁹

Causes:

Primary Adrenal Insufficiency

- ◆ Seventy percent of reported cases are due to autoimmune disorders
- ◆ Tuberculosis accounts for about 20% of cases in developed countries
- ◆ Less common causes of primary adrenal insufficiency are chronic infections (mainly AIDS and fungal infections), hemorrhage (secondary to anticoagulant therapy), cancer, amyloidosis, and adrenalectomy

Secondary Adrenal Insufficiency

- ◆ Lack of pituitary adrenocorticotropin (ACTH)

CUSHING'S SYNDROME

GUIDELINE GOALS

- ◆ To assist the practitioner in the initial laboratory investigation in patients with suspected Cushing's Syndrome
- ◆ To optimize the use of diagnostic laboratory tests

RECOMMENDATIONS

Cushing's Syndrome Clinical Features

- Central obesity
 - Severe fatigue and muscle weakness
 - Hypertension
 - Hyperglycemia
 - Easy bruising
 - Striae
 - In women, hirsutism and irregular menses
- ◆ Suspicion of Cushing's Syndrome warrants early specialist referral
 - ◆ In the case of borderline values, some tests warrant repeating
 - ◆ The measurement of cortisol in a 24 hour urine collection is the most sensitive and specific test for the diagnosis of Cushing's Syndrome. Urine creatinine levels should be checked as an indicator of completeness of 24 hour urine collection
 - ◆ Serum cortisol levels have low predictive value and are not recommended

BACKGROUND

Cushing's Syndrome is relatively rare. Studies suggest that the incidence of Cushing's Syndrome is 10 per million or approximately 1 in 5,000 hospital admissions.⁸⁰ Most cases of Cushing's Syndrome occur between the ages of 20 and 50 years. Cushing's Syndrome is the result of glucocorticoid excess, which can be endogenous or exogenous.

Endogenous causes of Cushing's Syndrome in order of frequency are: pituitary ACTH-secreting tumours, neoplastic disease (especially small cell carcinoma of the lung) and primary adrenal tumours. Other causes of elevated urinary cortisol include: depression and alcohol excess. In some studies, the diagnostic sensitivity and specificity of urinary free cortisol were 100 and 98% respectively. However, it is recognized that 5% may have normal levels due to episodic secretion and 5% of obese persons may have increased cortisol levels.⁸⁰⁻⁸²

The 1 mg dexamethasone suppression test has also been used for the diagnosis of Cushing's Syndrome. Although this test has a 95% diagnostic sensitivity, acute illness, psychiatric disorders, obesity and alcohol use can reduce the specificity of this test by decreasing suppressibility of the plasma cortisol. However, a normal result of the test excludes the possibility of Cushing's Syndrome.⁸³

HYPERCALCEMIA

GUIDELINE GOALS

- ◆ To use effective laboratory testing to facilitate the investigation of hypercalcemia
- ◆ To promote the optimal diagnostic laboratory testing strategy to enhance the quality of care for patients in Alberta and to improve laboratory ordering practices

RECOMMENDATIONS

- ◆ For initial investigation, albumin should be measured with serum calcium, e.g., for each 10g/L decrease of albumin from 40g/L, correct calcium by adding 0.20 mmol/L
- ◆ The specimen for calcium analysis should be obtained without application of a tourniquet
- ◆ Thiazide diuretics can mildly elevate calcium levels. In mild hypercalcemia, consider discontinuing thiazides for 1 month, then repeat serum calcium
- ◆ Parathyroid Hormone (PTH) level should be interpreted in relation to calcium concentration
- ◆ For patients with known malignancy, e.g., myeloma or carcinoma of bronchus, treatment of hypercalcemia may commence at mild to moderate elevations of calcium, without detailed investigation
- ◆ Refer to Algorithm 3, on page 9, for diagnostic options

BACKGROUND

The estimated incidence of hypercalcemia due to primary hyperparathyroidism and due to malignancy are 250 cases per million and 150 cases per million respectively. Overall, the incidence of hypercalcemia is about 0.6%.⁶⁴⁻⁶⁸ In the outpatient-ambulatory setting, hypercalcemia is usually mild and asymptomatic.

In the asymptomatic person over age 50 with long-standing mild hypercalcemia, the likelihood of the cause being primary hyperparathyroidism is over 90%.^{64,65,69} In contrast, a high proportion of hospitalized patients with hypercalcemia will have an underlying malignancy. Symptoms of hypercalcemia, (e.g., polyuria, altered mentation, nausea/vomiting and constipation) tend to be proportional to the rapidity of rise of the serum calcium as well as to the absolute level. The life threatening complications of hypercalcemia are primarily arrhythmia and profound volume depletion due to polyuria. Chronic mild hyperparathyroidism increases the risk of renal calculi, nephrocalcinosis and osteopenia.⁷⁰

Causes of Hypercalcemia

- Primary hyperparathyroidism
- Malignancy (especially lung, breast, myeloma)
- Vitamin D excess
- Sarcoidosis or other granulomatous disease
- Milk alkali syndrome
- Thiazide diuretics
- Other: hyperthyroidism, lithium, immobilization, familial hypocalciuric hypercalcemia

Approach to Abdominal distension and Ascites**Dysphagia****Gastro-esophageal reflux disease**

- Describe pathophysiology and elicit and interpret clinical features of GERD
- Investigation and lifestyle and pharmacologic management of patient with “heartburn”
- Identify potential serious complications of GERD

Peptic ulcer disease

- Use history and physical exam to diagnose peptic ulcer disease and its complications
- List risk factors for peptic ulcer disease
- Outline medical management of peptic ulcer disease and its complications
- Indications for surgery

Diarrhea

- **Acute diarrhea**
- **Chronic diarrhea:** Elicit and interpret data from the history and clinical examination and laboratory to support diagnosis and determine cause of steatorrhea and/or malabsorption
- Irritable bowel syndrome: Clinical features, therapy
- Inflammatory bowel disease: Clinical features and extra-intestinal manifestations
- Differentiate infectious colitis from inflammatory bowel disease

Gastrointestinal bleeding

- **Upper (see *clinical skills section on hematemesis*)**
- **Lower**

Constipation: Causes, complications, therapy, and prevention

Diverticular disease: Causes, complications

Hepatobiliary disease

- **Jaundice (with itching)**
 - Classify causes of jaundice
 - Use of clinical examination and lab to detect cholestasis and determine cause
 - Medical and surgical management of cholestasis and cholestatic pruritis
- Liver failure: Causes, Clinical features, complications, management
- **Alcoholic liver disease**

Pancreatitis

- Acute: Etiology, clinical and laboratory findings which predict poor prognosis in acute pancreatitis, management (including complications) and indications for medical and surgical care
- Chronic

Clinical Skills (see clinical skills section notes)

- Liver and gallbladder examination
- Extrahepatic stigmata of liver disease including alcoholic liver disease
- History taking for hematemesis
- History taking for dysphagia
- Ascites

Abdominal Distension and Ascites

Complaints of abdominal distension are common and may indicate significant underlying pathology. Most abdominal masses (other than stool) represent significant underlying disease that requires investigation.

Differential diagnosis:

- Air swallowing with gastric distension. This is common in patients with respiratory distress.
- Severe Constipation
- Ascites
- Mechanical intestinal obstruction. This may be intrinsic or extrinsic
- Intestinal pseudo-obstruction from toxic megacolon, or post-operative/post-traumatic
- Neurologic disease including complications of diabetes (dysautonomia), amyloid, scleroderma, or paraneoplastic syndrome, spinal cord injury or stroke. These may be acute or chronic processes
- Paralytic ileus from *Clostridium difficile*, Hypothyroidism, or Bacterial peritonitis
- Organomegaly (liver, spleen, kidneys, distended bladder), tumors (lymph nodes, primary or metastatic cancers), or aneurysms
- Subjective distension (irritable bowel, or anxiety or dyspeptic syndromes with eructation)

The history is important to determine risk factors and probabilities of any of these. A history of weight gain, increasing abdominal girth or ankle swelling makes ascites more probable. (See Ascites clinical examination for more details). Plain abdominal x-rays may be valuable to detect obstruction, and in the absence of excess abdominal gas or significant obesity, ultrasonography is useful for assessing ascites, organomegaly, lymphadenopathy or extramural neoplasm. A normal ultrasound does not rule out intestinal neoplasm. Paracentesis may be done for diagnostic and/or therapeutic reasons.

Management is as directed by the condition. Large volume (up to 6 liters) paracentesis for ascites is safe in patients who have not been diuresed to the point of severely contracted circulating volume.

Ascites is a common complication in patients with cirrhosis and portal hypertension, and the ascitic fluid exhibits a serum-ascites albumen gradient (SAAG) that is usually >11 . When the gradient is less than 11, suspect the presence of a condition, which causes ascites in the absence of portal hypertension such as tumor or tuberculosis involving the peritoneal surface. Controlled clinical trials have demonstrated that 10 or more litres of fluid can be removed by therapeutic paracentesis at one sitting. This is particularly safe if there is peripheral edema, and conversely should be approached with caution in patients with volume contraction. Many experts advise infusion of albumen during paracentesis if more than 5 litres of ascitic fluid are removed.

Together with portosystemic encephalopathy, jaundice, and coagulopathy, the development of ascites is associated with a poorer prognosis for survival, and may indicate the need to consider liver transplantation.

Alcoholic cirrhosis is commonly associated with the development of spontaneous bacterial peritonitis (SBP). In any patient with ascites exhibiting deterioration in well-being or hepatic encephalopathy, the presence of SBP should be suspected even in the absence of fever and leukocytosis. The diagnosis is made by finding an increased white blood cell count and positive bacterial culture of the tapped ascitic fluid. Patients with ascites secondary to portosystemic hypertension should be assessed for possible presence of esophageal varices, and if there has been a previous episode of SBP, then prophylactic antibiotics are indicated.

References:

Runyon BA. Management of Adult Patients With Ascites Caused by Ascites. *Hepatology* 27:264-272, 1998.

Dysphagia

Dysphagia for liquids as well as solids, is more suggestive of an esophageal motility disorder. The majority of patients with stricturing secondary to reflux have a history of heartburn, although it may be absent or remote in older patients or those with Barrett's esophagus. Typically dysphasia from reflux is slowly progressive. A Zenker's diverticulum should produce oropharyngeal dysphagia which characteristically creates problems in initiating swallowing, with regurgitation or symptoms of aspiration. A Schatzki's ring typically causes intermittent dysphagia for solids. Rapid/profound weight loss in the context of dysphagia favors neoplasm.

GERD and Heartburn

Heartburn or dyspepsia is a common gastrointestinal complaint with an incidence in adults of 20-40%. It is important to be able to differentiate dyspepsia from other causes of chest pain, and identify alarm symptoms.

Management should include counseling on lifestyle changes and being able to select patients who need specialized care

The sensitivity and specificity of heartburn and regurgitation for diagnosing GERD is 80% in patients with no alarm symptoms such as dysphagia or weight loss. In such a patient under the age of 50, a clinical diagnosis of GERD may be made and a treatment course of potent acid inhibition with a proton pump inhibitor may be prescribed. However, patients with alarm symptoms should have a prompt endoscopy, and patients who fail to respond to once or twice a day PPI therapy also need to go on to have endoscopic or motility studies.

Gastroesophageal reflux disease (GERD) is the commonest esophageal cause of noncardiac chest pain. The most sensitive test to detect reflux is a 24-hour ambulatory esophageal pH study. An upper endoscopy in most patients with an esophageal cause of noncardiac chest pain is a relatively expensive test that is not sufficiently sensitive. Only about half of patients with GERD have an abnormal esophageal mucosa. Although esophageal motility disorders occur in patients with noncardiac chest pain, the causal relationship of these disorders to the chest pain is not convincing, and other more readily treatable conditions such as GERD may coexist in patients with motility disorders.

Peptic ulcer disease

Peptic ulcer disease is usually caused by NSAID use or H. pylori infections. When peptic ulcer disease is suspected in a patient with no alarm symptoms, a diagnostic test (urea breath testing) is undertaken to determine the presence of H. pylori infection. If this is positive the patient should be treated with triple therapy including either a proton pump inhibitor or ranitidine bismuth compound plus two antibiotics such as metronidazole and clarithromycin, or amoxicillin and clarithromycin. These regimens are 85% effective in eradicating the H. pylori infection and healing the duodenal ulcer. Bland diets and antacids have no role in the first-line management of patients with ulcer disease. Associated anxiety should be treated and the diet should be tailored depending on the patient's needs. Only in setting where the urea breath testing is not available or where there are alarm symptoms should endoscopy be undertaken to make the diagnosis of H. pylori infection.

Am J of Gastroenterology 1999 94 9-11
Canadian J Gastroenterology 1998 12: 31-41
NEJM 1998 339:1869-1874
Gut 1999 45: 186-190

Gastroesophageal Reflux Disease: Adults

Summary of the Alberta Clinical Practice Guideline, July 2000

- Exclusion**
- This guideline does not apply to pregnant or lactating women or patients <18 years of age
- Etiology**
- Combination of conditions that increase the presence of gastric content in the esophagus, including:
 - transient lower sphincter relaxation
 - decreased lower esophageal sphincter tone
 - impaired esophageal clearance
 - delayed gastric emptying
 - decreased salivation
- Diagnosis**
- Diagnosis based on history (burning retrosternal pain with or without regurgitation) and physical examination
 - typical uncomplicated GERD generally does not require further investigation
 - **GERD is not caused by *H. pylori* infection**
- Management**
- Lifestyle modification (weight control, elevation of head of bed, eating smaller meals and avoidance of lying down within 1 hour of eating, reduction of alcohol, tobacco and caffeine intake, avoidance of spicy foods or drugs that affect sphincter tone)
 - Over the counter antacid or antisecretory medications
 - Assess response at 1 month
 - If patient fails to respond to above, add antisecretory or promotility therapy as therapeutic trial (below)

Proton pump inhibitor (PPI)

Once daily for 4 weeks

or

H₂ receptor antagonist (H₂RA)

Full dose - BID for 4 weeks

Treatment Failure or Recurrence of Symptoms

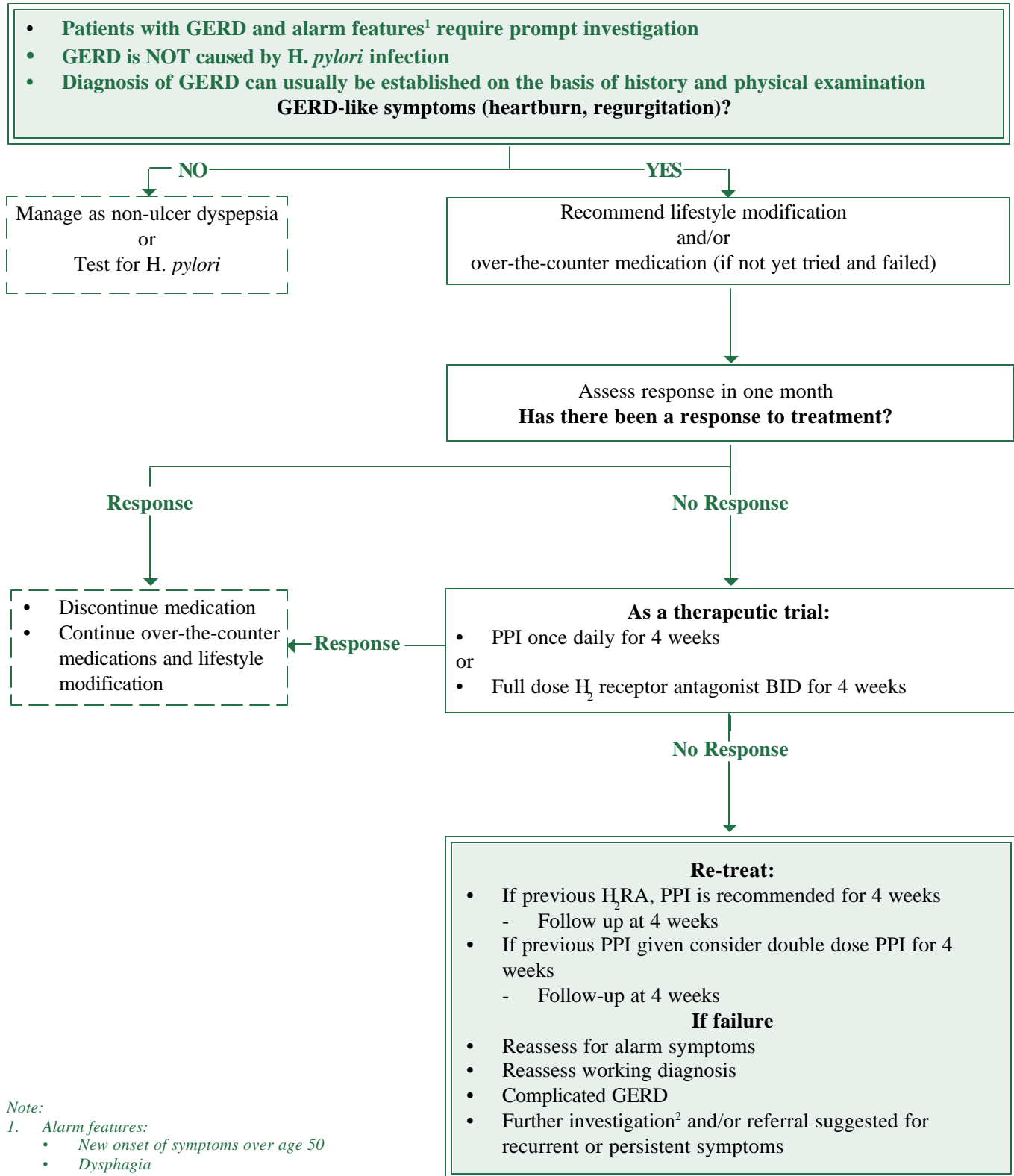
If previous PPI given, consider double dose **PPI** for 4 weeks

or

If previous treatment did **not** use PPI then, **PPI** is recommended for 4 weeks

- Follow-up**
- Follow- up at 2 to 4 weeks
- Alarm Features**
- Alarm features:
 - new onset of symptoms over age 50
 - dysphagia
 - odynophagia
 - bleeding/anemia
 - weight loss
 - Alarm features or complicated GERD (failure to respond to 4 to 8 weeks of therapy) require further investigation and/or referral
 - if further investigation warranted - endoscopy is preferred; however, barium examination is more readily available

Diagnosis and Management of GERD in Adults



Note:

1. Alarm features:

- New onset of symptoms over age 50
- Dysphagia
- Odynophagia
- Bleeding/anemia
- Weight loss

Other Indications for further investigation:

- Non-cardiac angina-like chest pain
- Respiratory symptoms secondary to reflux
- Failure to respond to 4 to 8 weeks of medical therapy

Chronic Undiagnosed Dyspepsia: Adults

Summary of the Alberta Clinical Practice Guideline, July 2000

- Exclusion**
- This guideline does not apply to pregnant or lactating women or patients <18 years of age
- Etiology**
- Disease of the upper gastrointestinal (UGI) tract. Most common UGI signs/symptoms suggest:
 - gastroesophageal reflux disease (GERD)
 - peptic ulcer disease (PUD) - 15 to 25% of cases
 - non-ulcer dyspepsia (NUP)
 - NSAID induced (20% of individuals using NSAIDs >12 weeks have endoscopic evidence of ulceration)
 - Consider non-UGI pathologies: cardiac, hepatobiliary, colonic or musculoskeletal
- Diagnosis**
- Based on symptom history, patient history and precipitating factors

Symptom History ¹	Alarm Features ²	Precipitating Factors
<u>Gerd-like</u> : heartburn, belching, bloating, early satiety, regurgitation <u>Ulcer-like</u> : nocturnal symptoms, burning epigastric discomfort, improvement with food <u>Dysmotility-like</u> : nausea, bloating, early satiety, worse with food	<ul style="list-style-type: none">• vomiting• bleeding/anemia• abdominal mass• unexpected weight loss• dysphagia• odynophagia	<ul style="list-style-type: none">• diet (caffeine, high fat)• medications:<ul style="list-style-type: none">- NSAIDs/ASA- calcium channel blockers- bisphosphonates• past family history of ulcer disease• family history of gastric cancer

- Not all patients require diagnostic testing (i.e., <50 years and previously well)
- Early endoscopy³ indicated for:
 - new onset >50 year (due to increase incidence of gastric cancer)
 - alarm features
 - repeat treatment failures
- If patient <50 has signs/symptoms suggestive of GERD refer to *Guideline for Treatment of Gastroesophageal Reflux Disease*
- If patient <50 has signs/symptoms suggestive of peptic ulcer disease urea breath test is recommended to test for *H. pylori* infection. If positive, refer to the *Guideline for Treatment of H. pylori Associated Peptic Ulcer Disease*

- Management**
- If patient is <50 years old and has no other organ pathology and no alarm symptoms, consider benign disease of UGI tract and modify precipitating factors
 - Consider trial of empiric therapy:

Proton pump inhibitor (PPI) for 2 to 4 weeks⁴
or
H₂ receptor antagonist (H₂RA) for 2 to 4 weeks⁵
or
Prokinetic agent for 2 to 4 weeks⁶

- Follow-up**
- Reassess at 2 to 4 weeks
 - success: stop treatment
 - partial success: repeat treatment one time
 - failure: investigate or refer

Notes:

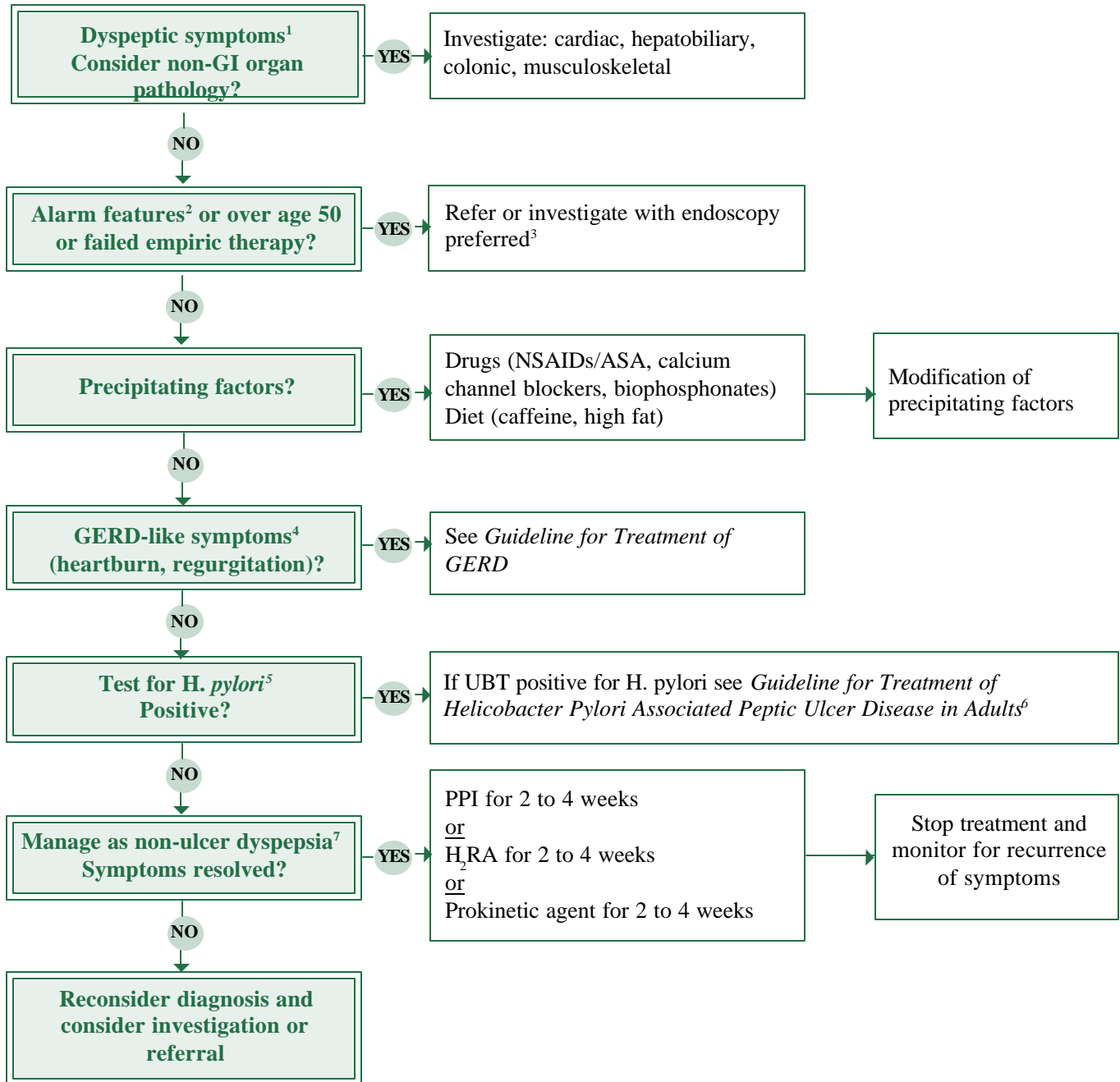
1. Some experts suggest that symptom type (i.e., GERD-like vs. PUD) may guide choice of empiric therapy.
2. It is critical to refer patient >50 with UGI bleeds & other alarm features
3. Upper GI barium X-ray may be considered as alternative (accuracy ~ 70%)
4. Recommended options for treatment include PPI, H2RA or prokinetic. There is no consensus to guide therapeutic choice, therefore consider symptoms to make a choice and prescribe for 2 to 4 weeks with reassessment
5. ~~Some experts would consider PPI or H2RA~~ as 1st choice for patients with ulcer-like dominant symptoms.
6. Some experts would consider prokinetic agents as 1st choice for patients with dysmotility-like dominant symptoms

For complete guideline refer to the Alberta Medical Association Web Site: www.albertadoctors.org
Guideline reviewed November 2001



Administered
by the Alberta Medical Association

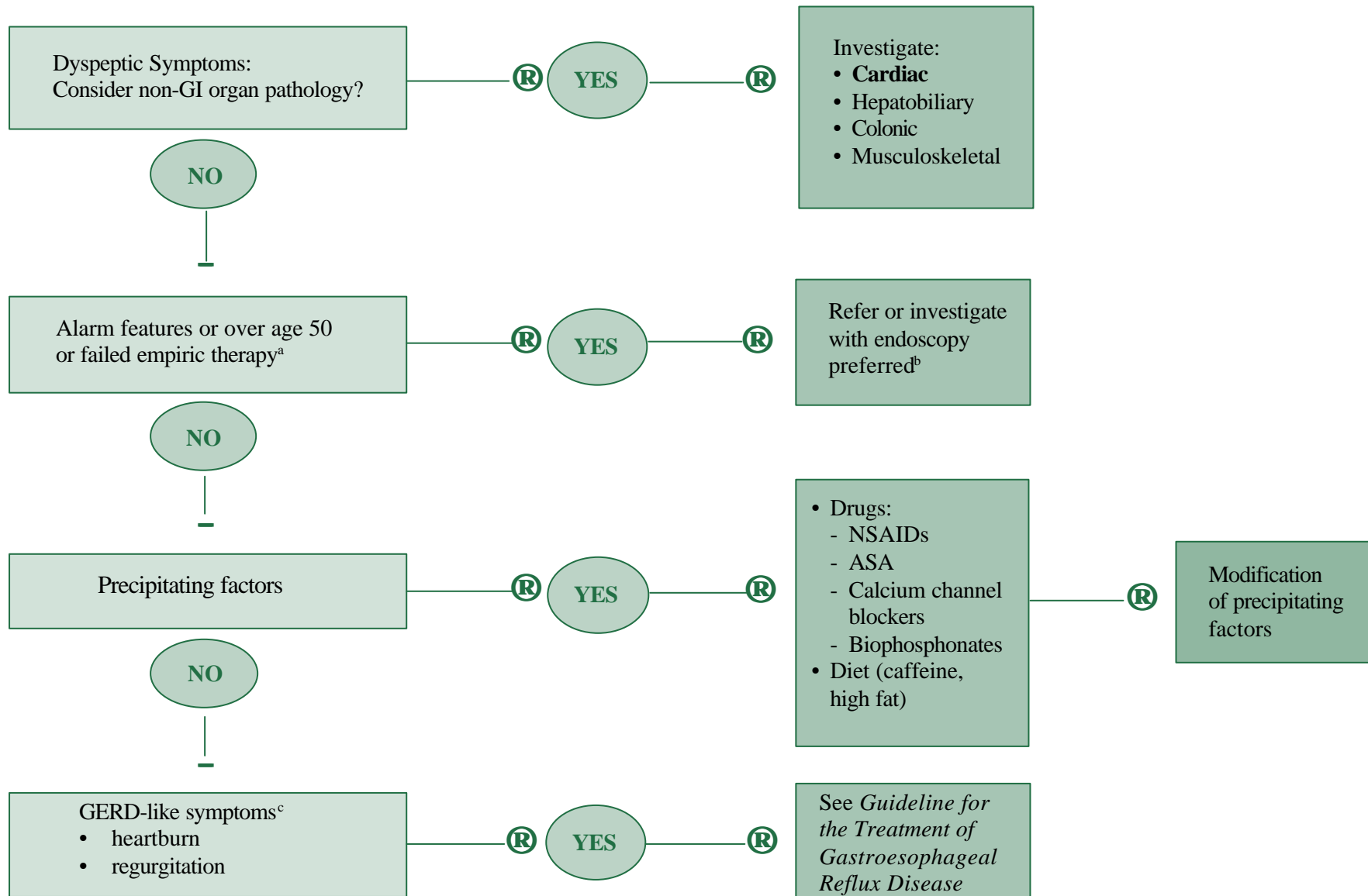
Diagnosis and Management of Chronic Undiagnosed Dyspepsia

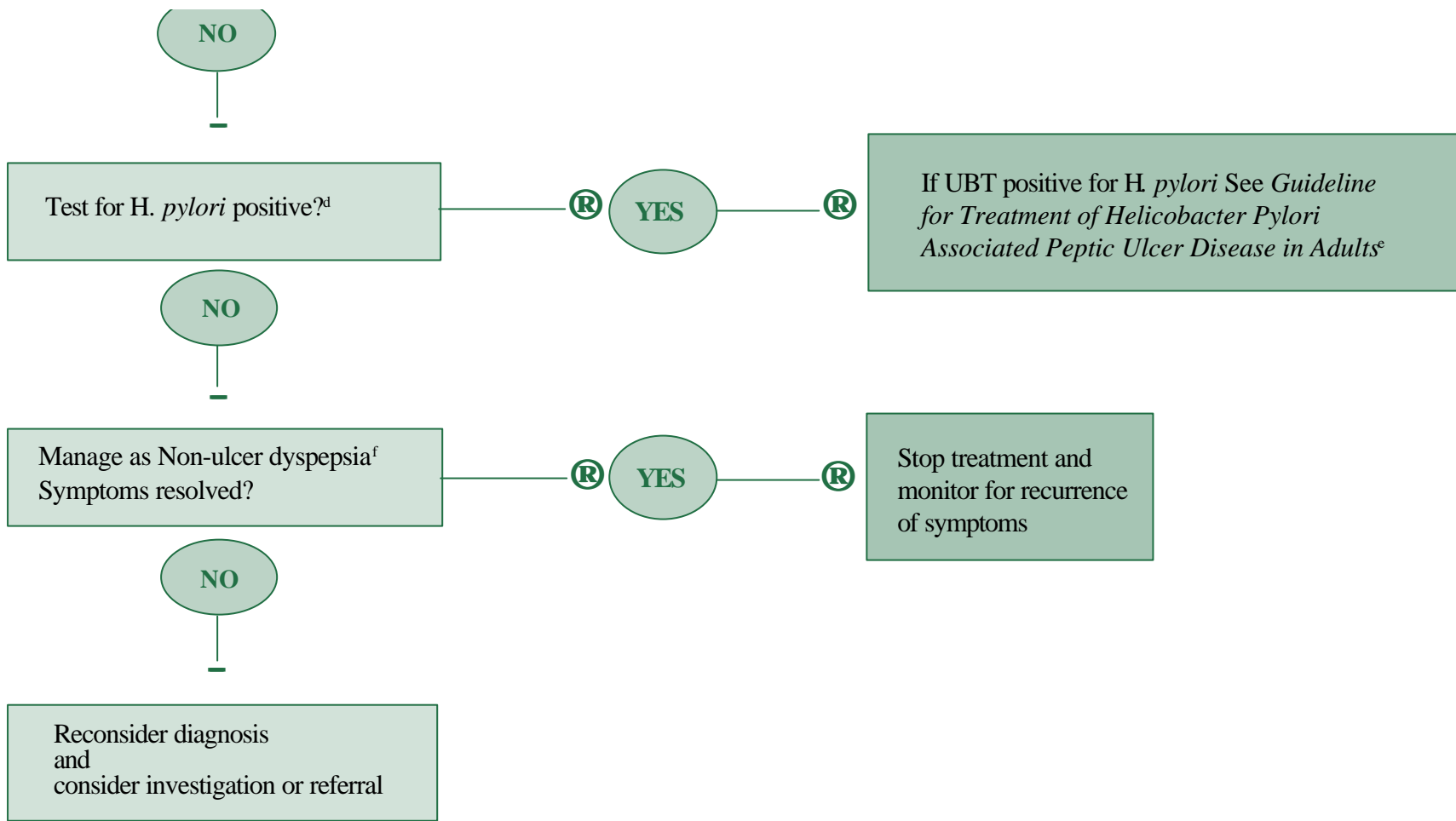


Notes:

1. Dyspepsia is a group of symptoms which alert clinicians to consider disease of the upper gastrointestinal tract. It is not a diagnosis and includes symptoms of upper abdominal discomfort, nausea, bloating, fullness and early satiety amongst others.
2. Alarm features: vomiting, bleeding/anemia, abdominal mass/unexpected weight loss, dysphagia/odynophagia.
3. Upper GI barium X-ray may be considered as alternative to endoscopy.
4. Symptoms suggestive of GERD: retrosternal burning, discomfort rising toward the throat, regurgitation.
5. One third of patients under age 50 without alarm features or GERD and not on ASA or NSAIDs will have *H. pylori* induced peptic ulcer disease.
6. *H. pylori* testing: test only if patient is willing to be treated if tests are positive. Do not trial *H. pylori* eradication therapy without testing. If *H. pylori* is associated with an ulcer, symptoms will improve with *H. pylori* eradication. If symptoms have stopped there is no need to retest to prove eradication. If there is non-ulcer disease, symptoms will not generally improve with *H. pylori* eradication. UBT is recommended for pre- and post-treatment testing. Serology is not recommended for post-treatment testing. Some potential exists for treatment side effects (allergies, *C. difficile* colitis, metallic taste). Patient compliance is essential to reduce potential for *H. pylori* resistance. Stop antibiotics 4 weeks before and PPI 2 weeks before re-testing with UBT.
7. Two-thirds of dyspepsia patients less than age 50 without alarm features, or symptoms suggesting GERD, or not taking ASA or NSAIDs will have NUD. There is limited symptomatic response to treatment for NUD.

ALGORITHM: DIAGNOSIS AND TREATMENT OF CHRONIC UNDIAGNOSED DYSPEPSIA IN ADULTS





EXPLANATORY NOTES

a. Alarm Features

- Vomiting
- Bleeding/anemia
- Abdominal mass/unexpected weight loss
- Dysphagia/odynophagia

b. Endoscopy

- Upper GI barium X-ray may be considered as an alternative

c. Gastroesophageal Reflux Disease (GERD)

- Symptoms suggestive of GERD:
 1. Retrosternal burning, discomfort rising toward the throat
 2. Regurgitation

d. Peptic Ulcer disease (PUD)

- One third of dyspepsia patients under age 50, without alarm features or GERD and not on ASA or NSAIDs will have *H. pylori*-induced peptic ulcer disease

e. Helicobacter pylori (*H. pylori*) testing

- Test only if patient is willing to be treated if tests positive for *H. pylori*
- Do not trial *H. pylori* eradication therapy without testing
- If *H. pylori* is associated with an ulcer, symptoms will improve with *H. pylori* eradication
- If symptoms have stopped, there is no need to re-test to prove eradication
- If there is non-ulcer disease (NUD), symptoms will not generally improve with *H. pylori* eradication
- UBT is recommended for pre and post-treatment testing
- Serology is not recommended for post-treatment testing
- Some potential exists for treatment side effects:
 - allergies
 - *C. difficile* colitis
 - metallic taste
- Patient compliance is essential to reduce the potential for *H. pylori* resistance:
 - 12% of Alberta *H. pylori* resistant to clarithromycin (1998)
 - 29% of Alberta *H. pylori* resistant to metronidazole (1998)
- Stop antibiotics 4 weeks before and PPI 2 weeks before re-testing with UBT

f. Non-ulcer dyspepsia (NUD)

- Two-thirds of dyspepsia patients less than age 50 without alarm features, symptoms suggesting GERD, are not taking ASA or NSAIDs will have NUD
- There is limited symptomatic response to treatment for NUD
- Recommended options for treatment include PPI, H₂RA, or Prokinetic. There is no consensus to guide therapeutic choice, therefore consider symptoms to make a choice and prescribe for 2 to 4 weeks with reassessment

H. pylori Associated Peptic Ulcer Disease: Adults

Summary of the Alberta Clinical Practice Guideline, July 2000

- Exclusion**
- This guideline does not apply to pregnant or lactating women or patients <18 years of age
- Etiology**
- Helicobacter pylori (H. pylori)
- Diagnosis**
- **It is critical to differentiate between PUD, ASA/NSAID-induced and malignant duodenal/gastric ulcers**
 - **Patient over age 50 with new onset of symptoms or those with alarm features warrant timely investigation, preferably by endoscopy**
 - H. pylori status (urea breath test) is recommended.
 - If negative consider trial of empiric therapy: proton pump inhibitor (PPI), or H₂A receptor antagonist, or prokinetic agent
- Management**
- **Treatment compliance is imperative**
 - Duration of therapy is 7 days for all treatment regimens
 - Therapy for eradication need not be followed by a curative course of acid suppression in uncomplicated ulcers

Suggested Treatment Regimens

First Line^{1,2}

PPI + Amoxicillin + Clarithromycin

Penicillin Allergic

PPI + Metronidazole³ + Clarithromycin

Macrolide Intolerance or Failure of 1st Line^{4,5,6}

PPI + Bismuth subsalicylate + Metronidazole³ + Tetracycline

Recommended Doses

PPI

= lansoprazole 30 mg BID or
= omeprazole 20 mg BID or
= pantoprazole 40 mg BID

Amoxicillin

= 1 gm BID

Clarithromycin

= 500mg BID

Metronidazole

= 500 mg BID or
= 250 mg QID in PPI + BMT protocol

Bismuth Subsalicylate

= 2 tablets QID

Tetracycline

= 500 mg QID

Notes

1. Eradication rates approximately 90%
2. Side effects occur in <5% of patients
3. Metronidazole resistance may occur in 10 to 20% of patients and will lower effective eradication rate from 90% to 75%
4. Eradication rates are >85%
5. May be used for triple therapy failures
6. Side effects that affect compliance have been reported for >50% of patients

Therapy NOT recommended

- Eradication therapy that include **ONLY** one antibiotic
- More than **ONE** course of antibiotic therapy without further investigations

Follow-up

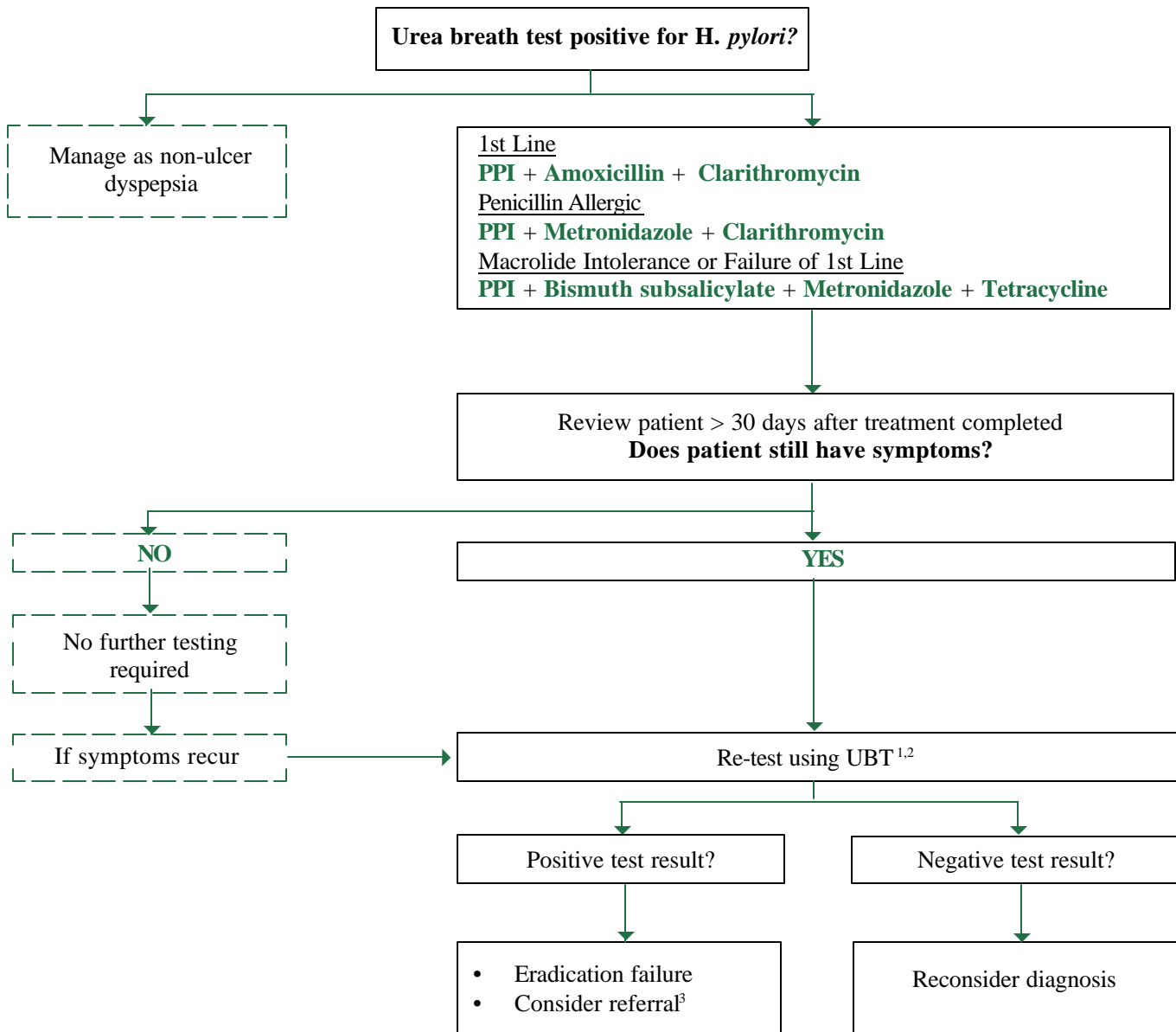
- If patient is asymptomatic, post-treatment testing is unnecessary
- If patient is symptomatic, re-test using UBT >30 days following completion of therapy
 - If UBT is negative, reconsider diagnosis or manage as non-ulcer dyspepsia
 - If UBT is positive, eradication therapy has failed - choose alternative protocol
- Serology is **NOT** recommended for post-treatment testing

Referral

- Specialist referral recommended for further treatment failures

Diagnosis and Management of *H. pylori* in Adults

- One third of dyspepsia patients under age 50, without alarm features or GERD and not on ASA or NSAIDs will have *H. pylori* induced peptic ulcer disease
- Test only if patient is willing to be treated if tests positive for *H. pylori*
- Patient compliance is essential to reduce potential for *H. pylori* resistance:
 - 12% of Alberta *H. pylori* resistant to clarithromycin (19(8))
 - 20% of Alberta *H. pylori* resistant to metronidazole (1998)



Notes:

1. Ensure that antibiotics have not been used in past 30 days, and PPI in past 14 days prior to UBT
2. Serology is not appropriate for post-treatment testing
3. PPI-BMT may be used for some triple therapy failures

Acute Diarrhea

Acute diarrhea is defined as more than 2-3 stools per day or more than 250 gms of stool/day for up to 2-3 weeks (diarrhea longer than 4 weeks is considered “chronic”).

Causes include:

Infections

Viral (rotavirus, CMV)

Travellers' diarrhea (E.Coli enterotoxigenic, E coli Enteroadherent, shigella, salmonella, campylobacter Iatrogenic (C. difficile)

Ischemic

Inflammatory (ulcerative colitis, crohns)

Irritable bowel

Drugs/toxic (antibiotics, laxatives, food poisoning, lactose intolerance)

Chronic diarrhea

By definition chronic diarrhea is greater than 4 weeks in duration. An organized approach to the investigation of patients with chronic diarrhea will result in earlier diagnosis and avoidance of serious nutritional deficiencies or other complications.

Causes may be divided into osmotic, secretory, motility disorder, and irritable bowel categories:

Osmotic

Small bowel disease (celiac, Bile acid malabsorption, Whipple disease etc)

Pancreatic disease (chronic pancreatitis, cystic fibrosis)

Lactase deficiency

Secretory

Inflammatory/exudative

Bleeding

Ulcerative colitis

Chronic bacterial infection

Non-bleeding

Crohn disease

TB AIDS

Neoplasms (villous adenoma, lymphoma)

Endocrinopathies (carcinoid, VIPomas, gastrin secreting tumors)

Motility disorders

Bacterial overgrowth Diabetic neuropathy

Scleroderma Short gut syndrome

Irritable bowel syndrome

Upper GI Bleeding

Hematemesis may be self-limiting but always warrants careful and urgent evaluation. The urgency of treatment and the nature of resuscitation depend on the amount and cause of the blood loss, and the underlying health status of the patient. Causes may include:

Ulcerative/Erosive

- Peptic ulcer disease
- Idiopathic
- Drugs (ASA, NSAIDS)
- Infectious (H. pylori, CMV, Herpes simplex)
- Stress ulcer

Esophagitis

- Peptic Infectious Pill induced (KCL, Bisphosphonate)

Porto-systemic hypertension (Esophageal varices, Gastric, Duodenal)

Traumatic or Post-surgical (Mallory Weiss tear) (This is often self-limited and may often be diagnosed from history and clinical examination alone.)

Vascular malformations (Angiodysplasia)

Tumors

Lower GI bleeding

Occult lower GI bleeding is commonly associated with neoplasm. The commonest causes of *painless frank* lower GI bleeding in the older age group are diverticular disease and angiodysplasia. The latter can easily be missed on colonoscopy. NSAIDs can also cause lower GI bleeding.

The highest yield procedure is colonoscopy, performed after rapid purge of the colon to remove as much blood as possible. If the source of brisk bleeding cannot be determined, angiography may be indicated (can also be used for therapy). Results are disappointing for lesions bleeding at slower rates or intermittently. Radionuclide scans can detect smaller bleeding volumes but will not localize the site of bleeding sufficiently to guide therapy. Barium enemas should be avoided given their low diagnostic yield and the interference of retained barium with subsequent colonoscopy or angiography.

Constipation

This may be defined as a change in a person's personal bowel habit to less frequent or more difficult defecation. It is common, NOT usually a manifestation of serious disease, and most commonly associated with low fiber intake and lack of activity.

Other causes may include:

- Irritable bowel syndrome
- Diverticular disease
- Secondary constipation from anal fissure, strictures or hemorrhoids
- Bowel tumors (Constipation occurs in < 1/3 of patients with cancer of the colon- diarrhea is more common. However, investigation for carcinoma of the rectum or colon should be considered in any patient over 40 who presents with recent, marked change in bowel habit without functional causes such as dietary change, immobility etc)
- Bowel obstruction
- Metabolic (hypothyroidism, diabetes, hypercalcemia)

Jaundice

Generally a person will have clinically detectable jaundice when the serum bilirubin exceeds 35 $\mu\text{mol/L}$. As ultraviolet light breaks down bilirubin, the jaundice may be more pronounced in non-light exposed areas (such as the portion of the conjunctivae covered by the eyelids, or the undersurface of the tongue). In addition elevated alkaline phosphate suggests the presence of cholestasis.

Causes include:

Unconjugated (indirect) hyperbilirubinemia

Hemolysis, ineffective erythropoiesis,

Decreased hepatic uptake (sepsis)

Decreased bilirubin conjugation (Gilbert syndrome transferase deficiency)

Conjugated (direct) hyperbilirubinemia

Drugs (Ocs, erythromycin)

Hepatitis

Cirrhosis

Primary biliary cirrhosis

- The "classic" presentation of fairly advanced Primary biliary cirrhosis (PBC) includes highest incidence in middle-aged women, jaundice, pruritis secondary to same, and alkaline phosphatase and (direct) bilirubin levels incommensurately elevated compared to transaminase levels. This pattern makes alcoholic hepatitis and viral hepatitis much less likely. Other stigmata of PBC include elevated total cholesterol, depressed HDL, and positive anti-mitochondrial antibodies.

Wilson's disease, Hemochromatosis, Alpha-1-antitrypsin deficiency

Alcohol cirrhosis

Fatty liver, sepsis

Extrahepatic cholestasis

Gallstones, sclerosing cholangitis, biliary stricture, cholangiocarcinoma, pancreatic cancer with duct compression. While gallstones may be asymptomatic, they are not usually associated with an elevated alkaline phosphatase unless there is common bile duct obstruction. Jaundice occurring in this setting is usually accompanied by abdominal pain.

Alcohol liver disease

In the Western world, depending upon the case series, in approximately 80% of patients with cirrhosis, the cause is alcohol. Hepatitis B and C, and idiopathic causes are less common. Remember that not all patients with alcohol abuse will develop alcoholic hepatitis or cirrhosis. In the patient with alcohol abuse and cirrhosis, other causes of cirrhosis must be looked for such as serum hepatitis B and C, or hemochromatosis.

Pancreatitis

By far the most common cause of pancreatitis in Western countries is alcohol-induced, with most such patients consuming at least 75 g of alcohol per day for 5 to 15 years.

Undifferentiated disorders

Dizziness

Fatigue

Tinnitus

Weakness

Fever of unknown origin

- **Criteria for FUO**
- **Assessment of likely causes on clinical and epidemiological grounds**

Syncope

- List Cardiac causes and other non-cardiac causes
- Elicit and interpret information from history and physical examination to distinguish among the major causes, and list and interpret basic investigations

Hypertension

- Diagnosis and basic management/guidelines for essential hypertension
- Describe target organ consequences of arterial hypertension
- **Discriminate between high blood pressure, hypertensive emergencies and hypertensive urgencies**
- **Pregnancy induced hypertension**

Venous Thromboembolism

- **Elicit and interpret clinical information to distinguish between acute DVT and other cause of calf swelling**
- **Elicit and interpret clinical information to distinguish between acute Pulmonary embolism and other causes for chest pain and dyspnea**
- Most appropriate investigations used to determine the presence of DVT or pulmonary embolism
- Management of DVT or PE and complications of anticoagulant therapy
- Prophylactic measures to prevent DVT and PE
- Arterial embolism and stroke prophylaxis in atrial fibrillation

Anaphylaxis

- Definition
- Elicit and interpret signs and symptoms of an allergic reaction
- Initial management of allergic reaction, advice to avoid further episodes
- Long-term management of patients who have had significant allergic reactions

Clinical Skills (see clinical skills section)

- Assessment of Chest pain (multiple causes including GERD, pancreatitis, CHD)
- Examination of the lymphatic system
- Taking a genetics history with construction of a relevant family history and pedigree

Dizziness

The complaint of “dizziness” must be clarified. It can be used to describe near-syncope, anxiety, ataxia, or vertigo. The sensation of dizziness due to near-syncope or hyperventilation is commonly referred to as “giddiness” or the sensation of an elevator descending too quickly.

A false sense of motion is called vertigo. This usually means dysfunction of the vestibular system. The most common type of vertigo is rotatory. When severe, vertigo is often associated with nausea and vomiting. To distinguish vertigo from ataxia, ask whether the symptoms are present only when walking. Symptoms present while sitting recumbent or standing cannot be explained as ataxia.

Causes of dizziness include:

Peripheral (Labyrinth)

- Seasickness
- Benign positional vertigo is fairly common, caused by loose or dislodged otoliths, and occurs with particular movement or positions of the head. Rapid extension and rotation of the head while the patient is supine, is called the Hallpike-Dix maneuver. It can elicit an attack, and is used to treat the condition.
- Acute labyrinthitis (bacterial or viral) is less common and is usually associated with hearing loss.
- Meniere’s disease. Vertigo is often severe, and attacks can last hours to days. In most patients deafness precedes the episodic vertigo. Acoustic neuromas seldom produce episodic vertigo of this kind.
- Drugs (aminoglycosides, alcohol)

Central

- Vertebrobasilar insufficiency
- Multiple sclerosis plaques on the 4th ventricle. Attacks usually last only a few days and usually are accompanied by other neurological signs and symptoms.
- Cerebellar Hemorrhage or neoplasm

Fatigue

Fatigue is a very commonly reported symptom in the primary care setting, but is uncommonly associated with organic causes. About 75% of patients will have fatigue from psychological causes. Fatigue is unlikely to be organically based if it is unrelated to activity, is not improved with rest. Try to elicit any history of sleep, sexual, eating, and bowel habit patterns. Fatigue that is a solitary symptom and is associated with a normal physical examination is unlikely to be associated with an identifiable organic cause, and further laboratory testing yields a cause in < 5% of cases.

If fatigue appears to be functional, outline a plan of management that includes 4 goals:

1. Accomplish activities of daily living
2. Return to work
3. Maintain interpersonal relationships
4. Perform some type of daily exercise

Tinnitus

Tinnitus is most commonly a harmless but annoying symptom only experienced subjectively. Any condition of the ear associated with the ear canal (wax, otitis media) cochlear hearing loss (Meniere disease, noise associated hearing loss) or central nervous system disease (acoustic neuroma, cerebellar pontine tumor) may cause tinnitus, but in the vast majority of patients (over 80%, especially in the elderly), the cause is idiopathic. Certain drugs may be associated with tinnitus, such as aspirin, amino glycosides, and digoxin.

Weakness

Many patients who complain of weakness are not objectively weak when muscle strength is formally tested. A careful history and physical examination will permit distinction between functional disease and true muscle weakness, and in turn, upper versus lower motor neuron or motor unit causes for weakness. Generalized weakness is more likely to be of functional origin than are complaints of an inability to perform specific tasks. (See clinical skills section for UMN versus lower motor neuron cause for paresis)

Fever of Unknown origin

Most febrile illnesses either resolve before a diagnosis can be made or develop distinguishing characteristics which lead to a diagnosis.

FUO refers to a prolonged febrile illness without an established etiology despite intensive evaluation and diagnostic testing. The "classic" definition from Petersdorf and Beeson's prospective analysis of 100 cases is [1]:

- Fever higher than 38.3°C on several occasions
- Duration of fever for at least three weeks
- Uncertain diagnosis after one week of study in the hospital

Proposed modifications to the definition include eliminating the in-hospital evaluation requirement because of the increased sophistication of outpatient evaluation [3] and reduction in duration to allow for nosocomial, neutropenic, and HIV-associated fevers which may not be prolonged [4,5].

With increasing diagnostic resources, the proportion of undiagnosed FUOs has dropped to fewer than 10 percent of cases. Generally, causes for the majority of "classic" FUO cases fall into three categories:

- Infections
- Malignancies
- Collagen-vascular diseases (eg, vasculitis, rheumatoid arthritis).

Infection remains the most frequent category, accounting for approximately one-third of cases.

Neoplasm is the second most frequent category, followed by collagen-vascular disease.

Note that connective tissue diseases seldom cause protracted fever without other stigmata of the disease becoming manifest. Prolonged fever of unknown origin (months) is most commonly associated with neoplasm and granulomatous diseases such as sarcoidosis. Medications may cause a [drug] fever of unknown origin, and may complicate the course of therapy in disease such as osteomyelitis or endocarditis were prolonged antibiotic therapy is required.

The causes of FUO vary dramatically with age. Undefined, self-limited viral syndromes are more common in children. In contrast, multisystem diseases such as rheumatic diseases, giant cell arteritis and polymyalgia rheumatica, and sarcoidosis may account for a third of cases of FUO over the age of 65.

Infective endocarditis has become a less common cause of FUO as it is usually detected by blood cultures and echocardiography. When endocarditis appears as FUO, it is more likely to be culture-negative or caused by difficult to isolate organisms such as *Bartonella quintana*.

Neutropenia-associated febrile episodes without a source are most frequently linked to bacteremia. Fungal infections replace bacterial infections in prominence after the acute period (after seven days) Fever, even if unexplained, usually abates with return of neutrophils. When fever persists or returns after the patient is no longer neutropenic, hepatosplenic candidiasis should be strongly considered.

Diagnostic approach

Of paramount importance are careful history taking, a thorough physical examination, and frequent reassessment of the patient frequently. Assessment should include travel, immunosuppression, drug and toxin histories, and localizing symptoms. Think of uncommon presentations of common diseases. Despite historical beliefs, the characteristics of the fever are not specific enough to guide the diagnosis of FUO. Fever patterns may be greatly modified in older patients, and or in those on steroids and nonsteroidal antiinflammatory drugs.

Laboratory investigations should involve few “routine” tests:

- Complete blood count, including differential and platelet count
- Routine blood chemistries, including liver enzymes, bilirubin, and lactate dehydrogenase
- Urinalysis, including microscopic examination
- Chest radiograph
- Routine blood cultures (times three) off antibiotics
- Tuberculin skin test with control(s)
- HIV antibody assay
- Heterophile antibody test in children and young adults
- CT scan of abdomen. This test is useful for detection of occult abscesses or hematomas, and abdominal lymphadenopathy. It outperforms abdominal ultrasound in this regard.

• Erythrocyte sedimentation rate (ESR) is likely also useful. A significantly elevated ESR suggests the presence of inflammation, infection, or neoplasm. One should know that the test is reasonably sensitive, but not specific, and may be positive in drug fever and renal disease, and negative in giant cell arteritis.

Unless other stigmata are present, antinuclear antibodies (FANA) and Rheumatoid factor are not helpful. Nuclear medicine imaging (gallium-67 and indium-111 labeled leukocyte scanning) is highly sensitive (scan whole body) but non-specific. It is best reserved for cases where the initial evaluation remains negative and a screening look at the entire body is desired.

Other tests should be directed by findings in history, physical examination and basic laboratory investigations. For example, central nervous symptoms or signs, for example, should prompt a lumbar puncture and imaging of the head and/or spine.

References

1. Petersdorf, RG, Beeson, PB. Fever of unexplained origin: Report on 100 cases. *Medicine* 1961; 40:1.
2. Jacoby, GA, Swartz, MN. Fever of undetermined origin. *N Engl J Med* 1973; 289:1407.
3. Petersdorf, RG. Fever of unknown origin: An old friend revisited. *Arch Intern Med* 1992; 152:21.
4. Durack, DT, Street, AC. Fever of unknown origin: Re-examined and redefined. In: *Current Clinical Topics in Infectious Diseases*, Remington, JS, Swartz, MN (Eds), Blackwell Science, Boston 1991. p.35.

Syncope

Syncope is defined as a sudden loss of consciousness due to impaired cerebral perfusion which resolves spontaneously. The common denominator of all causes is having cerebral blood flow interrupted for > 6-8 seconds, or a systolic BP drop to less than 70 mm Hg or a MAP to < 40 mm Hg.

Syncope is common, being responsible for 3% of ER visits and 1% of hospital admission. The incidence increases with age. Syncope is not a disease, but a symptom, and it has many causes. It must be distinguished from seizures, narcolepsy, hypoglycemia, hypoxia, and vertigo.

There is unfortunately no diagnostic gold standard against which various diagnostic tests for causes of syncope may be compared, and detected diseases may be correlational rather than causal. This accounts for the varying and wide estimates of relative contributions of various causes to syncope.

Causes of Syncope based on 5 population based studies of unselected patients

Neurocardiogenic (Vasovagal) (1-55%)

Cardiac:

- Arrhythmic (brady/tachy/conduction) (5-30%)
- Obstructive (aortic stenosis, IHSS etc) (10%)
- Orthostatic (4-12%)

Neurological

- Seizures (15%)
- Carotid Sinus hypersensitivity (< 1%)

Metabolic Drug (2-9%)

Psychiatric (1-3%)

Undiagnosed (30-40%)

Elderly patients may have situational syncope, with loss of consciousness associated with stool or urine elimination, or post-prandially, or after coughing or laughing. Since the prevalence of heart disease increases with age, elderly people are more likely to have a cardiovascular cause for their syncope. Cardiac causes are also more likely in patients presenting to the emergency department.

Venipuncture is the most common procedure done by health care providers and is a leading cause of syncope. In a study of 4050 venipunctures done over a 3-year period, syncope occurred in approximately 1% of the patients.

The most useful diagnostic elements in the diagnosis of syncope are the history, clinical examination, and a 12-lead ECG. This will yield the diagnosis in about 50% of cases. Other laboratory tests increase the yield to 60% and about 30-40% of causes remain undiagnosed (1).

Elements of the history that are useful in diagnosis include Duration and frequency, presence of any prodrome, including chest pain, dyspnea, particular circumstances at the time of the episodes (elimination, eating, position, exertion), the duration of unresponsiveness, the time to return to normal (post-ictal), and medication history. Vasovagal (neurocardiogenic) causes have "Near Misses" or averted spells, often a history of fainting as child, upright posture at onset, and prodromal sensations of warmth, diaphoresis, or nausea. The victim regains consciousness to normal within minutes. Sudden LOC, and palpitations often characterize Arrhythmic or conduction disturbance causes.

It is important to be able discriminate between seizures and syncope:

	Seizures	Syncope
LOC duration	Minutes	Seconds
Movement	Tonic-Clonic	Myoclonic/Extensor Spasm
Tongue Biting	++	-
Incontinence	++	-
ANS Prodrome	-	++
Post-ictal confusion	+++	+
EEG	Spike & wave	Diffuse slowing

Multifocal myoclonus has been observed in most patients who experience syncope. Syncopal convulsions have been reported in a much smaller proportion of patients who experience syncope. These convulsions are generally characterized by tonic stiffening, but patients may exhibit tonic-clonic seizures. These convulsions do not imply underlying seizure disorders. The absence of post-ictal confusion or drowsiness also militates against seizure.

Patients presenting with reported myoclonus or a generalized seizure clearly precipitated by syncope do not need additional testing or treatment. In such circumstances, EEG recordings have insufficient sensitivity to rule out seizure, and would not be indicated unless the clinical examination detected localizing signs, or the history also included seizures not precipitated by syncope.

Hospitalization indicated for patients with:

- Associated MI stroke or arrhythmias
- Accompanying chest pain
- Syncope associated with exertion
- History suggestive of arrhythmia or QT syndrome
- Clinical exam suggestive of CHD, CHF, or acute neurologic signs
- Abnormal ECG (VT, BBB, ischemia, B/T)
- Age > 70? Or sustain significant injury
- Frequent spells (> ½ -3 months) or recurrent despite Rx
- Mod-severe orthostatic hypotension

Syncope prognosis is dependent on the cause:

Cause	% Mortality/year (2)
Cardiac*	18-33
Non-cardiac	3-12
Unexplained	6-10

Although it is frustrating to not make a diagnosis despite extensive work-up, recurrence rates and bad outcomes are *much lower* in the unexplained group. In long-term follow-up, most patients with *inconclusive tests* and recurrent syncope have bradycardia as cause for symptoms

1. Kapoor, W. Medicine 1990; 69:160-75
2. Kapoor WN et al NEJM 1983;309:4

Hypertension

Contributions from P. Hamilton T.K. Lee

Arterial hypertension affects more than 20% of the adult population. Only half of hypertensive patients are recognized as having arterial hypertension, and only 16% are receiving appropriate therapy.

Cardiomegaly is a feature of end organ damage from uncontrolled hypertension and increases the risk of premature vascular events 5-fold. ACE inhibitors have been shown to have favorable impact on LVH and are most likely to have great impact on reducing morbidity and mortality. Additionally, in the presence of diabetes with proteinuria, ACE inhibitors are agents of choice.

Pregnancy Associated Hypertension

This may include pre-eclampsia, eclampsia, chronic pre-existing hypertension, transient gestational hypertension or pre-eclampsia superimposed on chronic hypertension. Although pre-eclampsia is generally a self limited disease with rapid resolution of hypertension and a low recurrence rate in future pregnancies (< 7%), when it is severe, and especially when it occurs in the second trimester, it is not so benign. Such patients are at a high risk for recurrence in subsequent pregnancies and for hypertension later in life. The incidence of fetal growth retardation is about 10%.

High blood pressure, Hypertensive emergencies and urgencies

Hypertensive emergencies and urgencies occur in about 1% of hypertensives, and is more common in men than women. High blood pressure (usually >210/120) is the finding common to hypertensive urgencies and emergencies, though elevated blood pressure alone does not constitute an emergency. **Hypertensive emergency** refers to elevated BP (usually but not necessarily) >210/120 with concomitant symptoms from target organ involvement, and **hypertensive urgency** (BP >210/120 without concomitant symptoms from target organ involvement).

For blood pressure values detected on the "first visit" between 140/90 and 180/105, and in the absence of target organ involvement and damage, at least 4 further visits are required to make the diagnosis of hypertension.

It is important to determine quickly whether a hypertensive emergency is present (aortic dissection, myocardial infarction, pulmonary edema, cerebrovascular hemorrhage, grade 3-4 retinopathy (papilledema or fundoscopic hemorrhages or exudates), or hypertensive encephalopathy) and make blood pressure lowering the first concern. Control of blood pressure in a patient with a hypertensive emergency may often involve CCU or ICU admission as careful monitoring, titration of medications, and treatment of the complication are all necessary. Initial targets for BP reduction should be to no lower than to 100-105 mm Hg diastolic or by no more than 25% of baseline diastolic, within several hours.

If the blood pressure has been poorly controlled for some time, the brain may have altered its autoregulation to adjust to higher pressures. Acutely lowering the blood pressure quickly to levels below 100-105 diastolic or by > 25% of baseline may induce cerebral hypoperfusion and stroke, and therefore should be avoided except under exceptional circumstances dictated by the treatment need of complications such as aortic dissection or worsening pulmonary edema.

For hypertensive urgencies, monitoring in a quiet room in the ER and institution or restarting of a medication such as sustained release calcium channel blockers may be all that is needed to lower the BP to acceptable levels. The target BP levels may be reached more slowly (over 6-24 hours). If the therapeutic response in the emergency department is favorable, the patient could be discharged with close follow-up as an out-patient 24-48 hours later.

Investigating the cause

Treatment takes precedence over investigation for secondary causes of hypertensive emergencies or urgencies. Select laboratory tests, which give the maximum possible diagnostic yield in the minimum amount of time.

Causes include:

Primary hypertension (long-standing, uncontrolled, medication-withdrawal).

Exacerbation of essential hypertension or poor adherence to medication account for about 60% of cases.

Secondary Hypertension (Found in about 40% of cases)

(The prevalence of secondary causes may be higher in Caucasian populations)

Renal disease: Uremia with fluid overload Acute GN, scleroderma crisis, Renal artery stenosis (accounts for 1/3 of secondary causes)

Primary hyperaldosteronism (although the commonest endocrinopathy causing secondary hypertension, it is an unusual cause for hypertensive crisis)

Pheochromocytoma

Drugs (cocaine, amphetamines, MAO inhibitor interactions)

Cerebrovascular accidents

In working up, remember that some drugs may interfere with investigations (labetolol in the work-up of pheochromocytoma, or drugs that effect the RAA system). Patients who have had poorly controlled hypertension may be hypokalemic from the activation of the RAA rather than a result of primary hyperaldosteronism. Renin and aldosterone levels may remain elevated for several months after a hypertensive crisis.

References and suggested reading material:

1. Kaplan NM: Hypertension crisis. Kaplan NM (ed) Clinical Hypertension 7th Edition. Williams & Wilkins, Baltimore 1998 p.p.: 265-80
2. Canadian recommendations for the management of hypertension. CMAJ 1999 161 (12 suppl)

Venous thromboembolism: Elicit and interpret clinical information to distinguish between acute DVT and other cause of calf swelling

Wells scoring system for pretest probability of deep-vein thrombosis

Clinical Feature		Points
Risk factors	Active cancer	
	Paralysis, paresis or recent plaster immobilization of the lower extremities	1
	Recently bedridden for > 3 days or major surgery within 4 weeks	1
Signs	Localized tenderness along the distribution of the deep venous system	1
	Entire leg swollen	1
	Asymmetric calf swelling (>3 cm difference, 10 cm below tibial tubercle	1
	Asymmetric pitting edema	1
	Collateral (nonvaricose) superficial veins	1
Other	Alternative diagnosis as likely or more likely than DVT	- 2

Interpretation:

Score	Probability of DVT
> 3	High
1-2	Moderate
0 or less	Low

Pulmonary Embolism: Elicit and interpret clinical information to distinguish between acute Pulmonary embolism and other causes for chest pain and dyspnea

Modified Wells Criteria for pre-test probability of pulmonary embolism Ann Intern Med 2001; 135:98

Clinical Feature	Points
Clinical symptoms of DVT	3.0
Other diagnosis less likely than PE	3.0
Heart rate > 100	1.5
Immobilization > 3 days or surgery in past 4 weeks	1.5
Previous PE or DVT	1.5
Hemoptysis	1.0
Malignancy (current or recent)	1.0

Interpretation:

Score	Probability of PE
>6.0	High
2-6	Moderate
<2.0	Low

Likelihood of Pulmonary embolism according to scan category and Clinical Probability in PIOPED study JAMA 1990;263:2753

Scan Probability	Clinical Probability		
	High	Intermediate /Moderate	Low
High	95	86	56
Intermediate	66	28	15
Low	40	15	4
Normal	0	6	2

Diagnosing pulmonary emboli in pregnancy

Determining the optimal diagnostic test involves a balance between diagnostic accuracy and radiation exposure to the fetus. If discussed with the nuclear radiologist, a V/Q scan can be performed with a lesser amount of radiation exposure, and constitutes significantly less radiation exposure than does a spiral CT scan. Doppler duplex scanning of the legs is reasonable for above knee thrombus detection, but would not rule out pulmonary emboli. Contrast venography would also not contribute to ruling out a pulmonary embolism, especially since pelvic veins would not be seen, and would expose the fetus to contrast and radiation. References: NEJM, 1998:339,2;93-104 NEJM, 1996:335,24;1816-1828

Acute DVT therapy

Use Low molecular weight heparins (LMWH) rather than heparin for acute DVT. They are as effective as unfractionated heparin (UFH), have a more predictable dose-response (based on body weight), and do not require monitoring. They may be given subcutaneously so that patients can receive the drug outside of the hospital setting. LMWHs are associated with less bleeding and heparin-induced thrombocytopenia, and are probably safe in pregnant women.

LMWH	SC Dose: DVT treatment	SC Dose: DVT prophylaxis (orthopedic)
Enoxaparin	1 mg/kg q12h or 1.5 mg/kg/day. Max single daily dose 180 mg	30 mg q12 start 12-24 hr post op or 40 mg od start 10-12 hr preop
Dalteparin	200 anti-Xa IU/kg/day. Max single daily dose 18,000 IU	2500 IU 6-8 hr post-op then 5000 IU daily or 5000 IU 8-12 hr preop and od starting 12-24 hr postop
Tinzaparin	175 anti-Xa IU /kg/day	75 IU/kg od starting 12-24 hr postop or 4500 IU 8-12 hr preop and od postop

Correct doses for massively obese patients have not been established. ?monitor plasma anti-Xa activity?

If UFH is to be used, use a dosing regimen that includes weight-based loading and maintenance doses, and a standardized adjustment scale based on aPTT monitoring. If your hospital does not have one, get one. Such regimens produce therapeutic (aPTT ratio > 1.5) anticoagulation sooner with no increase in bleeding and are associated with fewer recurrent DVTs. Aim for a aPTT ratio of 1.5-2.5.

Complications of Heparin use

Bleeding: Subcutaneous hematomas at injection sites (LMWH)

Major Bleeding: (defined as a drop in Hb > 2 gm, or need for transfusion, intracranial, or retroperitoneal bleeds) occurs in 1-2% therapies with LMWH and 6% with UFH. For heparin associated bleeding use Protamine sulfate. It is very effective for unfractionated heparin, but less so (requiring much higher doses) for LMWHs. Fresh frozen plasma (FFP) *does not* reverse the anticoagulant effect of heparin.

Osteoporosis with prolonged use (e.g. pregnancy)

Heparin-induced Thrombocytopenia:

Characteristics	HIT 1	HIT2
Incidence	25% of patients	5% UFH 1% LMWHs
Mechanism	Platelet aggregation with increased RES clearance	IgG-PF4-heparin immune complexes Result in platelet activation and procoagulant release-clotting
Onset	< 5 days after start heparin	5-10 days after start heparin. This trend seen regardless if heparin for first time or multiple times in past
Platelet count	Nadir typically > 100 T-1 0°	Nadir typically 20-150 X 10 ⁹ (median 50-70) or decrease > 50% from baseline (platelet count may still be in normal range in 10% of patients).
Consequence	Benign, reversible, usually recovers within 4 days of continued heparin	Potential significant thrombosis in 50-75%(80% venous 20% arterial), DIC and skin necrosis at injection sites
Therapy	None	Discontinue heparin. Use danaparoid (orgaron) or Lepirudin

*May be as early as 24 hours if used heparin in last 3 months (persistent circulating IgG)

The risk of HIT2 is dose dependant and is higher in therapeutic than in "lock" solutions. Warfarin alone is not a treatment option for HIT2, as it is associated with venous thrombotic limb gangrene in HIT2 when used alone (decreases Protein C). To be safe don't give until thrombocytopenia resolved on danaparoid or leuperidin. Although LMWHs are much less likely to trigger HIT antibodies than UFH they have 100% cross reactivity with existing HIT antibodies and are contraindicated in the management of HIT2.

Starting Warfarin: Choosing the 1st dose

The goal of treatment of acute venous thromboembolism is to provide prompt heparin therapy, and the early addition of warfarin. If there are no contraindications start warfarin on day 1 of heparin and monitor the INR daily. This strategy reduces the time to therapeutic INR without increasing bleeding. Use an "expected dose" (5 mg) or the patient's previous maintenance dose, rather than a larger loading dose. Large loading doses immediately deplete Protein C and Factor II without significantly reducing other factors. (2-3) This paradoxically increases bleeding and clotting risk. *Use a lower initial dose than 5 mg* if the patient is elderly, malnourished (or has low body weight or low albumin), has active cancer or heart failure, liver disease, or is on other medications, which might potentiate warfarin's effect (antibiotics etc), as they will be more sensitive to the warfarin.

It is important to continue the heparin for > 5 days and continue heparin for 2 days after the INR is in therapeutic range (therapeutic overlap), as this strategy has been shown to improve outcomes.

Warfarin: Choosing the 2nd dose

Measure the INR > 15 hours post-dose to accurately assess the effect of warfarin dose.

INR Day 2	Warfarin Dose
NO increase (commonest)	5 mg/day. If the INR is still 1-1.1 after the 2 nd dose, give 7.5 on the 3 day
1.2-1.4	2-3 mg/day
> 1.5	1 mg/day

Pulmonary embolism therapy

The existing standard of care is In-hospital adjusted dose intravenous unfractionated heparin. Randomized controlled trials of LMW heparin in hospitalized patients with "stable" PE (1,2) show therapeutic equivalence

Post Venous Thrombo-embolism (VTE) Prophylaxis:

Well-designed, randomized trials have compared different durations of full-dose warfarin anticoagulation (maintaining INR 2-3) for venous thromboembolism. (4-5). A minimum duration has likely been defined. Shortening the duration of therapy to less than 4-6 weeks in patients who, for the most part, had a first episode of VTE and did not have cancer, results in about a 2-fold increase in the rate of recurrent VTE after anticoagulants were stopped, without being associated with a convincing reduction in the rate of bleeding.

A consistent finding across studies is that 3 months of anticoagulant therapy is adequate for patients with VTE that has been provoked by a major transient risk factor, such as recent surgery, or immobility. However, this is not necessarily adequate for the higher risk patient group with "unprovoked" ("idiopathic") or recurrent VTE patient group. It is not clear from trial results in these groups, whether 3 months of therapy achieves as low a subsequent risk for recurrent VTE as 6 or 12 months of treatment. Unfortunately, continued anticoagulation is at the cost of persistent and significant risk of major bleeding episodes (5-7% incidence/year). On this basis, many experts recommend a minimum of 6 months of anticoagulant therapy for an unprovoked episode of VTE, provided patients do not have a high risk for bleeding. After this, the balance between benefit and harm of full dose warfarin become more difficult to determine, even in patients with a low risk for bleeding.

Recently published results from the PREVENT trial suggest that low dose warfarin (maintaining the INR between 1.5-2.0) may produce a significant reduction in long term VTE risk with negligible increase in bleeding risk, and with infrequent INR monitoring, at least for as long as 2-4 years of therapy.

Note that there have been no completed prospective studies to assess the optimal length of anticoagulation therapy in patients positive for anti-phospholipid antibody, anti-thrombin III deficiency, or in whom the first VTE episode was life threatening. Many clinicians consider lifelong therapy in these instances.

High INR management

When should you adjust Warfarin? Remember that a supra-therapeutic INR result may be due to a lab error if the tube was incompletely filled. True causes include excessive warfarin dosing, decreased oral intake, drug interactions, or recent diarrhea illness.

Avoid overly tight control with multiple dose changes as this strongly predicts INRs > 6! However, patients on warfarin are at increased risk for bleeding if the INR \geq 4.0. Expert opinion suggests the dose should be adjusted when 2 consecutive INRs are outside therapeutic range < 1.8 or > 3.4. When adjusting, avoid overly small or big changes (<5% to > 20% of dose), as these are either ineffective or increase the risk for overshoot.

INR	Action
4-5	Hold warfarin and investigate for cause. If next day INR < 4 can resume warfarin at lower dose
5-9	If bleeding risk high' hold warfarin and give Vit K (1-2.5 mg po) Otherwise, just hold warfarin and check INR next day. If INR decreased, restart warfarin at lower dose when INR 3-4. If next day INR increases then give Vit K po
>9	Give Vit K oral or IV. If substantial bleeding admit, give Vit K and FFP
Significant bleeding	Hold warfarin. Admit and give Vit K and FFP

Patients with elevated INRs are a higher risk of bleeding if there has been an upward trend in the INR values, or they have other underlying bleeding risks (Advanced age (3-4% if > 80), recent hemorrhage, alcohol binge drinking or liver disease, renal insufficiency, ASA or NSAID(including COX2) use, Cancer, low platelets, or uncontrolled hypertension)

Stopping Warfarin for surgery

There is usually no need to hold warfarin preoperatively for dental procedures, low risk procedures such as upper endoscopy with biopsy, colonoscopy with biopsy, or ERCP with stent insertion (but without sphincterotomy)(1), or other minor surgeries (with some exceptions).

For major surgeries it is usually sufficient and safe to stop warfarin 4-5 days pre-operatively. The INR will usually drop to < 1.4, which provides an acceptable level of hemostasis for surgery. The warfarin may have to be stopped sooner in patients > 70 years old, or if the maintenance INRs run > 3. (7) Patients at high risk for thrombo-embolism (arterial or venous events within last month, or metal mitral valve prostheses etc) usually require peri-operative coverage with heparin.

1. Hittlet A, Deviere J Can J Gastroenterol 2003;17:329-332

Geriatrics

Delirium and Dementia
Falls
Urinary Incontinence

Clinical skills : see clinical skill section

- **Gait and balance**
- **History taking for acute urinary incontinence**

Delirium and dementia

Delirium and dementia can both be "confusing" terms to differentiate. However, it is an important distinction to make because these two disorders vary greatly with regards to etiology. Synonymous terms for delirium include acute confusional state, toxic psychosis, metabolic encephalopathy, and acute brain syndrome. The hallmark symptom of delirium is an impairment of consciousness described by the DSM-IV as a "reduced clarity of awareness of the environment" along with failure to maintain attention. There is usually a global impairment of cognitive functions including, but not limited to, memory dysfunction. Since delirium is a syndrome and not a specific disease state, it has many potential causes. These include, but are not limited to, epilepsy, stroke, medications, CNS or systemic infections, endocrine dysfunction, hypoxia, heart, liver and kidney failure, head trauma, and deficiency states such as vitamin B₁₂ and thiamine (B₁) deficiencies. The major neurotransmitter thought to be involved in delirium is acetylcholine, and the primary site of dysfunction is thought to be the reticular formation..

Delirium may be diagnosed using the confusion assessment model developed by Inouye et al from the DSM IIR criteria. The diagnosis can be made if 2 major or 1 major and 2 minor criteria are met:

Major

- Acute onset and fluctuating course
- Inattention (hyper or hypoattentive)

Minor

- Disordered thinking
- Sensorium abnormalities(visual hallucinations etc)

Detection of minor criteria require the patient to be able to communicate with you.

Alzheimer's Dementia

Alzheimer's disease (AD) is a progressive neuro-degenerative disease of cortical neurons and the most common cause of dementia in individuals over the age of 60. The incidence of AD increases exponentially each decade after the age of 60. Pathologically, AD is characterized by predominant loss of cortical neurons in the association areas of the temporal, parietal, and frontal lobes. Dropout of cholinergic neurons in the nucleus basalis of Meynert appears to have an important role in the development of some of the neuropsychiatric sequelae of AD. Although the cause of AD remains unknown, several risk factors have been identified, including the gene for apo lipoprotein E4, a history of head trauma, and low educational background. No one risk factor is necessary or sufficient to cause AD.

Clinical manifestations of AD include loss of memory and other higher intellectual functions (e.g. orientation, attention, concentration, abstract reasoning, judgement, and motivation); disturbances of language (aphasia); loss of ability to performed learned activities (apraxia); and visual-spatial difficulty. Neuropsychiatric symptoms are also prevalent in AD and include agitation, anxiety, depression, apathy, paranoia, insomnia, and auditory or visual hallucinations.

There is no treatment for the primary degenerative abnormality of AD, although glutamate antagonists, nerve growth factors, estrogens, and non-steroidal anti-inflammatory agents are being studied as potential disease-modifying agents. However, symptomatic treatments are available.

The centrally active acetylcholinesterase inhibitors, tacrine and donepezil, have been demonstrated to provide temporary (up to 12 months) functional improvement in patients with AD; their effectiveness wanes due to inexorable disease progression and death of cholinergic neurons. Psychiatric symptoms of AD often respond well to antipsychotics (e.g. haloperidol) and antidepressants (e.g. paroxetine).

References and suggested reading material:

Lawlor PG et al. Occurrence, Causes, and Outcomes of Delirium in Patients with Advanced Cancer. *Archives of Internal Medicine* 2000; 160: 786-794

Pereira J, Hanson J, Bruera E. The Frequency and Clinical Course of Cognitive Impairment in Patients with Terminal Cancer. *Cancer* 1997; 79: 835-842

Ingham J, Breitbart W. Epidemiology and Clinical Features of Delirium. *Topics in Palliative Care* (1), pp7-19

De Stoutz ND, Stiefel F. Assessment and Management of Reversible Delirium. *Topics in Palliative Care* (1), pp. 21-43

Falls

Falls are common in the elderly and are associated with functional disability. About 95% of the causes of falls can be identified by a detailed history, physical examination, and environmental assessment. Interventions that prevent falls and their sequelae delay or reduce the frequency of nursing home admissions, and 1-2 year hospitalization rates, but do not change rates of mortality. History taking should try to determine potential extrinsic factors (environmental, medication, alcohol) and intrinsic factors (vision, inner ear, musculoskeletal, cardiovascular and cortical function). Only about 20% of falls are caused by a single specific cause: multiple causes are the rule. Evaluation should include a home environmental assessment for fall hazards.

Rubenstein L et al *Annals of Internal Medicine*. 1990;113:308

Urinary incontinence

There is an increasing incidence of involuntary micturition with age, and the prevalence of this disorder will increase as our population continues to age. The two commonest causes of chronic urinary incontinence are stress incontinence and dys-synergistic bladder (excessive detrusor contraction with urgency).

See clinical skills section for history taking for acute urinary incontinence.

Anemia

- **Approach to iron deficiency anemia**
- **Thalassemias**
- Investigation, differential diagnosis, and management of other micro-, macro- and normocytic anemias
- Pharmacology of erythropoietin
- Pathology of anemia of chronic disease
- Basic knowledge of Sickle cell anemia

Thrombocytopenia

- Understand mechanism and potential causes of decreased platelets
- Pathophysiology of TTP, ITP
- Management of thrombocytopenia

Bleeding disorders

- Elicit and interpret signs and symptoms of major underlying causes of bleeding disorders
- List and interpret basic investigations
- Hemophilia and Acquired Inhibitors, platelet disorders
- Management issues including platelet transfusions, vitamin K and various plasma derivatives

Transfusion medicine

- **Indications:**
- List and interpret information from the history and physical examination which indicates the presence of a transfusion reaction
- Knowledge of risks of blood borne infection
- Management of patient with transfusion reaction due to suspected ABO blood group incompatibility

Myeloproliferative disorders

- Polycythemia: Pathophysiology and approach to management
- Differential diagnosis of leukocytosis

Paraproteinemia

- Approach to monoclonal gammopathy and basic understanding of Multiple Myeloma including potential complications

Clinical Skills (see clinical skills section)

- Examination of the spleen
- Interpretation of laboratory findings in anemia

Anemia

In general, a CBC, peripheral blood smear, and reticulocyte count are the first steps in the investigation of any anemia. These results allow the determination of red cell size, and whether the bone marrow response to the anemia is appropriate. A reticulocyte index assesses whether the reticulocytosis is appropriately high for a given degree of anemia, and is calculated by:

$$\text{Reticulocyte index} = \text{Patient's Reticulocyte count (\%)} / (\text{patient's hematocrit} / 45)$$

With anemia, an index > 3 indicates a normal marrow response, whereas an index < 2 demonstrates an inappropriately low response. With a normal hematocrit an index of 1 is normal.

Iron Deficiency Anemia (IDA)

Investigation

- The initial steps in evaluation of IDA should include a CBC, peripheral blood smear, serum ferritin, and reticulocyte count.
- Progressive findings in IDA include:
 1. First, a decrease in ferritin, correlating with depleting iron stores in bone marrow. As IDA progresses one develops anisocytosis and elevated RDW as older cells maintain normal size and younger cells are now microcytic. As iron falls lower, there is a decrease in the reticulocyte count and serum iron concentration (serum iron/total iron binding capacity). At this point, all cells are hypochromic and microcytic on the peripheral smear and the MCV drops below 75 fL. Once anemia develops from iron deficiency, there should be no iron in the bone marrow (zero not just "low") because all the iron is shunted from the BM to the RBC before the body allows the Hemoglobin fall.
 2. A low serum ferritin is a useful index of iron body stores. There is no explanation for a low serum ferritin other than iron deficiency. In contrast, because it is an acute phase reactant which may be elevated with neoplasm infection or inflammation, a normal or increased value does not rule out IDA.
 3. In North America, IDA is more commonly due to excess iron loss from bleeding than from insufficient intake. Therefore IDA should always raise the suspicion for the presence of serious gastrointestinal disease. One requires about 3-4 cc of blood loss (1.5-2 mg iron) on regular basis to deplete stores.
 4. The commonest cause of gastrointestinal loss is likely gastric erosions: it is difficult for studies to accurately determine cause of blood loss because lesions detected may not be culpable. Up to 20% of GI losses are from cancer. Because colorectal cancer is the most life-threatening disease amongst causes of IDA, colonoscopy is recommended as initial procedure. A Barium enema with or without sigmoidoscopy is inferior methods of examination and should only be done if colonoscopy is not available. If colonoscopy is normal, the next step is gastroscopy-*if there are symptoms of upper GI disease*. The utility of gastroscopy in asymptomatic patients is more controversial.
 5. IDA may be the *only* manifestation of celiac disease, which may be found in 6% of patients with IDA. The transglutaminase (TTG) blood test is a useful method of detecting celiac disease.
 6. Most studies in patients with IDA do not show a correlation between a positive Fecal Occult Blood Testing (FOBT) and the presence or absence of a bleeding lesion in the bowel. Therefore, FOBT is best used for colorectal cancer screening, rather than in determining whether or not IDA is due to a bowel lesion.

Therapy for IDA

1. The goal of treatment is to not only correct the anemia, but to replenish stores. Ferrous sulfate 325 mg po qid taken 1-2 hours before meals and at bedtime will correct anemia in about a month, but it may take 6 months to replete stores because iron absorption by the

gut falls dramatically as the iron deficiency is corrected. Reticulocytosis peaks at about 7-10 days. Iron replacement should continue until the serum ferritin rises to > 50 ug/L, indicating total body iron stores of about 500 mg.

2. With Fe supplemental therapy described above, about 20% of people will get diarrhea or constipation, which is not dose-related and may be relieved by switching to another preparation. Gastric upset, and abdominal pain *are* dose-related and reflect the concentration of iron given. Sometime switching to ferrous gluconate or succinate may help reduce symptoms, although the delivery of elemental iron is only about half as much in these preparations (35 versus 60 mg per 325 mg tab) One can also try liquid formulation or taking the iron after meals. Again, less is absorbed, but it is worth it if adherence improves Parenteral iron therapy can have serious side-effects and should be reserved for exceptional circumstances.

Thalassemias

The thalassemias are inherited defects in globin chain production. They are more common in people of black or Mediterranean ancestry. American blacks more commonly have alpha thalassemia. Most people are heterozygous and have mild, asymptomatic disease, and it may be picked up on routine screening CBC as a microcytic anemia, typically with an MCV that is low for the degree of anemia seen.

In the normal adult 3 major hemoglobins are present in the mature RBC. Each hemoglobin consists of 4 heme groups and 4 globin chains. All hemoglobins have alpha chains but differ in which other globin chain they use:

Hb A: 97% alpha₂ beta₂
HbA₂: 2% alpha₂ delta₂
Hb F: 1% alpha₂ gamma₂

In heterozygous Beta-thalassemia the defect in production in beta globins causes a decreased production of HbA and compensatory increased production of HbA₂ and HbF. If there is combined iron deficiency and Beta thalassemia there can be a reduction in Hb A₂ production so that the electrophoresis is "normal". In alpha thalassemia, because all of the hemoglobins use alpha chains, decreased production does not alter the ratio of different hemoglobins. Other tests besides hemoglobin electrophoresis must be used.

The genetics of alpha thalassemia are more complicated

- 1 gene defect :clinical silent
- 2 genes: Similar to heterozygous B-thalassemia but normal hemoglobin electrophoresis
- 3 genes: Hg H disease with moderately severe anemia and Hb H (B₄) inclusions in RBCs
- 4 gene defect :death in utero! (hydrops fetalis)

Transfusion Medicine

Indications: Although the symptoms of anemia can include weakness, lassitude, dyspnea and palpitations, the correlation to hemoglobin concentration is poor until the Hb falls below 80 g/L. It is reasonable to assume that symptom improvement will occur with anemia correction only when the Hb is below 80, or when the anemia has occurred rapidly, or if concomitant heart or lung disease exists.

Antimicrobial therapy (Antiviral, Antibacterial, Antifungal)

- Spectrum of activity and major side effects of commonly used antimicrobial drugs
- Knowledge of hepatic versus renal clearance

Pneumonia

- Clinical and laboratory assessment to diagnose and grade severity of pneumonia
- Guidelines for hospital or outpatient care
- Pathogens & group-specific etiologies for community & hospital acquired pneumonia
- Patient populations at risk for unusual causes of pneumonia; specific pathogens involved
- Basic management, usual sensitivities and resistance of common pathogens
- Complications including empyema and lung abscess

Influenza**Central Nervous system infections (meningitis, encephalitis, brain abscess)**

- Recognition of bacterial meningitis as medical emergency.
- Clinical presentation, discrimination between bacterial versus viral meningitis.
- Know major pathogens and sensitivities. Knowledge of HSV encephalitis
- Indications for performance of a lumbar puncture, and interpretation of CSF findings

Soft tissue and skin infections (cellulitis, impetigo, erysipelas, necrotizing fasciitis)

- Pathogens involved in most cellulitis, and appropriate therapy
- Know when to suspect necrotizing soft tissue infections, and subsequent role of surgery

Urinary tract infections (UTI)

- Signs and symptoms useful in distinguishing between upper and lower UTI
- Basic laboratory test used to diagnose UTI and its bacterial etiology
- Catheter associated UTI Asymptomatic bacteriuria
- Outline management of acute pyelonephritis
- Predisposing factors for recurrent UTI and pyelonephritis

Osteomyelitis and Septic Arthritis**Infectious Endocarditis including risk factors and prophylaxis****Tuberculosis**

- Basic epidemiology and risk (foreign born and aboriginal)
- Understand primary versus reactivated TB
- Risk factors for reactivation or re-infection of tuberculosis
- Role of skin testing and management of "converted" or positive Mantoux test

Viral hepatitis

- Epidemiology, Risk factors for, natural history of viral hepatitis
- Signs and symptoms of acute hepatitis, and acute liver failure
- HAV, and HBV vaccines and existing therapy or a subset of patients

Sepsis including intra-abdominal sepsis**HIV infection and AIDS****Adult Immunizations****Clinical Skills (see clinical skills section)**

- Management of Community acquired pneumonia
- History taking for sexual, drug, and parenterally transmitted disease risk

Antibiotic Management of Community Acquired Pneumonia: Adults

Summary of the Alberta Clinical Practice Guideline, March 2002

- Decision to Hospitalize**
- Up to 80% of patients with CAP are treated as out-patients
 - For patients who require admission to hospital, calculation of Pneumonia Severity of Illness score (see reverse) is recommended to guide determination of site of care
 - Patient's recent antibiotic history is important. Previous beta-lactam and macrolide therapy are risk factors for penicillin resistant *S. pneumoniae*. Previous ciprofloxacin therapy is a risk factor for quinolone resistant *S. pneumoniae*

- General Management**
- Analgesics/antipyretics for control of pain/fever
 - Ensure adequate hydration
 - Oxygen therapy is indicated for hypoxemia
 - Patients with pleural effusions complicating pneumonia should be referred
 - Pleural empyema should be drained
 - Chest physiotherapy is controversial

- Antibiotics**
- Empiric therapy is recommended for all patients with physical findings of pneumonia and new infiltrate on chest X-ray
 - Need to do post-therapy chest X-ray

		Out-Patient	
		No Comorbid Factors¹	
Agent	Dose	Comments	
Azithromycin* Clarithromycin Doxycycline Erythromycin	OR 500 mg PO 1st day then 250 mg PO daily OR 250 to 500 mg PO bid OR 200 mg PO 1st day then 100 mg PO daily OR 500 mg qid	* Avoid azithromycin if there is a history of chills/rigors	
		Comorbid Factors¹	
Azithromycin* Clarithromycin Doxycycline	OR 500 mg PO 1st day then 250 mg PO daily OR 250 to 500 mg PO bid OR 200 mg PO 1st day then 100 mg PO daily	* Avoid azithromycin if there is a history of chills/rigors	
		Failure of 1st Line Agents²	
Gatifloxacin** Levofloxacin** Moxifloxacin** [Cefuroximeaxetil PLUS Erythromycin]	OR 400 mg PO daily OR 500 mg PO daily OR 400 mg PO daily OR 500 mg PO bid OR 500 mg PO qid	** Ensure no previous ciprofloxacin use. May be a risk factor for quinolone resistance	
		In-Patient	
		No Comorbid Factors¹	
Azithromycin* Clarithromycin Doxycycline	OR 500 mg PO 1st day then 250 mg PO daily OR 500 mg PO bid OR 200 mg PO 1st day then 100 mg PO daily	* Avoid azithromycin if there is a history of chills/rigors	
		Comorbid Factors¹	
Gatifloxacin** Levofloxacin** Moxifloxacin** [Cefuroximeaxetil PLUS Macrolide***]	OR 400 mg PO daily OR 500 mg PO daily OR 400 mg PO daily OR 750 mg PO daily	** Ensure no previous ciprofloxacin use. May be a risk factor for quinolone resistance *** Macrolide: azithromycin, clarithromycin, or erythromycin	
		Severe³	
[Cefotaxime/ceftriaxone PLUS Macrolide***] Alternative⁴ [Cefotaxime/ceftriaxone PLUS Quinolone****] Cephalosporin Allergy Quinolone**** PLUS Another antibiotic (clindamycin, macrolide, vancomycin)	1 g IV q8h/1 g IV daily See dosages above 1 g IV q8h/1 g IV daily See dosages above	*** Macrolide: azithromycin, clarithromycin, or erythromycin **** Quinolone: gatifloxacin, levofloxacin, moxifloxacin	

Notes:

1. Comorbid factors include: asthma, lung cancer, COPD, diabetes, alcoholism, chronic renal or liver failure, CHF, chronic corticosteroid use, malnutrition or acute weight loss, recent hospitalization (<3 months), HIV, smoking.
2. Failure of therapy = hemodynamic compromise or clinical deterioration after 72 hrs antibiotic therapy or no improvement after completion of antibiotic therapy.
3. Severe: PaO₂ <60 mmHg; respiratory rate >30/minute; sepsis with end organ dysfunction; extra pulmonary septic complications; cavitation; multilobar involvement.
4. The standard of care is a beta-lactam PLUS a macrolide. This combination should be effective but clinical data is lacking. Quinolone monotherapy is not adequate in severe pneumonia

For complete guideline refer to the Alberta Medical Association Website: www.albertadoctors.org



Administered by the
Alberta Medical Association

Pneumonia

Judging the severity of Community acquired pneumonia.

T Marrie 2001

There are a number of scoring systems that have been used to aid the clinician in deciding on the severity of community-acquired pneumonia. A number of the factors are intuitively obvious and include age – the older the individual the more likely the adverse outcome. Men have a worse prognosis of pneumonia than women do, and residents of a nursing home is also associated with a worse outcome. There are five comorbid illnesses – active neoplastic disease, liver disease, congestive heart failure, cerebrovascular disease, and renal disease- that are poor prognostic factors in patients with pneumonia. On physical examination the following factors have been found to indicate a poor prognosis. These include altered mental status, respiratory rate >30/min., systolic blood pressure of <90 mm of mercury, a temperature of <35°C or >40°C, and a pulse rate of 125 or more beats per minute. The following laboratory and radiographic findings indicate a poor prognosis. These are arterial pH < 7.35; blood urea and nitrogen > 11 mmol/l; serum sodium <130 mmol/l; blood glucose >14 mmol/l; hematocrit <30%; PO₂ <60 mm of mercury; and pleural effusion on chest x-ray.

Fine MJ, et al. A prediction rule to identify low risk patients with community-acquired pneumonia. NEJM 1997; 336: 243-50

Influenza

How to discriminate between a cold and Influenza

Symptom	Cold	Influenza
Fever over 38 C	Rare	Usual High fever of sudden onset, lasts 3-4 days
Headache	Rare	Usual, can be severe
Fatigue and weakness	Sometimes/mild	Usual, often severe, often early onset can last 2-3 weeks.
Body aches	Rare	Common
Runny/stuffy nose	Common	Common
Sneezing	Common	Sometimes
Sore throat	Common	Common
Chest discomfort, cough	Sometimes, mild to moderate	Usual, can be severe
Complications	Sinusitis, otitis	Pneumonia, respiratory failure, death

Central Nervous system infections

Aseptic Meningitis versus encephalitis

The distinction between aseptic meningitis and encephalitis is clinical and sometimes indistinct. The important distinguishing issue is whether there is normal brain function. Patients with meningitis may be uncomfortable, lethargic, or distracted by headache, but their cerebral function remains normal. In encephalitis, however, abnormalities in brain function are common, including altered mental status, motor or sensory deficits, and speech or movement disorders. Seizures and postictal states can be seen with meningitis alone and should not be construed as definitive evidence of encephalitis.

Aseptic meningitis occurring during the summer or fall is most likely caused by enteroviruses (Coxsackie, echovirus, poliovirus), while mumps is the leading cause in the winter or spring. Viral encephalitis, which develops in the summer or fall, is often due to arboviruses (including eastern and western equine and St

Louis encephalitis viruses), and in the winter or spring is usually secondary childhood such as measles, mumps, and varicella-zoster virus. Herpes simplex virus types 1 and 2 occur sporadically throughout the year, and cause either a life threatening encephalitis (HSV-1) or a self-limited meningitis (HSV-2). HIV infection can cause either syndrome and occurs throughout the year.

The clinical presentation of aseptic meningitis is generally nonspecific, with fever, headache, nausea and vomiting occasionally accompanied by photophobia and nuchal rigidity. Physical examination typically reveals signs of meningeal irritation. There are usually no diagnostic findings unless there are abnormalities strongly suggestive of a specific virus (such as swollen parotid glands with mumps).

Encephalitis can have a similar presentation, usually combined with an altered mental status ranging from subtle deficits to complete unresponsiveness. However, meningeal symptoms (photophobia and nuchal rigidity) may be absent with a pure encephalitis, as opposed to a meningoencephalitis. Seizures are common and focal neurologic abnormalities can occur, including hemiparesis, cranial nerve palsies, and exaggerated deep tendon and/or pathologic reflexes. HSV-1 has a particular affinity for brain tissue in the medial temporal and inferior frontal lobes. This focal involvement may produce the characteristic findings of bizarre behavior, olfactory hallucinations, and aphasia. The cerebrospinal fluid findings with aseptic meningitis and meningoencephalitis are generally indistinguishable (although there may be few, if any CSF abnormalities with a pure encephalitis): Red cells are usually absent; their presence in the appropriate setting suggests HSV-1 infection.

These findings are generally quite different from those associated with bacterial meningitis, which include a higher white count with neutrophil predominance, a higher protein concentration, and frequently a low glucose concentration

Consider CSF PCR for HSV, which is the most rapid and specific test available. The demonstration of focality by electroencephalography or MR imaging suggests HSV-1, but CSF PCR is more sensitive.

Dexamethasone in adults with bacterial meningitis

Dexamethasone appears to be a safe and beneficial *adjunctive* therapy (to antibiotics) in the treatment of moderate-to-severe acute bacterial meningitis caused by *S. pneumoniae*. A 10 mg dose should be administered intravenously just before or with the first dose of antibiotics in adults who present with suspected bacterial meningitis *without signs of systemic sepsis*, and should be continued for 4 days in those with documented pneumococcal meningitis, and discontinued if another microbiological cause of meningitis is found (1).

1. De Gans J et al NEJM 2002;347: 1549-56

Soft tissue and skin infections

S. Houston 2001

Cellulitis is very common. It is usually due to *Staphylococcus aureus* or Group A streptococcus (*S. pyogenes*). Gram-negative organisms are very uncommon in the absence of specific risk factors such as ischemic or necrotic tissue in diabetics or pressure ulcers, or unusual exposure related to trauma e.g. fresh water. The typical pace of clinical resolution often takes 48 hours or more before obvious “retreating” of the cellulitis margins occur, especially in elderly patients with preexisting lower limb problems such as venous stasis. A common error is to interpret this slower response as treatment failure, and to inappropriately change the antibiotic regimen to another (sometimes more costly or toxic) antibiotic.

Occasionally it can be difficult to distinguish cellulitis from venous thrombosis and the two conditions may coexist.

Necrotizing fasciitis, a medical emergency, is typically characterized by prominent or severe pain, prominent systemic features of sepsis and usually, rapid clinical progression.

Urinary tract infections (UTI)

The risk of bacteruria increases with the duration of catheterization, and it is virtually 100% with long-term catheters. An indwelling urinary catheter does confer a significant risk of serious urinary tract infection. Long-term antimicrobial prophylaxis will promote the development of more resistant organisms and is not known to improve outcome. Regular changing of indwelling catheters also does not improve outcome. If the patient develops systemic symptoms or signs of infection, or local signs and symptoms suggestive of UTI, alternative diagnoses should be ruled out by examination and appropriate investigations. If symptomatic UTI appears to be the likely diagnosis, urine C&S is indicated at that time (along with blood cultures if clinically indicated) to guide antimicrobial therapy.

Culture of urine, when the patient is not symptomatic, is not warranted.

Warren JW Nosocomial urinary tract infections. In Mandell, Douglas and Bennett. Principles and practice of infectious diseases.

Tuberculosis

Tuberculosis testing

Prior Bacille Calmette **Guerin** (BCG) can complicate interpretation of the tuberculin skin test. In general, a positive tuberculin reaction should not be attributed to BCG if vaccination was remote in time, if the diameter of induration is large, or if the likelihood of exposure to TB was high.

1. Menzies R, Am Rev Respir Dis 1992;145:621-5.

Viral hepatitis

S. Houston 2001

Hepatitis C is the most common and important cause of chronic hepatitis in Canada and the most common reason for liver transplantation in Edmonton. Intravenous drug use is by far the most common risk of infection. In the Edmonton area, up to 90% of IV drug users will be Hepatitis C positive. The risk of sexual transmission is variable but low in the absence of co-factors such as HIV co-infection: about zero to 4.4% among heterosexual partners of hepatitis C-infected individuals. Gay men with many sexual partners, in whom a high risk of sexually transmitted pathogens would be expected, have had a prevalence of hepatitis C which is marginally increased at most. (2) The risk of transfusion-related infection has been very low since blood donor screening was implemented in 1990.

About 85% of people who test seropositive for hepatitis C have active infection, whereas about 15% appear to have cleared the virus.

The long-term outcome of hepatitis C infection is incompletely understood primarily because a specific test has been available only since 1990 and the incubation period of disease due to hepatitis C is typically very long. Two studies involving 17 and 18 years of follow-up after transfusion-acquired infection showed a difference in overall mortality compared to a matched population. One large study showed a mortality difference mainly limited to subgroups determined by early age at diagnosis, presence of cirrhosis and increased alcohol consumption. However, most patients with hepatitis C infection show some degree of inflammation on liver biopsy.

Treatment for hepatitis C is evolving rapidly. Treatment response varies substantially depending on virus genotype and viral load. However, present therapies eliminate the virus in only a minority of patients. Sustained remission following 48 weeks of interferon therapy alone would be expected in $\leq 20\%$ of patients. A combination of interferon and ribavirin can lead to sustained remission in approximately 40%. (1) Treatment probably reduces the risk of serious sequelae of hepatitis C.

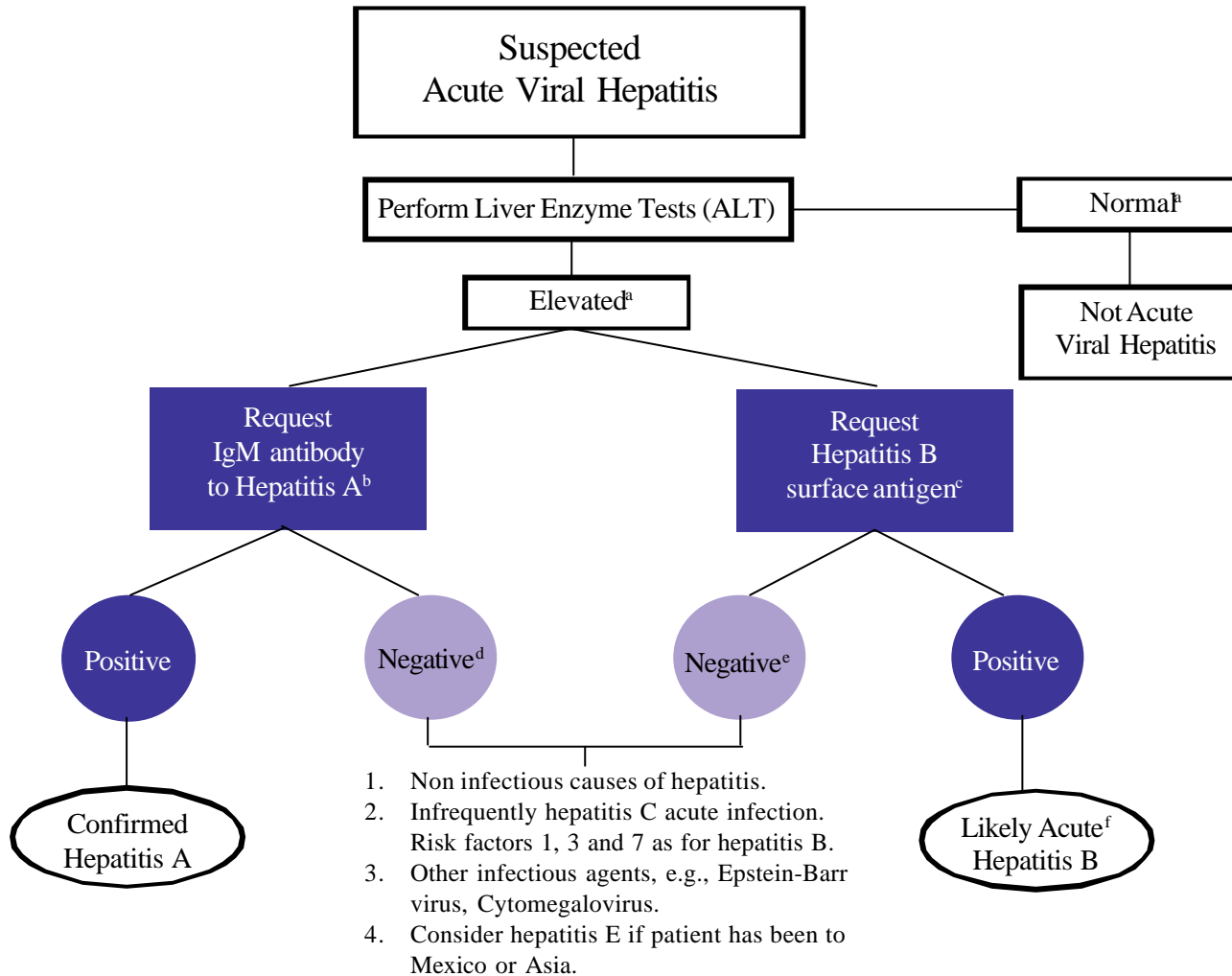
References

1. Poynard T, Marcellin P, Lee S. Lancet 1998;352:1426-32.
2. CDC. MMWR 1998;47(RR-19):1-39.
3. Niederau C et al. Hepatology 1998;1687-95.

Acute Viral Hepatitis



Administered by the Alberta Medical Association



- a. • Usually $\geq X5$ upper limit of normal in acute viral hepatitis.
- At the upper limit or mildly elevated.
 - Consider common non-viral causes, e.g., medication, alcohol; **OR**
 - Patient may be in the acute prodromol phase of viral hepatitis

Consider retesting ALT 2 to 3 days later when values will be significantly higher in acute viral hepatitis. Also consider requesting hepatitis serology at this point if indicated by the clinical history.

- b. If hepatitis A alone is being considered, request only anti-HAV IgM.
- c. If hepatitis B alone is being considered, request only HBsAg.
- d. May be negative in early infection. Repeat test if sample collected within 5 to 7 days of onset of symptoms.
- e. Consider requesting IgM antibody to hepatitis B core antigen **ONLY** if early “window period” is strongly suspected.
- f. Retest at 6 months to exclude chronic hepatitis B infection.

Risk Factors for Hepatitis A

1. Travel
2. Family & daycare contact
3. Poor hygienic circumstances

Risk Factors for Hepatitis B

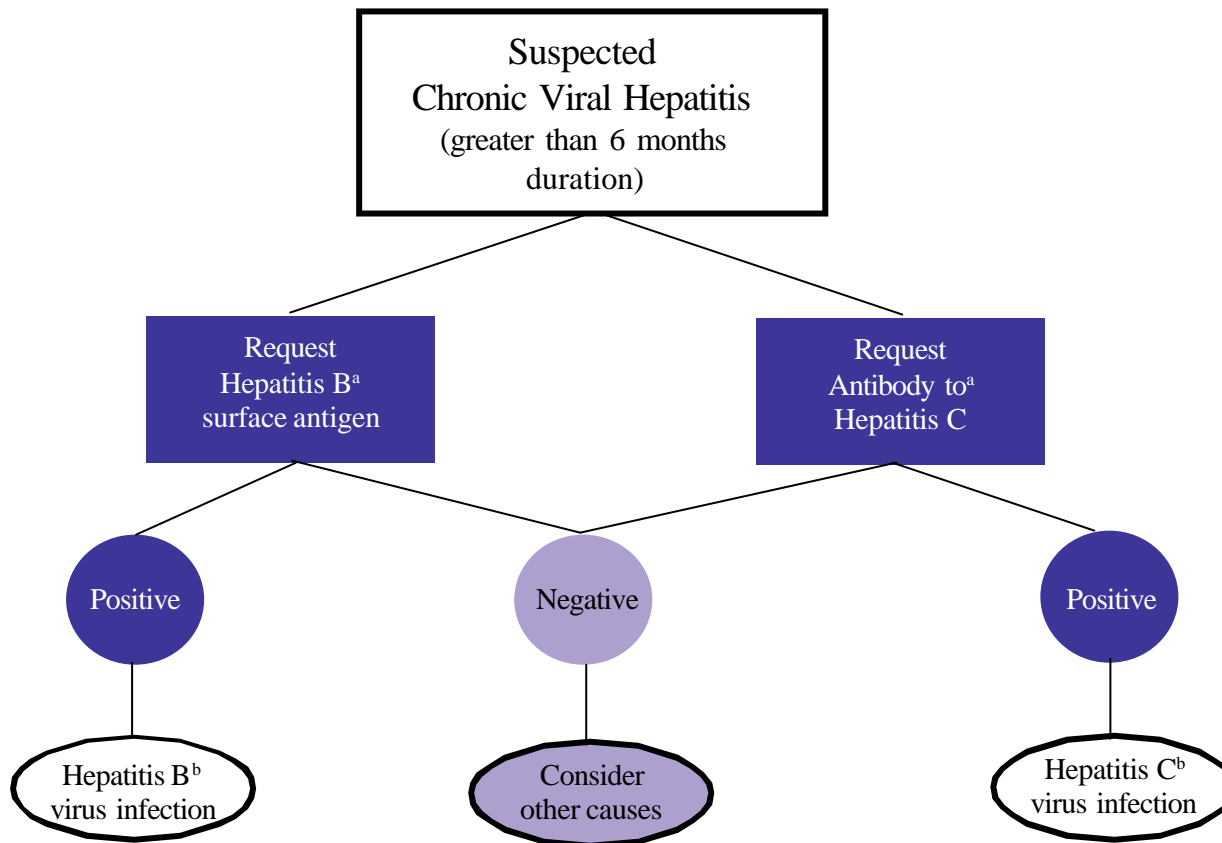
- | | |
|---|--|
| 1. Injection drug use | 5. Renal dialysis |
| 2. Sexual transmission | 6. Immigration from endemic region |
| 3. Percutaneous/per mucosal exposure, e.g., Health Care Providers | 7. Blood transfusions & blood products |
| 4. Perinatal transmission | 8. Close family contact |

March 1997

Chronic Viral Hepatitis



Administered by the Alberta Medical Association



- a. If hepatitis B or C is suspected, such as after receipt of a letter of notification by the Red Cross, then request HBsAg or anti-HCV as indicated.
- b. Further tests may be required to determine extent of liver inflammation and cirrhosis.

March 1997

Risk Factors for Hepatitis B

1. Injection drug use
2. Sexual transmission
3. Percutaneous/per mucosal exposure, e.g., Health Care Providers
4. Perinatal transmission
5. Renal dialysis
6. Immigration from endemic region
7. Blood transfusions & blood products
8. Close family contact

Risk Factors for Hepatitis C

1. Injection drug use
2. Percutaneous exposure, e.g., tattooing and needle stick exposure
3. Blood transfusions & blood products

Pathophysiology

The pathophysiology of HIV infection, with CD4 cell depletion, is well understood. Populations of CD4 lymphocytes are in a state of constant flux, and are in constant struggle with the rapidly reproducing virus. A large pool of activated infected CD4 cells continuously produce new HIV virions. Their half-life is several days. A smaller pool of latently infected CD4 cells (half life of about 6 months) can become “activated” and produce virions under situations of immune stimulation. Other CD4 cell types include activated uninfected cells, and long-lived non-activated, non-infected cells and memory cells. Although the immune system is quite efficient at clearing HIV, enough virions remain to survive, mutate, and multiply.

Both HIV infection and acquired immune deficiency syndrome (AIDS) are now reportable diseases under public health legislation in all provinces and territories, but anonymous testers are excluded. There is no jurisdiction where prenatal HIV testing is mandatory; however, in some jurisdictions women are informed that HIV testing is routine and given the option to decline (the “opt-out” approach).

Pre-test and post-test counseling should be carried out. Giving patients information about HIV risks and testing rather than asking intrusive questions can also be a useful way to begin the discussion. Guidelines for HIV testing are available through the Canadian Medical Association.

Steben M, et al: Counseling guidelines for HIV testing. CMAJ 1995. www.cma.ca/cpgs%2Df/hiv/index.htm.

Test Counseling

Pre-test counseling informs patients about:

- Their risk for HIV
- Ways to decrease risky behaviours
- The risks and benefits of the test
- The accuracy of positive and negative test results (over 99% sensitive and specific)
- The seroconversion “window period” for HIV antibody tests to become positive (98% within three months of infection)
- The confidentiality of test results

Obtain informed consent

Post-test counseling:

Provides an opportunity to reinforce all of the above information, carried out in person, especially if the test is positive.

Clinical presentation of acute HIV infection

Only a minority of HIV-infected patients is identified during an acute seroconversion illness, although when high-risk patients are followed prospectively, a large proportion of them have a clinical illness at the time of seroconversion. Fever is the most common feature, rash may occur in more than half, and lymphadenopathy, pharyngitis or oral lesions are relatively common. Aseptic meningitis can also occur. Thrombocytopenia is common and mild transaminitis may occur.

It is important to recognize this illness because 1) it will resolve spontaneously and the opportunity for counseling and treatment will be missed if it is not diagnosed. 2) Patients with a clinically apparent acute seroconversion illness may have more rapid disease progression than those with asymptomatic infection, and they may benefit from early or immediate antiretroviral therapy. Incidentally, these patients characteristically have very high HIV viral loads and may be particularly infectious, for example through sexual contact, during the seroconversion illness. PCR is now the test of choice.

HIV and Pregnancy

Vertical transmission from women with HIV to their newborns is 25% to 30% without intervention, but as low as 1% with aggressive treatment in pregnancy. The mainstay of perinatal prevention is highly active antiretroviral therapy (HAART) during pregnancy, during delivery, and for the newborn. An additional decrease in risk may be achieved with elective cesarean section for women who do not have an optimal response to HAART. All women with HIV should be discouraged from breast-feeding, which also transmits the virus.

Treatment of chronic HIV

In the developed world, the 3-year survival for those taking HAART is > 95%, and many have been living with HIV for more than 15 years. Although very high viral loads correlate with poor prognosis, the best correlation for treatment initiation is the CD4 count. There is substantial evidence to support initiating HAART when the CD4 count is < 200 cells/mm³, or when a person has AIDS or symptomatic HIV. Prior to this stage, the optimal time to begin antiretroviral therapy is debated, and decision to treat patients with CD4 counts between 200-350 should also factor in viral loads > 55,000 copies/ml, rate of CD4 count decline, adherence issues, potential drug interactions and adverse drug reactions.

Once started, HAART should be considered a lifelong intervention. The therapeutic goals are to durably suppress viral load, preserve immune function, and improve longevity and quality of life. Response to treatment can be followed with viral load determinations, with a goal of complete HIV suppression (undetectable viral load).

Viral load and CD4 counts should be monitored every three months for those on medication, and more frequently when treatment changes are made. Continued monitoring is important for determining ongoing effectiveness of therapy, and for making changes to treatment when resistance develops or adherence is poor. HIV-infected patients not on HAART with CD4 counts > 350 cells/mm³ should be assessed every three to six months. Many clinicians would consider starting therapy for viral loads > 55,000 copies/ml.

Virologic failure is defined as the failure to achieve a viral load <50 copies/mL or any sustained return of the viral load to >400 copies/mL. Viral resistance is driven by viral replication. Undetectable HIV viral loads are linked with the least risk of viral resistance. Amongst a number of factors, the single most significant factor determining viral resistance is the inappropriate use of ARV therapies.

There are currently four different classes of antiretroviral available:

- nucleoside reverse transcriptase inhibitors (NRTIs);
- non-nucleoside reverse transcriptase inhibitors;
- protease inhibitors; and
- a fusion inhibitor.

Antiretroviral therapies combining drugs from different classes prolong survival and significantly reduce the risk of opportunistic diseases. A minimum of three compounds from at least 2 classes taken together is considered standard care, and the most potent and durable combinations include drugs from at least two classes. Antiretroviral combinations need to be individualized to suit the acceptable dosing and side-effect profile of the specific patient. Monotherapies or double drug regimens promote viral resistance and should not be used. Commonly used combinations include 2 NRTIs, and a PI, or 2NRTIs and a NNRTI.

Class	Available agents
NRTI (nucleoside reverse transcriptase inhibitors)	Zidovudine (ZDV) 3TC ddI ddC d4T Abacavir
NNRTI (non-nucleoside reverse transcriptase inhibitors)	Nevirapine Delaviridine Efavirenz
PI (protease inhibitors)	Indinavir Saquinavir Ritonavir Nelfinavir Amprenavir
Fusion Inhibitor	

Immunization

Varicella Vaccine

The National advisory committee on immunization recommends vaccination for all health persons ≥ 12 months of age who are susceptible to disease, especially if:

- Health care workers
- Childcare workers
- Individuals in close contact with pregnant women

The vaccine offers 70-90% protection against varicella of any severity and 95% protection against severe varicella for at least 7-10 years. Avoid pregnancy for at least 1 month post-vaccination.

Influenza vaccination (annual)

- High risk: Adults with chronic cardiac, or pulmonary disorders, diabetes, cancer, immunodeficiency (including HIV), immunosuppression (e.g. renal transplants), chronic renal disease, Residents of nursing homes or long-term care facilities, or people aged ≥ 65
- Health care workers and other personnel with continuous direct care contact with people at high risk
- People who provide essential community services

The vaccine provides protection starting 14 days post-vaccination, and lasts up to 6 months. It is safe to administer during pregnancy.

Meningococcus vaccine

- Persons 2-24 years of age in CHA region
- Asplenic patients
- Individuals traveling to areas of endemicity (e.g. sub-Saharan Sahel region of Africa)

Vaccine takes about 14 days to become effective offers $> 90\%$ protection in individuals ≥ 2 years, lasts about 5 years, and is NOT contraindicated in pregnancy or breast-feeding

Pneumovax vaccine

Strongly recommended for high risk:

- Asplenia (traumatic, surgical, or congenital)
- Splenic dysfunction
- Sickle cell disease

Whenever possible, give the vaccine 10-14 days before splenectomy. Vaccine failure may occur in these groups.

Recommended:

- All persons ≥ 65 years
- All residents of long term care facilities
- Patients with chronic cardiac, pulmonary (excluding asthma), or renal diseases, diabetes, cirrhosis alcoholism, HIV infection, and other conditions associated with immunosuppression

The vaccine may be administered simultaneously with influenza, at a separate injection site.

Tetanus-diphthera vaccine

- Recommend booster every 10 years.

Hepatitis A vaccine

Recommendations include:

- Long term or frequent travelers to or residents of areas of endemicity
- Residents and staff of institutions for mentally handicapped
- Persons with underlying chronic liver disease (e.g. hepatitis B or C)
- Members of the armed forces or emergency relief workers
- Persons working with non-human primates

Hematuria: Major causes and investigation**Proteinuria: Major causes and investigation**

- **Nephrotic range**
- **Non-nephrotic range**

Electrolytes and acid-base balance

- **Anion and non-anion gap acidosis**
- List and classify major causes
- List signs and symptoms of severe acidemia
- Differentiate metabolic from respiratory acidosis on basis of biochemical tests
- Basic “cause-dependent” management
- **Calculate Plasma Osmolar gap and list major causes**

- **Hyperkalemia: causes and basic management**
- **Hypokalemia: causes and basic management**
- **Hyponatremia: causes and basic management**

Acute renal failure

- **Recognize conditions and factors which may pre-dispose to renal failure**
- **Distinguish among pre-renal, renal or post-renal causes**
- **List and interpret laboratory and imaging investigations in diagnosis**
- **List indications for emergency renal dialysis in patients with acute renal failure**

Chronic renal failure

- **Knowledge of common causes of chronic renal failure**
- List common drugs, which are contraindicated in people with chronic renal failure
- Discuss dosage adjustment for commonly used medications in patients with renal failure
- List common medical consequences of chronic renal failure (uremia)
- Indications and relative contraindications for renal dialysis and transplantation

Interpretation of creatinine and microscopic urinalysis

Hematuria

The prevalence of hematuria ranges from < 1% for < 40 years to 13% for older individuals. Proteinuria is less common. Both may indicate serious pathology in kidneys or urinary tract. It is important to distinguish red urine (rifampin, dyes, rhabdomyolysis with myoglobinuria) from hematuria, transient from persistent hematuria, and glomerular from extra-glomerular hematuria.

Causes may include:

Transient

Urinary tract infections	Exercise-induced
Calculi	Trauma
Endometriosis	Thromboembolism (renal vein thrombosis)

Persistent

Extraglomerular renal
Tumors
Tubulointerstitial disease (PCK, Pyelonephritis)
Vascular (papillary necrosis, Sickle cell disease)
Collecting system (Tumors or stones)
Glomerular
Isolated (IgA nephropathy, Thin membrane disease)
Post-infectious (Post-streptococcal)
Systemic (Vasculitis, SLE)

Measurement

Reagent “dipstick” strips cannot differentiate between Red blood cells, free hemoglobin or myoglobin, so a positive dipstick should prompt urinalysis microscopic examination. Make sure the presence of RBCs or hemoglobin is not from menses or lesions of reproductive tract. Note that urinary tract infections can cause microscopic hematuria. After these considerations, try to confirm if there are glomerular sources.

Interpretation

The history and physical examination should look for evidence of systemic inflammatory disease, edema, hypertension, or purpura suggestive of glomerular disease. Exposure to carcinogens, a history of smoking, or cyclophosphamide suggests uro-epithelial malignancy.

Order microscopic urinalysis (use a clean catch AM sample if possible-urine is more concentrated and acidic and RBC will last longer). The presence of ≥ 3 RBC /high-powered field in at least 2 of 3 samples constitutes hematuria. The presence of red cell casts or urinary protein ≥ 3 gm/l ($\geq 1+$) suggest glomerular sources as well. Order serum Creatinine, and urea (and 24-hour determinations of protein if proteinuria is present). If there is no indication of glomerular origin, do ultrasonography and urine cytology. If the patient is of African origin, check hemoglobin electrophoresis. An IVP and/or cystoscopy may be of additional value if there is increased risk for uro-epithelial tumors.

A number of individuals with asymptomatic microscopic hematuria will have normal renal function, and no proteinuria, calculi, or malignancy. Failure to confirm hematuria on repeat testing is reassuring, and repeated testing over a year thereafter is probably sufficient to rule out occult disease. If the hematuria persists, likely diagnoses include IgA nephropathy, thin membrane disease, hypercalcuria or hyperuricosuria. The prognosis of asymptomatic hematuria is generally favorable, and it is reasonable to follow these patients with annual urinalysis and serum creatinine, provided they remain asymptomatic, have no gross hematuria or significant proteinuria.

Proteinuria in excess of 500mg/24 hours is of renal origin. The possible mechanisms include tubular dysfunction, glomerular permeability alterations, and overflow proteinuria (ie light chain overproduction). Proteinuria in excess of 3 g/24hrs, which is dipstick positive (to exclude primarily light chains), is of glomerular origin.

Proteinuria is defined as the excretion of protein in the urine in excess of the normal limit of 0.15 g/day. Proteinuria is often discovered on dipstick analysis. Very alkaline or concentrated urine may result in an overestimate by dipstick method of the daily excretion of protein, so that it will not correspond to the 24-hour collection value. Generally, 1+ means 3g/L or greater. Standard dipsticks lack the sensitivity to detect microalbuminuria (30-300 mg albumin/day) so it is not sufficient for screening diabetic patients who may have incipient diabetic nephropathy.

Asymptomatic proteinuria is often benign transient phenomena, but in a minority of patients may be the first sign of significant renal or systematic disease. The history, physical examination and simple lab testing can usually distinguish between functional, glomerular, tubular or overflow causes. Functional proteinuria occurs with exercise or fever, or orthostatic changes. The latter may be suspected if an “AM urine” (after emptying bladder before going to bed) has relatively little protein compared to a sample obtained later on in the day.

If proteinuria persists in 2 or more samples the amount should be quantified with a 24-hour collection. If it is confirmed to be above 150 mg/day, obtain Creatinine, urea, fasting glucose, and urinalysis to detect infection or hematuria, and an ultrasound. History taking should focus on potential systemic illnesses such as diabetes, multiple myeloma, connective tissue diseases, chronic infection, primary renal disease, malignancy and vasculitis. Blood pressure and volume status should be checked. Proteinuria > 3.5 gm and mostly albumin on electrophoresis suggests nephrotic syndrome. Lesser amounts of protein may be tubular or glomerular. “Overflow” proteinuria, such as seen with light chains of multiple myeloma, tends to be a single peak. Protein of tubular origin tends to consist of multiple globulins and therefore has multiple peaks.

Unless contraindications exist, patients with proteinuria and diabetes should be treated with ACE inhibitors or angiotensin II receptor blockers.

Reference: House AA and Cattran DC. Nephrology: 2.Evaluation of asymptomatic hematuria and proteinuria in adult primary care. CMAJ 2002; 166: 348-353

Electrolytes and acid-base balance

To calculate the Anion Gap = $([Na] + [K]) - ([Cl] + [HCO_3])$ Normal ≤ 16

To calculate Plasma Osmolar gap:

- Osmolar gap = Measured - Calculated Osmolality
- Calculated osmolality (mmol/L) = $2[Serum Na] + Serum urea + serum glucose$
- Normal calculated osmolality is 270-290 mmol/L
- Normal osmolar gap is less than 10 mmol/L (mosm/kg H₂O)
- Causes of increased plasma Osmolar gap:

Causes of increased plasma Osmolar gap: With Anion Gap Metabolic Acidosis

- Ethylene glycol ingestion
- Methanol ingestion
- Formaldehyde ingestion
- End stage renal disease with GFR < 10 and without regular dialysis
- Diabetic ketoacidosis
- Alcoholic ketoacidosis (rarely contributes more than 10 to the gap)
- Lactic acidosis

Causes of increased plasma Osmolar gap: Without Metabolic acidosis

- Isopropyl alcohol ingestion
- Mannitol use

Electrolytes: Hyperkalemia

True hyperkalemia is a potentially life threatening condition. Rule out pseudo-hyperkalemia from hemolyzed lab specimens or excess cells in the sample (e.g. major thrombocytosis), treat urgently if real, and look for causes. Except in patients with established significant renal failure, the 12-lead ECG is helpful in determining the presence of true hyperkalemia. A plasma (instead of serum) potassium assay can also be done if excess cells are thought to be the cause.

Differential diagnosis

Increased intake (seldom an independent cause)

Redistribution

Insulin deficiency

Metabolic acidosis (only if anion gap is normal (RTA type 4))

Cell lysis (rhabdomyolysis, trauma-crush syndromes, hemolysis, tumor lysis)

Reduced Urinary Excretion

Acute or chronic renal failure

Decreased secretion from hypoaldosteronism, adrenal insufficiency, RTA type 4, or drugs (NSAIDs, ACEIs, potassium sparing diuretics)

Treatment involves cardiac protection (calcium chloride), potassium shift into cells (insulin and glucose/B-mimetics/bicarbonate), removal (potassium binding resins, dialysis), modifying or removing exacerbating factors (dietary indiscretion, ACE-inhibitors, potassium-sparing agents), and addressing underlying causes.

In chronic renal failure patients, hyperkalemia unresponsive to conservative management is an indication for starting regular dialysis.

Electrolytes: Hypokalemia

Hyperkalemia is most often discovered on routine analysis of serum electrolytes or ECG analysis. Symptoms usually develop much later when depletion is quite severe. It is most commonly caused by renal loss.

Differential diagnosis

Decreased intake (e.g. anorexia nervosa)

Redistribution (e.g. during treatment)

Increased loss

Renal losses

Diuretics, hyperaldosteronism, adrenal hyperplasia, Cushing's, Renal tubular acidosis

Gastrointestinal losses

Vomiting and diarrhea (including bulimia and laxative abuse)

Electrolytes: Hypomagnesemia

Hypomagnesemia is common in seriously ill patients. The serum measurement for magnesium is not a very reliable estimate of intracellular stores.

Differential diagnosis

Severe malnutrition

Gastrointestinal loss from diarrhea, malabsorption, short gut syndrome, acute pancreatitis

Renal loss from

Diuretics (loop, thiazide)

Hypercalcemia

Volume expansion

Tubular dysfunction (alcohol abuse, aminoglycosides, amphotericin, cisplatin, cyclosporin, primary causes, acute tubular necrosis in diuretic phase)

GI and renal loss may be discriminated by measuring urinary magnesium excretion

Cellular uptake of magnesium is slow so replacement requires sustained supplementation. Potassium sparing agents may help to reduce diuretic associated hypomagnesemia.

Electrolytes: Hyponatremia

Hyponatremia is often discovered incidentally because of the frequent measurement of serum electrolytes. It may mean water gain, sodium depletion or often both. Identifying the main process is important because it will affect choice of therapy and rate of correction.

Pseudohyponatremia may exist, and has been attributed to hyperglycemia, hyperlipidemia, and hyperproteinemia. The false decrement in sodium value from hyperlipidemia and hyperproteinemia does not occur if the laboratories use sodium selective electrodes on undiluted plasma. Most laboratories in Alberta use this method. For hyperglycemia, correction can be made by calculating for excess serum glucose (the measured sodium value drops by 3 mmol/L for every 10 mmol/L increase in serum glucose above 5 mmol/L).

Differential diagnosis

Water gain: Primary polydipsia or Iatrogenic

Decreased excretion of water: SIADH or solute deficiency

Sodium depletion

 Renal Loss (diuretics, mineralocorticoid deficiency, tubular defects)

 Gastrointestinal loss

 Third space and skin losses

Edema states (cirrhosis, CHF, nephritic syndrome)

Electrolytes: Hypernatremia

Hypernatremia is almost always caused by water loss rather than by sodium gain. It is particularly common in elderly (especially cognitively impaired) patients who may lack the ability to respond to thirst by drinking water. Decreased water intake is therefore commonest, but increased loss (renal, GI, Insensible) may be important in given situations. Sodium gain is rare but may be seen with the use of hypertonic solutions or with primary hyperaldosteronism. Diuretic agents (especially the thiazides) are more likely to produce hyponatremia.

What is Acute Renal Failure?

Acute renal failure is defined loosely as rapidly deteriorating renal function over the course of days (rapidly progressive) to a few months. It usually presents with ↓ urine outputs (esp if in hospital), edema, and symptoms of azotemia/uremia. When faced with a patient with renal failure (ie ↑ creatinine), it is vitally important to determine the temporal sequence, as the distinction between acute and chronic renal failure has implications diagnostically, therapeutically, and prognostically.

What Numbers are Important?

When assessing renal function, most people initially use serum creatinine as a surrogate for GFR. However, while convenient, it is not overly accurate:

- At high GFR, most of creatinine is cleared by filtration (95%) and a small portion is actively secreted by tubular cells (5%). As GFR falls, this proportion becomes 50%-50% and so serum creatinine (and creatinine clearance calculated from 24hr collections) over-estimates true GFR.
- Because of compensation by remaining nephrons and the wide range of “normal” creatinine values, one can lose almost 50% of their renal function before the serum creatinine becomes “abnormal”.

Thus, when the serum creatinine begins to rise, significant damage has already occurred. Conversely, at the opposite end of the spectrum, a rise from 800 umol to 1600 umol, which might seem drastic, signifies a loss of only about 6.25% of total renal function. A general rule of thumb is that creatinine doubles for every time you lose half of your remaining renal function.

What About Oliguric vs Non-oliguric Renal Failure?

ARF can present either oliguric (<400ml urine per day) or non-oliguric (more than 400ml per day). This is not a clue to etiology (although abrupt, complete anuria usually signifies significant obstruction) but rather a reflection of severity. However, non-oliguric ARF can still be severe. Consider that glomerular ultrafiltration is ~ 180 liters daily. If only 1% of nephrons are filtering, up to 1.8 liters of urine can be produced daily (it will be poor quality urine, but urine nonetheless). Similarly expressed, a GFR of 1 ml/min is potentially able to produce 1.44 liters of urine daily.

Because non-oliguric ARF probably represents milder disease, the prognosis for recovery is better. However, there is no difference in terms of renal or overall survival if an oliguric pt is converted to a non-oliguric pt with high dose loop diuretics. It does make the pt easier to manage and their lives more tolerable as fluid restriction is not as big of a concern.

Factors that help to Separate Acute from Chronic Renal Failure

- Previous creatinine values (or urinalysis, urea, etc): anything that points towards renal dysfunction is helpful, and the older the data the better. You must therefore call the lab, call the family doctor, look in old charts to find old values. This is the most definitive means but often these values do not exist.
- Hemoglobin: as renal mass declines, erythropoietin production falls and RBC production also declines. However, it takes about 3 months for the drop in Hgb to be noticeable. If the patient is anemic and no other obvious cause is found, it points to a chronic renal process.
- Renal ultrasound: another way of helping differentiate. As disease progresses, the kidneys become scarred and shrunken (in most diseases, but diabetes, amyloidosis, and HIV nephropathy can be

exceptions). If renal ultrasound shows small kidneys, the process was chronic and has the kidneys are irreversibly scarred.

- Renal biopsy: most definitive way to determine if process is chronic (ie irreversible) or acute. However, is usually not performed for this reason as decision can usually be made before biopsy required.

What Causes Acute Renal Failure?

You must have a means of categorizing this HUGE list of causes of acute renal failure if you are to remember them all (or most anyways). The most popular method is to classify according to anatomic site of injury.

Pre-Renal Causes

Anything that affects renal function before the renal arteries; usually resulting in impaired perfusion to the kidneys. ie dehydration/hypovolemia, hepatorenal syndrome, CHF, nephrotic syndrome.

Intrinsic Renal Causes

Everything that affects the renal arteries to the renal veins and all structures in between. Anatomic Sub-categorization helps.

Vascular--renal artery stenosis, large vessel vasculitis (Takayasu's, PAN), microangiopathy (HUS), renal vein thrombosis

Glomerular--any proliferative glomerulonephritis (particularly those causing crescentic or RPGN..lupus, Goodpastures, Wegeners, post-infectious, IgA, cryoglobulinemia et al).

Tubulointerstitial--includes ATN (drugs or ischemic), acute interstitial nephritis, tubular obstruction (heme pigments, myeloma proteins, drug crystals such as acyclovir toxicity)

Post-Renal Causes

Obstructive problems of the ureters (stones, retroperitoneal fibrosis, tumor) or urethra (stones, prostate, congenital valves).

How to Differentiate Between Them?

History

The differential diagnosis of ARF will be different for hospitalized pts vs outpatients. A very common cause for both is drug-induced ATN, so take a detailed med list. Ask esp. about over the counter NSAIDs and COX-2 inhibitors ('arthritis pills' or 'painkillers'). Other common culprits include ACEi, antibiotics (esp penicillin/cephalosporins, aminoglycosides, and vancomycin), contrast agents, and diuretics. Ask about anti-cholinergic meds that could cause retention. With in-patients, the cause is drugs until proven otherwise. Outpatients are more likely to have retention (esp males) or intrinsic renal problems.

Physical

The most important aspect is assessing volume status, to help separate pre-renal from others. Also look for signs of vasculitis, prostatism, or bladder distention, CHF etc. Inserting a Foley catheter helps to rule out urinary retention at the level of the prostate.

Laboratory

Urinalysis is a simple but very useful test. In both pre-renal and post-renal conditions, the kidneys themselves are normal (at least in the early stages of the process). Therefore, the urine produced, although diminished in amount, should be normal. However, if the process has been present for some time or is severe, intrinsic renal damage may occur and the urine could become more concerning.

Pre-renal

No protein, no Hgb, no casts, specific gravity high $FE_{Na} < 1\%$ Urine Na $< 10mEq/l$
Creatinine may fluctuate daily

Post-renal

No protein, no Hgb, no casts

Renal

Variable proteinuria, hematuria, casts
May see signs of tubular dysfunction (acidosis, hypokalemia, glycosuria) in interstitial nephritis.
 $FE_{Na} > 1\%$ and urine Na $> 20mEq/l$ Urine specific grav. or osmolarity same as plasma
Distinctly unusual to have normal urinalysis Usually steady 50-100 $\mu mol/l$ \uparrow in creatinine daily

The commonest dilemma is in differentiating pre-renal failure from ATN. Determining the urine Na, osmolarity, and FENa can usually sort this out. Other tests that are routinely useful include renal ultrasound (to rule out obstruction, although lack of hydronephrosis does not absolutely rule out obstruction as acute obstruction $< 24hrs$, or retroperitoneal fibrosis will not show as hydronephrosis).

Management

By far the most common cause of ARF in hospital will be nephrotoxic ATN, so most of the following will pertain to that entity. Treatment of pre-renal and post-renal ARF involves prompt correction of the abnormality (eg. fluids, TURPs, or improved heart function). If this does not immediately improve renal function, then the insult has likely progressed to ATN anyways. Treatment of GNs and interstitial nephritis are talks unto themselves.

Although a wide variety of agents can cause ATN, there are common predisposing risk factors for all. These include:

Pre-existing renal dysfunction Elderly age (as normal GFR \downarrow by 1ml/min/yr after age 40yrs)
Diabetes mellitus Dehydration
Multiple nephrotoxic hits (ACEi plus NSAIDs very common and deadly)

Prevention:

The best treatment is prevention. Avoid using nephrotoxins in these high-risk patients. If unavoidable (eg angiograms) then prophylaxis is mandatory. No consensus exists on what is most effective, but ensuring good hydrated throughout is essential. Furosemide and mannitol may offer benefits but data is unconvincing (Solomon *et al*, NEJM 1994 331:1416). N-acetyl cysteine has also become popular despite the weak evidence for its efficacy (Tepel *et al*, NEJM 2000 343:180).

Treatment:

Once ATN is established, little can be done except to deal with the complications through fluid management and dialysis if necessary, and importantly, prevent further insults (ie no nephrotoxic drugs, watch for drugs requiring dose adjustments, and avoid hypotension esp during dialysis). Using loop diuretics to convert oliguric to non-oliguric renal failure makes fluid management easier and everyone happier, but renal outcome will not change. Most healthy pts will recover from ATN within 7-21 days after the insults are stopped (Myers *et al*, NEJM 1986 314:96), but ATN may persist until up to 8 weeks post-insult. Usually serum creatinine falls enough to stop dialysis but often remains 100-200 μmol above previous baseline.

Management of the patient with pre-end stage (ESRF) chronic renal failure (CRF) is probably the most common situation encountered by the generalist. The incidence of end-stage renal disease (ESRD) is also increasing at an annual rate of about 7% per year, with almost 1 in a 1000 Canadians requiring dialysis at present.

What is Chronic Renal Failure?

Two aspects are important; the duration of the dysfunction, and the rapidity of the decline. Both of these address, indirectly, the potential of reversibility. When this potential is minimal, we call this chronic (irreversible) renal failure.

Diabetes accounts for about 40% of all new cases of end-stage renal disease (ESRD), and is the most common cause. Hypertension is the second most common cause. Chronic glomerulonephritis, chronic interstitial nephritis, and polycystic kidney disease are important but much less common causes. Renal failure from PCKD takes years to develop and is almost always coupled with hypertension and renal failure, and is associated with mild proteinuria.

Despite multiple possible etiologies, in most cases CRF progresses in a predictable fashion with a common histologic endpoint of glomerular sclerosis and tubulointerstitial fibrosis, and thus it is often impossible to establish a firm diagnosis once end-stage has been reached, even through biopsy.

In many cases the inciting event was acute (eg glomerulonephritis) and was unrecognized or, despite treatment, resulted in a sub-optimal response. In many cases the event is irreversible and progressive (eg hereditary nephritis). Even in those cases in which the disease is no longer “active” (ie post-obstructive nephropathy), progression to ESRF often occurs. Anything that accentuates intraglomerular hypertension or atherosclerotic damage will accelerate the whole process. This includes:

- Systemic hypertension: a risk factor for progression regardless of underlying disease.
- Proteinuria: once felt merely to be a marker of dysfunction, it now appears that the filtered protein (but unlikely albumin) is toxic to the tubules and likely contributes to the damage. Increased proteinuria associated with poorer prognosis for renal survival. Experimental evidence shows that increased protein intake leads to hyperfiltration and accelerated renal decline, but studies in humans fail to conclusively show that restricting protein is beneficial in preventing loss of renal function
- Hyperlipidemia: evidence suggests that this accelerates renal injury, probably in similar fashion to coronary atherosclerosis (many people believe that coronary atherosclerosis and glomerulosclerosis are similar processes in different vascular beds).

Thus, treatment to prevent progression is limited and non-specific. The best advice is to prevent further injury (ie from radiocontrast dye procedures, NSAIDs, antibiotics etc), control hypertension aggressively and control hyperlipidemia. Also, there is accumulating data to suggest that **ACE inhibition** slows progression in non-diabetic nephropathy of a variety of causes, so this **should be your first choice in antihypertensives**.

What are the Specific Concerns with CRF and loss of nephron mass?

Anemia

The exact site of kidney Epo production is unknown, but as functional renal mass declines, Epo production (and RBC production) declines leading to anemia, which is present in the majority of patients with ESRF. The anemia is normocytic with decreased reticulocyte production. There is no good correlation between GFR and Hgb levels. Some patients can get quite anemic with GFR~30-40ml/min, while others have a

GFR of almost zero and have a normal Hgb. All renal patients should be subjected to a good anemia workup when it is first discovered, as many patients will have a co-existent reason for anemia. Iron deficiency, (occult GI blood loss and poor absorption) and chronic inflammation/infection are common. Most patients are treated with recombinant Epo (Eprex®) when anemic. There is evidence that keeping Hgb levels above 110g/l is beneficial, but the exact targets are debatable. The usual dose of Eprex is 100-200units/kg/week, given SC/IV in divided doses 2-3 times weekly. This is then modified up or down depending on response, which should occur in 1-3 months. Most patients also require supplemental iron. If patients can't tolerate (or afford) Epo, then transfusions or androgen injections (nandrolone decanoate, Deca-durabolin®) may be necessary.

Electrolytes/Acid-Base

Hyperkalemia

The most common problem encountered in this population of patients. Again, no good correlation between GFR and risk of hyperkalemia as many factors are active (intake, degree of tubulointerstitial damage, presence of RTA IV etc). Most patients with slowly progressive CRF can be managed until ESRF with dietary restriction to <60mEq daily and occasional K-binding resins (Kayexalate®).

Acidosis

The average intake ~ 50-100mEq of H⁺ daily (from protein), which the kidney must excrete. Can usually compensate until GFR reaches ~ 40ml/min., then acidosis occurs (anion gap acidosis) Patients with chronic tubulointerstitial disease may develop a non-anion gap acidosis earlier in the course of their disease. It is usually not severe, with HCO₃⁻ usually no less than 15mEq/l. Many people suggest treatment with NaHCO₃ as needed when HCO₃⁻ drops below 20mEq/l.

Calcium-Phosphate Balance

The kidney involved in Ca-Phosphate balance in 2 ways:

- Major route of inorganic phosphate elimination (derived from protein ingestion). As GFR decreases, phosphate retention occurs.
- Major site of conversion of 25 hydroxyvitamin D₃ [25-(OH)D₃] to 1,25-dihydroxyvitamin D₃ [1,25-(OH)₂D₃], the active form of vitamin D₃. As renal mass decreases, vitamin D₃ production falls

Most likely with increased phosphate and decreased Vit D₃, serum calcium levels fall, stimulating parathyroid hormone (PTH) production, and leading to a release of calcium from bones. The price paid for normalization of serum Ca is a persistently elevated PTH level (secondary hyperparathyroidism), bone resorption/demineralization, tendon ruptures, and metastatic calcifications in skin and vessels. This is termed osteitis fibrosa and is one of three types of bone diseases seen in renal failure collectively termed **renal osteodystrophy**. Treatment is aimed at prevention and is accomplished in three ways:

- Dietary phosphate restriction.
- Use of phosphate binders (Ca-carbonate, Ca-acetate, or aluminum containing binders like Amphogel®) with meals to limit phosphate absorption in gut.
- Use of oral or IV vitamin D₃ to increase gut absorption of Ca and suppress PTH production.

Goals of therapy are to maintain a normal serum calcium, phosphate under 2.00 mmol/l and PTH 2-3x normal levels. There is a risk of increased calcification if calcium-phosphate product >5.4mmol/l. Some pts may require parathyroidectomy for resistant hyperparathyroidism, but this is uncommon.

Uremic Complications

Renal failure affects practically every body system, so symptoms attributable to uremia can be seen everywhere. It should be noted that the “uremic toxin(s)” is unknown. It is unlikely urea, but it seems that accumulation of these toxins occurs in concert with urea accumulation, so urea is used as the surrogate marker. Common or important uremic complications:

- General malaise, weakness
- Neurological: decreased memory and concentration, asterixis, distal polyneuropathy, confusion, seizures, coma
- Pleural effusions.
- Pericarditis
- Platelet dysfunction/bleeding, anemia
- Nausea, vomiting, gastritis
- Pruritus, frost, sallow

The presence of any of these is usually a good indication that the patient requires renal replacement therapy (RRT), either dialysis or transplantation.

When Should These Patients Start Dialysis?

In the acute setting, dialysis is initiated if any of the following are present (“AEIOU”):

- Acidosis: Severe, and resistant to bicarbonate therapy.
- Electrolyte disturbances: eg: hyperkalemia resistant to binding resins and dietary discretion.
- Intoxications such as lithium, methanol or digoxin
- Fluid Overload unresponsive to diuretics and fluid restriction
- Uremic symptoms such as pericarditis, seizures or encephalopathy

In the chronic setting, as well, most nephrologists prefer to initiate dialysis while the patient is still feeling well and is well nourished, and before these life-threatening complications occur. However, the exact timing can be difficult, as patients are often resistant to starting dialysis, and many patients are started too late. Some general indications for dialysis in CRF include:

- Malnutrition: renal failure progresses, appetite and protein intake fall and patients become malnourished. Consider dialysis if albumin $<35\text{g/l}$.
- $\text{GFR} < 10\text{ml/min}$ or creatinine clearance $<15\text{ml/min}$.
- Serum creatinine $>1000\ \mu\text{mol/l}$ or urea $>30\text{mmol/l}$. However, often by the time the creatinine rises to 1000 or more other indications have been met, and the need can be sooner in some patients, so don't use numbers alone.
- If any acute indications are present.

Metabolic acidosis is rarely a reason to initiate chronic dialysis, because the acidosis of renal failure is not from overproduction but is from under excretion of daily acid production, and is therefore not severe (usually 12-15 mMol/L).

It is better to start too soon than too late. Early referral for education and access planning (ie at least 1 year before anticipated need for dialysis) is recommended and appreciated.

Interpretation of creatinine and microscopic urinalysis

Even small increases in serum creatinine may represent real and significant changes in GFR. It is advisable to calculate the estimated creatinine clearance or actually measure a 24 hr creatinine clearance to get a better estimate of the actual renal function. Automated Cockcroft calculators (part of Medcalc) may be down loaded to PDAs for free from the site: <http://medcalc.med-ia.net>

Severe muscle injury associated with crush injuries, and rhabdomyolysis associated with drugs, malignant hyperthermia, or repetitive seizures may lead to increases in creatinine, but this is not expected after uncomplicated surgery and anesthesia. Uncomplicated urinary tract infections are not associated with elevation of serum creatinine.

Stroke and Transient ischemic attacks

- List and classify causes of new-onset focal neurological deficits
- Use clinical examination to differentiate among the major categories of new-onset focal neurological deficits
- Determine on clinical grounds the anatomical site of the neurological lesion
- Basic investigations to determine the cause of a new-onset focal neurological deficit
- Initial management of stroke and transient ischemic attacks
- List acute complications of stroke and their management

Seizure Disorders

- Use clinical examination to differentiate a seizure from syncope and other conditions
- List and classify major causes of seizure
- Definition of status epilepticus
- Acute emergency management including drugs

Parkinson's Disease

- Clinical presentation: See clinical skills section
- **Basic management**

Demyelinating disease

- Multiple sclerosis diagnostic criteria
- Guillain-Barre Syndrome and Subacute combined degeneration: diagnostic findings and clinical presentation

Mononeuropathies

- **Carpal tunnel syndrome**
- Clinical examination to detect carpal tunnel syndrome
- Commonest causes or precipitants of carpal tunnel syndrome (nerve compression, diabetes, occupational, hypothyroidism, pregnancy, rheumatoid arthritis, acromegaly)
- List and interpret investigations used in the diagnosis of carpal tunnel syndrome
- Outline general management

Coma

- *See clinical skills section*
- Elicit and interpret information from the history and physical to distinguish among the major cause of coma
- List basic investigations and management

Headache

Clinical Skills (see clinical skills section)

- Cranial Nerve examination (2,3,4,6)
- Upper versus lower motor neuron lesions

Stroke and Transient Ischemic attacks

Stroke

Approximately 85% of all strokes are ischemic. 50% of these are secondary to large vessel atherosclerosis, or intracranial small vessel (lacunar) disease, about 20% are cardiac thrombo-embolic, and 20-30% are of undetermined source. About 15% of strokes are hemorrhagic.

Factors that can worsen the course of a stroke include fever, hyperglycemia, hypertension or hypotension, and hypoxia.

Transient ischemic attacks

Definition: Focal neurological deficit of sudden onset lasting less than 24 hours (most last < 20 minutes). In the first year following a TIA the average (untreated) risk of stroke is 12 %.

Amaurosis fugax is the painless sudden onset of vision loss in one eye. It is often described as a curtain being pulled over eye. Ask your patient to cover each eye in turn to confirm mono-ocular loss. Amaurosis fugax has a more favorable prognosis than other kinds of TIA.

Refer patients for emergency assessment if

1. Multiple TIAs occur over a short period of time (crecendo). This often indicates high grade carotid stenosis
2. A TIA occurs in the context of recent head trauma*
3. A TIA occurs in a patient already taking anticoagulants*

*Need to rule out bleeding

Lacunar Stroke Syndromes

Lacunar infarctions involve the deep white matter in the regions of the internal capsule, pons, or thalamus. They are the result of lipohyalinosis of small penetrating arteriolar branches of the anterior, middle, and posterior cerebral arteries, such as the lenticulostriate arterioles. Lipohyalinosis is characterized by blockage of the arteriole by medial hypertrophy and a lipid-fibrinoid mixture. Hypertension is a common pre-association with lacunar stroke syndromes. Discrete clinical presentations exist:

1. Pure motor stroke: lesion in pons or internal capsule. Although speech may be slurred, there is no aphasia, and if a R-sided lesion no apraxia or other parietal lobe findings
2. Pure sensory stroke: lesion in the thalamus
3. Clumsy hand-dysarthria stroke: lesion in the anterior limb of internal capsule or rarely the pons. Slurred speech and clumsiness and mild weakness in one arm
4. Crural (leg) paresis and ataxia: lesion in pons or internal capsule or cerebellar peduncle.

Parkinson Disease (PD) Contributions from R. Camicioli

The prevalence and incidence of PD is age dependent with an incidence ranging from 2/1000 at ages 60-69 years to 20/1000 in people older than age 80 years, with ranges varying between studies. The diagnosis is based on the presence of at least two of:

- rest tremor (in most but not all)
- bradykinesia
- rigidity

There are guidelines for the treatment of mild parkinsonism (1). A young patient with parkinson's disease, if suffering from functional difficulties, should be treated with a dopamine agonist, not levodopa/carbidopa. The rationale for using an agonist in younger patients (under 70 years of age) is that it may minimize the development of wearing off and dyskinesias in the long term. In older patients this risk is not as great and the risk of side effects from dopamine agonists, (including confusion, psychosis, hypotension) increases with age. The decision is not an easy one in a young patient though, because sleepiness and sudden episodes of sleep may occur with treatment. Patients need to be warned of these potentially serious side-effects. (2)

There are several dopamine agonists available: bromocriptine, pergolide, pramipexole, and ropinerole. There are efficacy data that are summarized in the guidelines cited above.

References:

1. J. M. Miyasaki, W. Martin, O. Suchowersky, W. J. Weiner, and A. E. Lang Neurology 2002 58: 11-17)
2. Excessive Daytime Sleepiness and Sudden-Onset Sleep in Parkinson Disease. A Survey by the Canadian Movement Disorders Group Douglas E. Hobson; Anthony E. Lang; W. R. Wayne Martin; Ajmal Razmy; Jean Rivest; Jonathan Fleming JAMA. 2002;287:455-463)

Mononeuropathies

Carpal Tunnel Syndrome

The diagnosis of carpal tunnel syndrome can often be made on the basis of the clinical presentation alone. A negative Tinel's sign does not rule out the condition, and in the absence of other neurological findings, further investigations are not required. The best course of action would be night-time wrist splints.

Headache

Causes may include:

Migraine

 With aura (classic migraine)

 Without aura (common migraine)

Tension-type headache and headache with medication overuse

Cluster headache

Headache associated with vascular disorders

 Subarachnoid hemorrhage

 Temporal arteritis

 Venous thrombosis (e.g. cavernous venous thrombosis)

 Intracranial hematoma (Subdural, Epidural)

 Severe arterial hypertension

Headache associated with non-vascular intracranial disorders

 Elevated CSF pressure (Intracranial mass lesion or Hydrocephalus)

 Intracranial infection (Meningitis, Abscess, Sinusitis)

Systemic viral infections

Psychological disorders

Medication use (nitrates) or withdrawal (analgesic)

Usually, primary headache disorders do not arise from grave underlying diseases. Migraine headaches are likely under diagnosed. A comprehensive patient history is the single most important diagnostic "test" in evaluating patients with headaches. The most useful diagnostic information can be by asking **POUN**Ding headache (**p**ulsatile, **o**ne day, **u**nilateral, **n**ausea, **d**isturbing):

- (1) Are the headaches pulsating?
- (2) Without medication, do the headaches last between 4 and 72 hours?
- (3) Are the headaches typically unilateral?
- (4) Do you become nauseated?
- (5) Do the headaches disturb your daily activities?

If the patient answers yes to 3 or more questions, it is very likely that the patient has migraine headaches by the International Headache Society (IHS) classification. Conversely, if a patient responds yes to two or fewer questions, it is unlikely that they have migraines.

The patient's statement "this is the worst headache of my life" does not efficiently diagnose a subarachnoid hemorrhage, while its absence provides similarly little information.

Typically, patients with primary headache disorders have a normal neurologic examination. Fewer than 1% of patients with acute headaches and normal neurologic examinations will have significant abnormalities on CT scan or MRI.

Patients with episodic migraine headaches can often be managed with over-the-counter nonsteroidal anti-inflammatory agents or acetaminophen.

For many patients, additionally avoiding situations or foods that trigger their headaches may be sufficient. When these measures and medications begin to fail, ergotamine derivatives, and a new class of serotonin antagonists (5-HT₃ receptor antagonists [sumatriptan]) are all effective for acute treatment of migraine.

Prophylactic medications may be useful for patients with frequent disabling attacks. β -blockers have been the most well studied preventive drugs. NON-ISA Beta-blockers such as propranolol, metoprolol, and timolol, verapamil and tricyclic antidepressants may all be effective.

After 6 consecutive months of successful prevention, one can attempt to wean the patient from prophylactic medications and reassess whether further treatment is required.

Oncology and Palliative Care

Colorectal Cancer

Prostate Cancer

Breast Cancer

Lung Cancer

Clinical presentation, diagnosis and initial management of Oncological Emergencies and Urgencies:

- Spinal Cord compression
- Malignant hypercalcemia
- Impaired level of consciousness in a patient with malignant disease

Palliative Care TIPS

This is an excellent series of practical handouts that is produced by the Edmonton Regional Palliative Care Program (www.palliative.org)

Recommended reading includes:

- Cancer Nausea and Vomiting
- Constipation in the Cancer Patient
- Dyspnea
- Depression or Delirium
- Hydration
- Hypercalcemia of malignancy
- Pain Assessment
- Pain Management
- Commonly administered sub-cutaneous medications in palliative care

<http://www.palliative.org/PC/ClinicalInfo/PCareTips/PCareTipsIDX.html>



Administered by the Alberta Medical Association

Guideline for Use of PSA and Screening for Prostate Cancer

GOALS

- ◆ To provide guidance about appropriate use of prostate specific antigen (PSA) testing
- ◆ To help physicians and their patients make informed decisions about screening for prostate cancer in asymptomatic men of any age

RECOMMENDATIONS

- ◆ The appropriate use of PSA testing includes:
 - ◆ follow-up of a patient with prostate cancer
 - ◆ evaluation of a patient with symptoms of prostatism
 - ◆ evaluation of a patient with an abnormal digital rectal examination (DRE)
- ◆ PSA testing should be discussed with the following patient groups (see text):
 - ◆ those at higher risk for the development of prostate cancer
 - ◆ those who express a concern about the development of prostate cancer
- ◆ PSA testing is inappropriate in patients with a reduced life expectancy

- ◆ PSA testing detects prostate cancer at an earlier stage. However, this benefit is unproven as a routine screening test in asymptomatic, low risk males. Thus:
 - ◆ given the widespread use of PSA, men should be advised of its availability, reliability, and the potential risks and benefits of treatment
 - ◆ if proceeding with screening then both DRE and PSA should be performed

OVERVIEW OF THE EVIDENCE

BACKGROUND

According to the National Cancer Institute of Canada (1996), prostate cancer is the most frequent cancer and the second leading cause of death from cancer in men, exceeded only by lung cancer.¹ Prostate cancer accounts for 27% of all male cancers and 13% of male cancer-related deaths. While the incidence has increased significantly over the past 35 years, the mortality rate has increased only slightly. It is estimated that in 1996 there will have been 33,600 deaths from cancer in men of which 4,200 will be due to prostate cancer. The lifetime risk for developing prostate cancer is 12%.

The above recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making

Risk factors for prostate cancer include: age, race, diet, and family history. The risk of getting prostate cancer increases rapidly after age 50. The incidence of prostate cancer in men 75 years of age is thirty times greater than that in men 50 years of age.¹ A high intake of dietary fat also seems to be associated with a higher risk for developing cancer.² African-American men have a 30% greater incidence of prostate cancer compared with white men. There is an increased risk for the development of prostate cancer in men who have first degree relatives with the disease.

The reason for the dilemma in prostate cancer screening relates to the following two conflicting factors:

- 1) Not all prostate cancers are serious and clinically important. Most men will die with, rather than from, the disease. Autopsy studies report that more than 30% of all men over the age 50 have histologic evidence of prostate cancer, but only 3% will die from it. How we identify those requiring potentially curative therapy from those who can be safely followed without treatment remains to be elucidated.
- 2) Locally advanced or metastatic prostate cancer is very serious. It can cause premature death and painful suffering. Ten-year survival rates are as follows:
 - ◆ 75% when confined to prostate
 - ◆ 55% with regional extension, and
 - ◆ 15% with distant metastases.

USE OF PSA TESTING

Use of PSA testing PSA is a protein produced by both normal and cancerous prostate tissue. Elevated serum levels of PSA may identify the presence of cancerous and non-cancerous abnormalities of the prostate gland. 60–75% of men with prostate cancer will have elevated PSA levels.³ Mild elevations of PSA are commonly associated with benign prostatic disease. For a given individual there may be variations in PSA levels independent of disease.

Investigation and follow-up of a patient with prostate cancer

In patients with prostate cancer, serum PSA levels are often proportional to the clinical stage of the disease and the volume of prostate cancer found in the gland. Thus PSA may help predict the likelihood of discovering lymph-node or seminal-vesicle involvement.

Increasing PSA values after definitive radiotherapy or radical prostatectomy for localized prostate cancer can predict residual localized cancer or the development of metastases. Following the initiation of hormone therapy in metastatic disease, PSA values are useful in predicting response to therapy. The Alberta Uro-oncology group⁴ has produced recommendations on the use of PSA for follow up of patients with prostate cancer.

Evaluation of symptomatic patients

Benign prostatic hyperplasia (BPH) and prostate cancer are both common diseases in men as they age. Prostatism, a symptom of both conditions, warrants further investigation based on a number of factors which may include age and life expectancy of the patient. It remains unclear at this time whether BPH is associated with increased risk for prostate cancer. However, symptoms of BPH associated with urinary tract obstruction are similar to those of prostate cancer.

Various methods have been proposed to detect and diagnose cancer in men with BPH. It should be remembered that some men with BPH will have mildly elevated PSA levels. The most appropriate way to detect prostate cancer in these men is a combination of DRE and PSA. Transrectal ultrasound (TRUS) of the prostate is not useful as a screening test for prostate cancer. TRUS does provide an excellent means of guiding transrectal biopsies of the prostate.

Evaluation of a patient with an abnormal DRE

Digital rectal examination is easy to perform and is the traditional test to detect changes in the prostate gland. DRE is useful in detecting other colorectal disease. Suspicion arises when irregularities are found in the prostate gland. However, DRE has a limited sensitivity and specificity in the detection of prostate cancer.⁵ A suspicious DRE is an indication for serum PSA testing.

Evaluation of a patient with risk factors for prostate cancer

African-American men and men with first degree relatives diagnosed before the age of 70 have a higher risk than the general population. However there is no evidence to suggest that early detection efforts will provide more benefit to such individuals than to normal risk patients. One study revealed, however, that when presented with information about PSA testing, patients with risk factors show a greater interest in pursuing PSA screening than those with no risk factors.⁶

BENEFITS AND RISKS ASSOCIATED WITH SCREENING FOR PROSTATE CANCER

Unfortunately, prostate cancer does not lend itself well to screening for the following reasons:

- ◆ The natural history of the disease is poorly understood as it is not possible to predict reliably the biological potential of a given tumour in any single individual to progress to significant morbidity and mortality.
- ◆ There has been little or no impact of improvements in detection and treatment of prostate cancer on overall mortality of the disease. Mortality from prostate cancer has not significantly changed over the last 30 years.
- ◆ Screening tests with high sensitivity and specificity do not exist.
- ◆ It is not clear that the benefits outweigh the risks of screening for prostate cancer.

There is little evidence to suggest that patients who are screened have better health outcomes than those who are not screened. Some researchers suggest that early detection increases survival because men who are diagnosed with localized tumours and receive treatment have a greater chance of being cured than those with more advanced disease.^{7,8}

Others argue that some men with early stage prostate cancer have good outcomes with delayed or conservative treatment.⁹ No controlled studies have ever addressed the question of health benefits associated with screening for prostate cancer. Trials are underway in Canada, the United States and Europe, but the results will not be available for more than a decade.

In assessing the potential benefits of any screening test the problems of false positive results, the potential harm of testing and the risks of treatment must also be evaluated. For example, in men over 50 the positive predictive value of a PSA >4.0 & g/L is only 31%. Two out of three men with abnormal results on routine screening will not have cancer. Before cancer is ruled out, these men must undergo additional testing such as repeat PSA testing, ultrasonography and biopsy. Anxiety and its consequent health problems may become a significant issue for patients with a positive PSA and a negative work up.

Risks associated with radical prostatectomy and/or radiotherapy include incontinence, urethral stricture, bowel damage, erectile dysfunction and complications arising from anaesthesia and major surgery, including death.⁸ The treatment of patients with clinically insignificant cancer would lead to unnecessary morbidity.

Notwithstanding these issues, however, definitive treatment of prostate cancer is potentially curative if the disease is confined to the prostate gland when diagnosed. Although the evidence is not conclusive, there are data that suggest a greater proportion of cancers being detected by screening are organ confined and that the majority of these tumours may be clinically significant. Whether or not this will result in an improvement in the survival rates in prostate cancer remains to be seen.¹⁰

ADVICE TO PATIENTS

The Alberta Clinical Practice Guidelines Program supports the right of the patient to make an informed decision about his health care options. Patient decisions will vary as a result of individual fear of cancer (which may be associated with family history), the potential impact of iatrogenic complications on the quality of life, and individual interpretation of the evidence relative to health benefits.

Patient education is paramount in decisions surrounding prostate cancer. It is important for asymptomatic men to be aware of the consequences of their decisions to be screened or not screened.

Before deciding on testing, the patient should consider the procedures that would necessarily follow an abnormal result and whether or not he would want to be treated if cancer were diagnosed. "In particular, men with a life expectancy of less than 10 years should be advised that screening is unlikely to be helpful and may worsen the quality of their lives."⁸

If a patient wishes to proceed with screening after discussion of the risks and benefits associated with diagnosis and treatment of prostate cancer, then DRE combined with PSA is indicated. The positive predictive value of the two tests is better than each alone.^{11,12}

DEFINITIONS

Sensitivity: the proportion of men with prostate cancer who have a positive test result.

Specificity: the proportion of men without prostate cancer who have a negative test result.

Positive predictive value: the proportion of men with a positive test result who have prostate cancer.

SELECTED REFERENCES

1. National Cancer Institute of Canada. Canadian Cancer Statistics. Canadian Cancer Statistics. 1996:57.
2. Pienta K, Esper PS. Risk factors for prostate cancer. *Annals of Internal Medicine* 1993; 118:793-803.
3. Garnick MB. Prostate cancer: screening, diagnosis, and management. *Annals of Internal Medicine* 1993;118:804-818.
4. Alberta Cancer Board. Recommendations for the use of PSA in the follow-up of patients with prostate cancer.
5. Guinan P, Bush I, Ray V. The accuracy of the rectal examination in the diagnosis of prostatic carcinoma. *New England Journal of Medicine* 1993;16:425.
6. Wolf A, Nasser J, Wolf A, Schorling J. The impact of informed consent on patient interest in prostate specific antigen screening. *Archives of Internal Medicine* June 24 1996;156:1333- 1336.
7. Catalona WJ, Smith DS, Tatloff TW. Measurement of prostate specific antigens in serum as a screening test for prostate cancer. *New England Journal of Medicine*, 1991;324:1156-1161.
8. Woolf SH. Screening for prostate cancer with prostate specific antigen – an examination of the evidence. *New England Journal of Medicine* 1995;333:1401-1405.
9. Chodak GW, Thisted RA, Gerber GS. Results of conservative management of clinically localized prostate cancer. *New England Journal of Medicine* 1994;330:242-248.

10. Dugan A, Bostwick D, Myers R. The definition and preoperative prediction of clinically insignificant prostate cancer. *JAMA* 1996;275:288-294.
11. Cooner W, Mosley B, Rutherford C. Prostate cancer detection in a clinical urological practice by ultra-sonography, digital rectal examination and prostate specific antigen. *Journal of Urology* 1990;143:1146-1152.
12. Babaian R. The relationship of prostate specific antigen to digital rectal examination and transrectal ultrasonography. *Cancer* 1991; 9:1195.

THE ALBERTA CLINICAL PRACTICE GUIDELINES PROGRAM

The Alberta Clinical Practice Guidelines Program promotes appropriate, effective and quality medical care in Alberta by supporting the use of clinical practice guidelines. The program is administered by the Alberta Medical Association under the direction of a multi-stakeholder steering committee.

Alberta Clinical Practice Guidelines Steering Committee

Alberta Health and Wellness
Alberta Medical Association
College of Family Physicians of Canada,
Alberta Chapter
College of Physicians and Surgeons of Alberta
Physicians at Large
Public Representative
Regional Health Authorities
University of Alberta
University of Calgary
Alberta Association of Registered Nurses
Alberta College of Pharmacists

TO PROVIDE FEEDBACK

The Alberta CPG Working Group on Prostate Cancer Screening is a multidisciplinary team composed of family physicians, urologists, a medical oncologist, medical biochemist, radiologist, pathologist, registered nurse, public representative and CME educator. The Working Group encourages your feedback. The scientific review supporting this guideline is available upon request. If you need further information or if you have difficulty applying the guideline, please contact:

The Alberta Clinical Practice Guidelines Program
12230 – 106 Avenue NW
EDMONTON, AB T5N 3Z1
(780) 482-2626
or toll free 1-800-272-9680
Fax: (780) 482-5445



Administered by the Alberta Medical Association

Guideline for The Early Detection of Breast Cancer

This guideline has been developed by the Early Detection of Breast Cancer Working Group and is based on current scientific evidence. Due to the addition of important research related to breast screening, a regular review of this CPG will be undertaken.

SCOPE OF GUIDELINE

The recommendations in this guideline apply to asymptomatic women. **Any woman who has signs or symptoms suggestive of breast cancer needs appropriate evaluation, regardless of age.**

GOALS

- ◆ To provide guidance about the appropriate use of screening tools for breast cancer;
- ◆ To help physicians and patients make informed decisions about screening for breast cancer in asymptomatic women of all ages;
- ◆ To decrease mortality due to breast cancer.

EXCLUSIONS

The recommendations in this guideline do not apply to:

- ◆ Women with signs and symptoms suggesting breast cancer;
- ◆ Women with a history of breast cancer;
- ◆ Men.

DEFINITION OF SCREENING FOR BREAST CANCER

Breast cancer screening refers to the application of a procedure to asymptomatic women for the purpose of detecting unsuspected breast cancer at a stage when early intervention can affect the outcome.

The above recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making.

SCREENING PROCEDURES

Mammography, clinical breast examination and breast self-examination can be used as screening procedures.

RECOMMENDATIONS

General

- ◆ Women with a family history of early onset of breast cancer or multiple relatives with breast cancer may need special consideration. Some experts suggest that mammography screening among this population should commence five to ten years prior to the age of onset of breast cancer in their family member. Consideration may be given to referral to the Cancer Genetics Research Clinics. (*See Discussion of Mammography Recommendations and Appendix 1*).

Women aged 50 to 69

- ◆ Women aged 50 to 69 years should have a screening mammogram at least every two years.
- ◆ Annual mammography screening should be considered in circumstances of increased risk.

Women aged 40 to 49

- ◆ Women aged 40 to 49 should have the opportunity to access screening mammography. Physicians should discuss with patients, the benefits and risks of screening.
- ◆ There remains controversy regarding the degree of benefit of screening mammography in this age group. (*See Discussion*)
- ◆ If a woman chooses to participate in mammography screening, the recommended interval between screens in this age group is one year.

Women Over 70 Years

- ◆ The risk of breast cancer in this group is high.
- ◆ Mammography screening should be considered every two years taking into account individual patient health factors and preferences.

Women Under 40 Years

- ◆ Routine mammographic screening for women under 40 is not recommended.

Clinical Breast Examination and Breast Self Examination

- ◆ Clinical breast examination (CBE) and breast self examination (BSE) detect some breast cancers which are not evident on mammography. CBE and BSE should be seen as complementary examinations to mammography. (*For CBE See Appendix 2*)
- ◆ Primary care physicians should discuss breast self examination with all women by age 30.

Breast Implants

- ◆ Women with breast implants should be referred for diagnostic mammography at age appropriate intervals.

BACKGROUND

Epidemiology

Breast cancer is one of the most serious health concerns of Canadian women and is the most common form of cancer in women excluding non-melanoma skin cancer. Breast cancer accounts for 30% of all new cancer cases.^{1,2,3,4} Over 1,500 new cases of breast cancer were reported in Alberta in 1997⁵ and approximately 410 Alberta women die from this each year. Breast cancer accounts for nearly 21% of all cancer deaths in Alberta women.¹

Risk Factors

The lifetime risk for breast cancer is one in nine. The risk however, varies over a woman's lifetime. Table One reflects the age specific risk of breast cancer for women.⁵

Table One
Probability of Developing Breast Cancer in the Next Five Years, by Age, for Women Who Reside in Alberta and Currently Do Not Have Breast Cancer

Age	Probability
35	1/384
40	1/208
45	1/128
50	1/109
55	1/94
60	1/78
65	1/70
70	1/65

Increasing age, being born in North America and northwest Europe, and having two or more first degree relatives with a history of breast cancer are identified as the strongest risk factors.

There are many other identifiable risk factors, but few are amenable to change. It is estimated that up to 80% of women who develop breast cancer have no risk factors other than being female, and in a higher risk age group.⁶

Available evidence suggests that the effect of hormone replacement therapy (HRT) on the risk of breast cancer is small.⁷

DISCUSSION OF MAMMOGRAPHY RECOMMENDATIONS

A normal screening mammography does not rule out breast cancer in the presence of persistent palpable abnormalities. Further evaluation may still be required.

Women Aged 50 to 69 Years

Many studies have shown the efficacy of mammography screening for breast cancer for women aged 50 to 69 years. Regular mammographic screening in this age group is estimated to reduce mortality from breast carcinoma by approximately one third. Because additional benefit with annual screening has not been demonstrated,⁸ screening every two years is often recommended.

Women Aged 40 to 49 Years

In women aged 40 to 49, breast cancer is the single leading cause of death.^{3,4} Some of the reservations about making population-based recommendations for women in this age group, are based on limitations in the scientific evidence available to date. While there is emerging evidence of benefit from some combined analyses of the randomized trials, the benefit is smaller than in older women, and is of borderline statistical significance.^{9,10}

There has been a lot of debate in the literature regarding the reasons for the apparent decreased benefit of screening. Evidence to date suggests that screening mammography is less sensitive for women in their forties than for older women.¹¹ It has also been suggested that due to more rapid growth of tumours in this age group that the interval between screens in some studies has been too long to show a benefit.¹² Data suggests that annual mammography in this age group will be required¹³ in order to detect breast cancer at its earliest stages and achieve a reduction in breast cancer mortality similar to that seen in older women.^{13,14} Finally, there may be statistically insufficient numbers of women in this age group included in the controlled trials to definitively show a benefit.¹⁵

Concerns have also been raised about the decreased positive predictive value of any of the three breast screening procedures in women in their forties when compared to older women. In other words, the probability that a younger woman would have a benign biopsy as a consequence of screening is higher than for older women.

Women Over 70 Years

The incidence of breast cancer increases with age, and therefore women over 70 years continue to be at high risk. Although no randomized clinical trials have specifically addressed the efficacy of screening in this age group, it should be considered in the context of individual health factors and personal preference.

Women Under 40 Years

Randomized controlled studies have not included women in this age group.¹⁶ Routine screening is not recommended.

Women With A Family History of Breast Cancer

Women with a strong family history of breast cancer should be advised of the availability of counselling and information provided by the Cancer Genetics Research Clinics. (*See Appendix 1 for referral criteria*)

Radiation Risk

The risk of mammographically-induced cancer is generally considered to be negligible. Some experts have expressed concern over the theoretical risk of radiation-induced breast cancers, especially among younger women. However, the studies which have raised this concern involved much higher levels of radiation than are found in present day mammography.^{17,18} The radiation dose delivered by mammography is lower than that of an ordinary chest X-ray.

FACTORS AFFECTING ACCEPTANCE OF SCREENING RECOMMENDATIONS

The strongest stimulus for a woman to participate in mammography screening is the recommendation from her physician. Studies indicate that many factors affect a woman's choice to participate in breast cancer screening. Adverse factors include age, i.e., younger (40-49) and older (70 plus) women; socioeconomically disadvantaged; limited contact with a physician; single marital status; unemployed and retired; country of birth and fewer years since immigration, i.e., Asia, South and Central America, Caribbean and Africa; lower educational attainment; and, rural residence.^{19,20,21} Physicians should ensure that all women who would benefit from screening be informed of its potential advantages.

SELECTED REFERENCES

1. National Cancer Institute, Canadian Cancer Statistics, 1997.
2. Statistics Canada. HEALTH REPORTS. Catalogue 82.003XPB.1997;9(1).
3. Gaudette LA, Silberger C, Altmayer CA et al. Trends in breast cancer incidence and mortality. HEALTH REPORTS. Statistics Canada, Catalogue 82.003-XPB. 1996;8(2):29-37.
4. Bondy M, Luskbader E, Halabi S, et al. Validation of a breast cancer risk assessment model in women with a positive family history. Journal of the National Cancer Institute 1994;86:620-25.

5. Bryant HE, Brasher PMA. Risks and probabilities of breast cancer: short term versus lifetime probabilities. *CMAJ* 1994;150(2):211-216.
6. Alberta Cancer Board. A Snapshot of Cancer in Alberta. 1996.
7. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52,705 women with breast cancer and 108,411 women without breast cancer. *Lancet* 1997; 350:1047-59
8. Tabar L, Faberberg G, Day N, et al. What is the optimum interval between mammographic screening examinations? An analysis based on the latest results of the Swedish two-county breast cancer screening trial. *International Journal of Cancer*, 1987; 55: 547-551.
9. Smart C, Hendrick R, Rutledge J, Smith R. Benefit of mammography screening in women ages 40 to 49. Current evidence from randomized controlled trials. *Cancer*, April 1995; 75(7): 1619-1626.
10. American Cancer Society. Workshop on Guidelines for Breast Cancer Detection. Chicago, March 1998.
11. Kerlikowske K, Grady D, Barclay J, et al. Effect of age, breast density, and family history on the sensitivity of first screening mammography. *JAMA*, July 1996; 276(1): 33-38.
12. Feig S. Determination of mammographic screening intervals with surrogate measures for women aged 40-49 years. *Radiology*, 1994; 193: 311-314.
13. Duffy S, Chen H, Tabar L, et al. Sojourn time, sensitivity and positive predictive value of mammography screening for breast cancer in women aged 40-49. *International Journal of Epidemiology*, 1996; 25(8): 1139-1145.
14. Tabar L, Fagerberg G, Chen H, et al. Tumour development histology and grade of breast cancers: prognosis and progression. *International Journal of Cancer*, 1996; 66: 413-419.
15. Kopans D, Halpern E, Hulka C. Statistical power in breast cancer screening trials and mortality reduction among women 40-49 years with particular emphasis on the national Breast Screening Study of Canada. *Cancer* 1994; 74: 1196-1203.
16. Liberman L, Dershaw D, Deutch B, et al. Screening mammography: value in women 35 to 39 years old. *American Journal of Roentology*, July 1993; 161: 53-56.
17. Mettler F, Upton A, Kelsey C, et al. Benefits versus risks from mammography: a critical reassessment. *Cancer*, March 1996; 77(5): 903-909.
18. NIH Consensus Statement. Breast Cancer Screening of Women Ages 40-49. January 1997; 15(1).
19. Dodd GD. Screening for Breast Cancer. *CANCER SUPPLEMENT*. August 1, 1993; 72(3):1038-1042
20. Maxwell CJ, Parboosingh J, Kozak JF, Desjardins-Denault SD. Factors Important in Promoting Mammography Screening among Canadian Women. *Canadian Journal of Public Health*, Sept 1997; 88(5):346-350.
21. Gentleman JF, Lee J. Who Doesn't get a Mammogram? Statistics Canada, Catalogue 82-003-XPB, Health Reports, Summer 1997. Vol.9, No.1
22. Bates B. A Guide to Physical Examination and History Taking. (pp317-328) 4th Edition, 1987 J.B. Lippincott Company, Philadelphia

THE ALBERTA CLINICAL PRACTICE GUIDELINES PROGRAM

The Alberta Clinical Practice Guidelines Program promotes appropriate, effective and quality medical care in Alberta by supporting the use of clinical practice guidelines. The program is administered by the Alberta Medical Association under the direction of a multi-stakeholder steering committee.

Alberta Clinical Practice Guidelines Steering Committee

Alberta Health and Wellness
 Alberta Medical Association
 College of Family Physicians of Canada,
 Alberta Chapter
 College of Physicians and Surgeons of Alberta
 Physicians at Large
 Public Representative
 Regional Health Authorities
 University of Alberta
 University of Calgary

TO PROVIDE FEEDBACK

The Early Detection of Breast Cancer Working Group is a multidisciplinary team composed of a family physician, general practitioners, radiologists, general surgeons, a gynecologist, oncologist, pathologist, epidemiologist, Medical Officer of Health, nurse, medical student, public representatives, the Canadian Cancer Society, and Breast Cancer Policy Council representatives.

The Working Group encourages your feedback. If you need further information or if you have difficulty applying this guideline, please contact:

The Alberta Clinical Practice Guidelines Program
 12230 - 106 Avenue NW
 EDMONTON, AB T5N 3Z1
 (780) 482-2626
 or toll free 1-800-272-9680
 Fax: (780) 482-5445
 E-mail: cpg@albertadoctors.org
 Website: <http://www.albertadoctors.org>

Pain Management: Pearls and pitfalls

Classify the pain to understand cause:

- Somatic pain- Localized, tender, often dull ache
- Visceral pain- less well localized, deep, aching or throbbing pain. Sharp if serosa involved or colicky if viscera obstructed.
- Neuropathic (dysesthetic or neuralgic)-Often along a dermatome. Burning or stinging with sensory changes (eg: hyperalgesia (dysesthetic pain). Occasionally shooting, lancinating pain (neuralgic pain).

Measure the intensity:

- Visual Analog Scale (10cm) No pain j-----|Worst possible pain or Numerical Rating Scale (1-10)

Treat any underlying causes: Anxiety, fear, and despair make pain worse

Identify poor prognostic factors for pain control:

- Neuropathic pain, paroxysmal pain, psycho-social distress, cognitive impairment, alcohol/drug abuse

Consider non-pharmacological or combined regimens

- Massage, heat/cold, TENS, acupuncture, biofeedback, physiotherapy/OT, anesthetic blocks, surgery, radiotherapy
- NSAIDS, acetaminophen, bisphosphonates, calcitonin
- Adjuvants: muscle relaxants, sedative/anxiolytics, Tricyclic antidepressants, anticonvulsants, steroids

Anticipate and treat side effects

Basic analgesic management

For intermittent pain or if the patient has acute renal failure, PRN dosing often appropriate.

For continuous severe pain, use regular around the clock (RTC) regimens of opioids with rescue doses available (10% of 24 hour dose). Start with a short-acting opioid for titration until pain control is stabilized, then give 50-75% of the total daily dose of immediate release as an equianalgesic dose of slow release opioid. Use break-through pain (BTP) orders to determine if additional doses are needed. Each BTP dose (q1-4 hours) should be about 10% of the 24 hr consumption of opioid. Review the total BTP doses used in last 24 hours to calculate needed increases in baseline regimen, and continue daily assessment until adequate pain control is achieved.

Considerable individual variability exists in analgesia and toxicities experienced, both with different opioids within the same individual and between different individuals on same opioid. Reasons may include genetically determined expression of opiate receptor subtypes, and opioid metabolite accumulation. Evidence suggests benefits in analgesia-toxicity balance with the switching of opioids. See table for choices and comparable doses.

Complications of Opioid use

Complications are more common with higher doses, longer duration of use, or renal failure. Avoid Meperidine (Demerol) due to excess of side effects with chronic use.

Constipation: the hand that writes the opiate order writes the laxative order.

Obtundation and respiratory depression: Attend to ABCs, and reverse with Naloxone if necessary. Beware of sudden relief of cause of pain and "unopposed" analgesic.

Opioid-induced nausea: Treat with Metoclopramide/domperidone

Delirium: Avoid misdiagnosing delirium as increasing pain (if opioid-induced, then vicious cycle soon escalates)

Myoclonus: This is intermittent, irregular, involuntary, jerking movements generally involving the limbs. It is more common if higher doses or renal failure. Correct existing renal failure and dehydration. Change the opioid and decrease equianalgesic dose by 20 to 30 %. It is rarely necessary to use benzodiazepines (clonazepam)

Hyperalgesia: This is a paradoxical reaction to opioids where the patient has increasing pain with increasing opioid doses. Thought to be secondary to opioid metabolite toxicity. Ensure adequate hydration and renal function, change opioid and decrease equianalgesic dose by 20 to 30 %.

Commonly used Opioids

Drug	Notes	Duration hrs	Equianalgesic dose po mg	Equianalgesic dose IM/IV mg
Morphine	Usual first choice. Effective, well tolerated, safe, and cheap. Start with a low dose of immediate release 10-20 mg po q4h RTC, and increase by 25% a per day until relief of pain.	3-7	60	10
Hydromorphone (Dilaudid) (Hydromorph Contin)	Usual alternative to morphine	4-5	7.5	1.5
Fentanyl transdermal (Duragesic: Sublimaze)	Transdermal patches convenient for maintenance dosing but not suitable for rapid titration or for uncontrolled pain. Conversion ratio from other opioids is less certain, and drug is costly.	Several days	100 ug/hr	
Oxycodone		4-6	30	-
Codeine		4-6	200	130

Colorectal Cancer

Colorectal cancer is extremely common. In fact, approximately 5% of the North American population will develop colorectal cancer in their lifetime. It is important to know that current recommendations are based on a combination of age and family history. When there is no family history, baseline line risk is still sufficient to begin screening and the recommended age is 50. Current American Cancer Society recommendations have been adopted by the American College of Gastroenterology and are routinely followed by gastroenterologists in Canada. Genetic screening is for high-risk patients only as defined by a significant family history. While NSAID use is currently under investigation for prevention of colorectal cancer, the literature must be considered suggestive rather than proven..

References and suggested reading material:
American Cancer Society Guidelines on Colorectal Cancer Screening
Colorectal Cancer. Lancet 353:391-399 1999

Prostate Cancer

Prostate cancer is now the second most common cancer in men, after non-melanoma skin cancer. According to the National Cancer Institute of Canada (1996), prostate cancer is the most frequent non-skin cancer and the second leading cause of death from cancer in men, exceeded only by lung cancer.¹ Prostate cancer accounts for 27% of all male cancers and 13% of male cancer-related deaths. While the incidence has increased significantly over the past 35 years, the mortality rate has increased only slightly. The lifetime risk for developing prostate cancer is 12%. The level of PSA rises with age as the prostate becomes hypertrophic, so that the test becomes less specific. Most men with a PSA level above 4 ng/ml DO NOT have prostate cancer.

Lastly most men who develop prostate cancer die with the disease rather than from it. To date, it remains unclear how to accurately identify those patients who will have a benign course and benefit from “watchful waiting”, from those whose prostate cancer will follow an aggressive course and who would benefit from early aggressive surgical, radiotherapeutic, or chemotherapeutic interventions.

References:

Prostate cancer: progress and perplexity. Hoey,J. CMAJ 1998; 159: 491-492
Screening for prostate cancer. McGregor M, Hanley JA et al. CMAJ 1998; 159: 1368-1372
AMA CPG

Clinical Pharmacology of:

- Proton pump inhibitors and H2 Blockers
- Furosemide
- Hydrochlorothizide
- Nitrates
- Digoxin
- ACE Inhibitors
- Angiotension Receptor blockers
- Aminoglycosides
- Non-steroidal anti-inflammatories
- **Diabetes therapy: Insulin, Sulfonylureas, biguanides, thiazolidinones, acarbose**
- Thyroxine
- Unfractionated heparin, Low molecular weight heparin, Warfarin
(See General Internal Medicine Section)
- Corticosteroids : List potential complications of corticosteroid use and withdrawal, measures to prevent iatrogenic adrenal insufficiency

Drugs and the Kidney

- Common drugs requiring adjustment in renal failure
- Nephrotoxic drugs

Toxicology, Drug overdoses, and Withdrawal syndromes

- Acetaminophen
- Tricyclic antidepressants
- Aspirin
- Alcohols (ethanol, methanol, ethylene glycol)
- Opioids
- Cocaine
- Benzodiazepines
- Knowledge of drugs prolonging QT interval of ECG
- Digoxin
- Initial management of Alcohol Withdrawal and delirium tremens
 - State criteria for alcohol related disease/CAGE score
 - Major complications of alcohol related disease
 - Initial management in patient who is comatose, combative or undergoing withdrawal

Oral Hypoglycemics: General

All of the oral hypoglycemic agents described below can be used as initial monotherapy in patients where diet and exercise manipulation has been insufficient. Clinical factors may affect choice of agent – e.g., avoiding metformin or acarbose in individuals who already have gastrointestinal complaints, or avoiding thiazolidinediones in patients with heart failure. The UKDPS study in 1998 demonstrated that metformin is the best first-line drug for obese patients with type 2 diabetes. (1) Classes of oral hypoglycemic agents can be effectively and safely combined (sulphonylureas and meglitinides counting as a single class of insulin secretagogues). Progressive increases in the number of combined agents are to be expected with disease progression – at least up to three different agents.

Biguanides: Metformin (Glucophage)

The primary action of metformin is to suppress hepatic glucose production. Significant gastrointestinal side effects such as diarrhea, nausea, vomiting and anorexia may occur. Often, side effects can be reduced or avoided if the metformin dose is very gradually increased and taken with a meal. There is a historical concern about the risk of lactic acidosis with metformin. Although probably very rare, caution should be exercised in patients at risk, and the drug is contraindicated in the presence of active liver disease, significant renal impairment, acute or chronic metabolic acidosis, acute myocardial infarction, ethanol abuse, and perhaps congestive heart failure.

Thiazolidinediones (TZDs): Pioglitazone (Actos), Rosiglitazone (Avandia)

TZDs bind to peroxisome proliferative-activated receptors (PPARs), causing proliferation of insulin receptor genes involved in glucose production, transport, and utilization. They improve insulin sensitivity, particularly in skeletal muscle (but also in adipose). Glucose control from the TZDs may take several weeks to commence, and the full effect may not be evident for up to 12 weeks after initiating therapy. Being metabolized by liver, no dosage adjustment is necessary for renal failure.

Do not use TZDs in active liver disease (ALT greater than 2.5 times the upper limit of normal at baseline). Check liver enzymes before initiation, every two months for the first 12 months, then periodically thereafter. The drugs do not by themselves lead to hypoglycemia, but can lead to weight gain. TZDs can also cause fluid retention with increased plasma volume with edema and may precipitate congestive heart failure in susceptible individuals. The CHF can be hard to treat until the TDZ is stopped. TZDs are expensive but can be covered by special authorization via Alberta Blue Cross if the patient meets the criteria for coverage.

Insulin secretagogues**Sulphonylureas Glyburide (Diabeta), Gliclazide (Diamicron)**

Patients who are not obese (BMI <27) are candidates for sulphonylureas. These drugs stimulate release of insulin from pancreatic beta cells. About 50% of newly diagnosed T2 diabetic patients can achieve acceptable control with these medications. Sulphonylureas also provoke hyperinsulinism, which in turn accounts for the most troublesome adverse effects: weight gain and hypoglycemia (which can be serious, is often unappreciated or unrecognized and can cause significant morbidity in seniors). Gliclazide may be less prone to inducing hypoglycemia.

Meglitinides Repaglinide (Gluconorm), Nateglinide (Starlix)

Meglitinides are nonsulphonylurea agents that stimulate insulin release from the pancreatic beta cells. Repaglinide provokes hyperinsulinism, so concerns about hypoglycemia and weight gain are similar to sulphonylureas. Repaglinide's onset of action is much more rapid than glyburide or gliclazide. Insulin levels increase within 15 minutes of the oral dose and the total duration of hyperinsulinism is shorter. The drugs are administered at meal times and may be more appropriate in patients who have relatively erratic or unpredictable eating patterns, to avoid hypoglycemia. The drug is not renally excreted and can be given in the presence of renal insufficiency. It is about twice the cost of glyburide.

Alpha-glucosidase inhibitors: Acarbose (Prandase)

Acarbose interferes with intestinal carbohydrate digestion and reduces rate of glucose absorption, resulting in a reduction of postprandial hyperglycemia. It can cause significant gastrointestinal symptoms (flatulence, diarrhea and abdominal pain), which can be minimized by starting on a low dose and titrating slowly.

Combined therapy

In type 2 diabetes, it is frequently possible to combine insulin with oral agents –typically using an intermediate acting insulin (NPH or Lente) administered at bedtime. The peak action of these insulins usually coincides with the highest rate of hepatic glucose production and their use can assist in securing improved fasting glucose levels. If an improvement in fasting glucose still does not secure good daytime glucose control, multiple dose insulin regimens may be required, (and some oral agents may be stopped.)

Insulin

For patients with T2 diabetes who are underweight (BMI < 25) it is reasonable to start insulin. If diet is not controlled there is a tendency to gain weight and insulin resistance can lead to escalating doses of insulin without improved control. For reasonably tight control a twice-daily regimen of NPH and regular insulin might be appropriate. However this requires a constant diet and activity schedule, and many patients do better on a more intensive schedule, with background insulin requirements provided by 1 or 2 injections of NPH and additional injections of regular insulins or fast-acting (and shorter duration of action) insulin analogs (lispro) are given at meal times. When the intent is to control blood sugars with insulin only to the degree necessary to keep patients asymptomatic and out of risk of hyper osmolar coma, one can use a fixed regimen of NPH and regular insulin (such as 30/70).

Use of ACE inhibitors

The HOPE trial (2) looked at the effects of ramipril, on cardiovascular events in patients at high risk for coronary heart disease who did not have left ventricular dysfunction or heart failure. About 1/3 of patients in the study had diabetes mellitus. Ramipril (10 mg/day) reduced cardiovascular morbidity and mortality as well as microvascular endpoints, independent of blood pressure lowering. (BP reduction in HOPE was small with mean of 3/2 mm Hg). In the ramipril group, the combined outcome was reduced by 25%: myocardial infarction alone was reduced by 22%, stroke by 33%, and cardiovascular death reduced by 37%. With respect to secondary outcomes, the development of overt diabetic nephropathy was reduced 24%, and the need for laser therapy for retinopathy by 22%. Overall, 15 high-risk patients with diabetes would require therapy with ramipril for 4.5 years to prevent one of the primary endpoints. (NNT for 4.5 years= 15). ACE inhibition should probably be added to the other therapeutic regimes that we use in diabetic patients such as aspirin, statins, beta-blockers, etc. Whether other ACEI produce the same effect, as Ramipril is not clear, and other similar trials in progress (PEACE) and (EUROPA), using other ACEIs (e.g. perindoril), may provide an answer.

References:

1. UKDPS study Group. Lancet 1998; 352: 837-53
2. Effects of Ramipril on Cardiovascular and Microvascular Outcomes in People With Diabetes Mellitus: Heart Outcomes Prevention Evaluation (HOPE) Study Investigators: Lancet 2000; 355 (January 22): 253-259a

Pulmonary Medicine

Wheezing, and Asthma Acute and Chronic

- Physiology of airflow obstruction
- Criteria for diagnosis, and differential diagnosis of dyspnea with wheeze
- List precipitants of an acute exacerbation
- Initial (including emergency) and maintenance management
- Judgment of severity and recognition of complications of acute asthma (*see clinical skills section*)

Chronic bronchitis and emphysema

- **List factors, which may result in exacerbation of dyspnea in patients with COPD**
- List indications for hospitalization
- List complications of chronic hypoxia
- Strategies for Smoking cessation
- Oxygen and Drug treatment

Chronic Cough

Chronic dyspnea : List and categorize common causes

Approach to hemoptysis

- List and categorize major causes
- List features which suggest life threatening /massive hemoptysis
- Outline management of massive hemoptysis
- Outline management of patient with recurrent hemoptysis

Pleural effusions

- List major causes of:
- Differentiate transudate and exudate and infected (empyema)

Pulmonary hypertension and cor pulmonale

Cyanosis

- Definition and differentiate clinically between central and peripheral cyanosis
- Elicit and interpret information from the history and physical examination to differentiate among the major causes of cyanosis

Clinical skills (see clinical skills section)


- Basic Interpretation of blood gases
- Examination and laboratory findings in COPD
- Clinical assessment of asthma



Administered by the Alberta Medical Association

Guideline for The Management of

Acute Asthma in Adults and Children

This guideline has been adapted from the CAEP guidelines for Acute Asthma Management and new information has been added. 

RECOMMENDATIONS see Algorithm A (Adult) and Algorithm B (Pediatric) for specific recommendations.

Assessment of Severity



- ◆ In addition to vital signs and clinical measures, an objective measure of the severity of airflow obstruction should be determined. (see Algorithms A and B)

Bronchodilators

- ◆ Inhaled β -agonists are first line therapy for the emergency management of asthma.
- ◆ Bronchodilators should be administered by the inhaled route in preference to the parenteral route for the majority of asthmatics.
- ◆ Bronchodilators should be titrated using objective and clinical measures of airflow obstruction to guide the dose and frequency of administration.
- ◆ Anticholinergic bronchodilators should be added to β -agonists for severe asthma and may be helpful for moderate asthma.

Corticosteroids

- ◆ Corticosteroids are recommended in the early management of acute asthma
 - Oral agents are preferred to IV agents except in those too ill to swallow.

- ◆ All patients discharged from the site of emergency management (ED) for acute asthma should be considered for a course of oral corticosteroid therapy. 
- ◆ In addition to oral corticosteroids, inhaled corticosteroids should be considered for all patients with asthma at discharge. 

Additional Therapies



- ◆ IV magnesium sulfate treatment should be considered for patients with severe asthma.
- ◆ Other drugs that can be used in the management of severe asthma are: adrenaline, IV salbutamol, and inhaled corticosteroids. (see Algorithms A and B)
- ◆ Antibiotics are commonly over-used in acute asthma; they should be reserved for obvious bacterial infection.

Delivery Devices

- ◆ A metered dose inhaler (MDI) with a spacer device is as effective as nebulization in patients with mild to moderate acute asthma.
 - In children, an MDI with spacer produces fewer side effects than nebulization.

Discharge

- ◆ A discharge plan and clear instructions for follow-up should be prepared for patients discharged from the ED.
 - A written action plan is recommended. (Refer to Chronic Asthma Guideline for further management)

The above recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making.

BACKGROUND

Asthma is a common disease in both children and adults; current Alberta estimates suggest 13% of children and 7% of adults have this disorder.¹ The burden of disease related to asthma in Canada is hard to quantitate because deaths and hospitalization rates are underestimates of the disability and loss of enjoyment of life experienced by Canadians with this condition.² Fatal asthma is increasing worldwide, and Alberta has one of the highest rates of fatal asthma in Canada. Acute asthma costs in Canada are high, with emergency department (\$22 million) and in-patient costs (\$84 million) exceeding \$100 million per year.³ Despite improved understanding of the disease and pharmacological options, death and hospitalization still occur.^{2,5} Appropriate emergency department (ED) or equivalent management of acute asthma will have an impact on these statistics. Reviews of ED care in Canada have concluded that the condition is often under treated in this setting.^{4,5}

Assessment of Severity

- ◆ In addition to vital signs and clinical measures, an objective measure of the severity of airflow obstruction should be determined (See Algorithms A and B).

Methods of assessment include past asthma history, clinical (vital signs, including pulse oximetry where available, and physical examination), and pulmonary function testing. It has been consistently shown that the severity of airflow obstruction in asthmatic exacerbations correlates poorly with the traditionally assessed clinical signs of obstruction (e.g., wheezing). Many patients may have near normal physical findings yet will have clinically important obstruction when spirometric tests are performed. Similarly, changes in clinical signs after treatment do not always reflect changes in spirometry results. Furthermore, it has been shown that physician predictors of peak expiratory flow rates (PEFR) are frequently inaccurate.

The standard outcome measures used in the ED to assess severity of airflow obstruction are PEFR and forced vital capacity in 1 second (FEV₁).⁶ There is a high correlation between improvements in these two parameters following bronchodilator treatment. The best value of 3 attempts at each measurement should be recorded when possible. Because optimal results are patient effort dependent, specially trained

personnel (Respiratory Therapist, Nurse, MD) should be present to monitor the procedure.

Studies have suggested that percent predicted values are not more useful than absolute values in making clinical decisions.⁷ However, subjects were young (<40 years old) and unlikely to have had any component of fixed airway obstruction (e.g., COPD). To be consistent with all patient groups, recording the PEFR or FEV₁ according to the percent of previous best, if known, or the percent of predicted based on simple nomograms, is recommended. Observing the change over time of pulmonary function test results is an important component in the assessment of response to therapy.

Physician estimates of response to therapy are often inaccurate in acute asthma, yet several studies have shown that failure to substantially improve PEFR or FEV₁ in response to initial bronchodilator therapy is predictive of a more prolonged attack course, or even the need for hospitalization. Thus, objective measurement of post-bronchodilator response is the best method of predicting outcome of the asthma attack.

Treatment

Bronchodilators

- ◆ Inhaled β -agonists are first line therapy for the emergency management of asthma.
- ◆ Bronchodilators should be administered by the inhaled route in preference to the parenteral route for the majority of asthmatics.
- ◆ Bronchodilators should be titrated using objective and clinical measures of airflow obstruction to guide the dose and frequency of administration.

Inhaled β -agonists produce the fastest relief of acute bronchospasm with the fewest side effects.⁸⁻¹⁰ Prior treatment with aerosolized (MDI or wet nebulization) β -agonists does not preclude successful reversal of airway obstruction in the ED.¹¹ Two multicentre trials comparing aerosolized β -agonists to IV β -agonists demonstrate that aerosolized β -agonists are more effective and safer than intravenous salbutamol for acute asthma.^{12,13} Use of intravenous bronchodilators should be restricted to selected patients with severe sentation or becomes so despite inhaled therapy).

asthma (i.e., when response to nebulized therapy is incomplete or if the patient is moribund at preThe dose of aerosolized or intravenous β -agonist necessary to reverse an asthmatic attack has not been standardized. A patient's ability to use the aerosol route, the efficiency of the delivery system, the relative amounts of bronchospasm versus airway narrowing due to inflammatory mucosal edema and secretions, and unpredictable patient factors such as reduced sensitivity or down regulation of beta receptors in severe asthma all influence drug dosing. Relief of bronchospasm in response to aerosolized bronchodilators is best achieved if the principle of cumulative dosing is followed, in which sequential doses build upon the therapeutic effects of previously administered doses.¹⁴⁻¹⁶ The frequency of dosing will be determined by the patient's response and by the time required to completely nebulize the dose. Dosing every 15-20 minutes by wet nebulization, or even continuous wet nebulization, may be necessary initially, because of the inherent low efficiency of these devices.^{16,17} The optimal number of puffs, from an MDI with spacer, in the setting of acute asthma is not known. The British Thoracic Society¹⁸ recommends 20 - 40 puffs may be necessary, CAEP¹⁹ suggests 4-8 puffs Q 15-20 minutes with the recognition that it may be necessary to increase the dose to 1 puff Q 30-60 seconds.

Ventilated asthmatics with refractory bronchospasm, not responding to conventional bronchodilators may respond to inhalational anaesthetic agents with bronchodilating properties such as ether, halothane, enflurane, or isoflurane. Problems encountered with this approach include the potential for hypotension and cardiac dysrhythmias, probably exacerbated by the hypoxemia often seen in these patients.

Bronchodilator dose adjustment should be made by following objective measures of airway obstruction and symptoms. Once maximum relief of obstruction has been achieved by bronchodilators, administering further doses by any route will provide no further clinical benefit, but may have the potential for toxicity.

Anticholinergics

- ◆ Anticholinergic bronchodilators should be added to β -agonists for severe asthma and may be helpful for moderate asthma.

A systematic review of the use of anticholinergics in children²⁰ and a recent study²¹ have demonstrated evidence of improvement in lung function and reductions in admission rates (30%) in children with severe asthma. The studies done on mild to moderate asthma using single doses of ipratropium have shown limited benefit. However, some lung function improvements in moderate asthma may warrant its use in this setting as well.

Less consensus exists for the use of ipratropium bromide in adults with acute asthma.²² Disparate findings suggest that a conservative approach should be adopted. In adults, the use of anticholinergics should be reserved for patients not responding to β -agonists or with severe symptoms.

Corticosteroids

- ◆ Corticosteroids are recommended in the early management of acute asthma
 - Oral agents are preferred to IV agents except in those too ill to swallow.
- ◆ All patients discharged from the ED for acute asthma should be considered for a course of oral corticosteroid therapy.
- ◆ In addition to oral corticosteroids, inhaled corticosteroids should be considered for all patients with acute asthma at discharge.

The early use of systemic corticosteroids has been recommended on the basis of a systematic review.²⁴ These reviews suggest that the early administration of corticosteroids may reduce admissions to hospital. Moreover, the treatment appears to be most effective in the patients who have severe asthma and who have not received inhaled corticosteroids during their presentation. The delivery of corticosteroids in the ED is an important consideration. Research suggests that oral and IV agents function equally effectively. Therefore, it is recommended that the

corticosteroid be administered early, and by mouth; IV treatment should be reserved for those too dyspneic to swallow. The number of patients requiring intravenous agents should be small. Oral prednisone/prednisolone (1 mg/kg for children; 50 mg for adults) or intravenous corticosteroids (solucortef or methylprednisolone) may be used.

Additional Therapies

Magnesium Sulfate

- ◆ IV magnesium sulfate treatment should be considered for patients with severe asthma.

A number of randomized clinical trials have examined the use of intravenous magnesium sulfate for the treatment of acute asthma in the ED;²⁵ two involve children and the others involve adult subjects. In general, the use of magnesium is not supported for all patients seen in the ED. However, there is evidence that in severe asthma (children: <50% predicted PEFR and not responding to therapy; adults: <30% predicted PEFR and not responding to therapy), magnesium does provide additional benefit when combined with standard medications (e.g., corticosteroids, oxygen, β -agonists, etc). Specifically, it provides approximately 10% improvement in the percentage predicted pulmonary functions (PFT's). There is also evidence that patients respond faster, are discharged earlier, and that the admission rate is lower when magnesium is used. In general magnesium is inexpensive to administer, is safe in the doses prescribed for asthma, and is well tolerated (no major side effects reported in the trials). In adults, magnesium should be administered over 20 minutes and the dose is generally 2 grams.

In children, the dose is 25 mg/kg IV over 20 minutes. Magnesium can be administered more rapidly in severe cases. The use of magnesium is recommended for severe cases of asthma presenting to the ED and not responding to traditional measures.

- ◆ Other drugs that can be used in the management of severe asthma are: adrenaline, IV salbutamol, aminophylline, and inhaled corticosteroids.

Aminophylline

Over the years, the use of aminophylline in acute asthma has fallen from favour. Systematic reviews evaluating randomized controlled trials of aminophylline compared to placebo in the acute treatment of adults²⁶ and children²⁷ with acute asthma, both clearly demonstrated a lack of benefit in major outcomes such as pulmonary functions and admissions. It is interesting to note both reviews identified excessive side effects, which outweighed the benefits of aminophylline in this setting. Currently, this agent would constitute an option only for patients where all other modalities had failed (β -agonists, corticosteroids, ipratropium bromide, magnesium, oxygen, intravenous salbutamol, etc.), and should be used cautiously.

Additional therapies have been used in acute severe asthma. For example, high dose inhaled corticosteroids have been shown to improve pulmonary functions in some asthmatic patients.²⁸ In addition, epinephrine has a long history of use in acute allergic reactions such as asthma, and should be considered in severe asthma. Antibiotics are NOT effective in the early management of acute asthma, unless the patient has obvious signs and symptoms of a bacterial infection. If the patient is not responding to the therapies in this guideline, early patient referral or transfer is recommended.

Delivery Devices

- ◆ A metered dose inhaler (MDI) with a spacer device is as effective as nebulization in patients with mild to moderate acute asthma.
 - In children, an MDI with spacer produces fewer side effects than nebulization.

In a large systematic review, aerosolized bronchodilators administered by wet nebulization or metered dose inhalers during acute asthma were shown to be equally efficacious.²⁹ In both adults and children, comparisons between the two failed to demonstrate superiority of either method with respect to traditional outcomes such as pulmonary functions and admission rates. However, especially in children, the use of the wet nebulizers produced more of the autonomic side effects. Since the dose

comparisons for MDI with spacer to nebulizer in these studies were unequal, caution is warranted when deciding on therapy. Therefore, site specific decisions on the method of delivery must be based on other issues such as cost, physician familiarity, and supporting resources (i.e., respiratory therapy and nursing staff availability).

Discharge

The PEF/FEV₁ values are general guides to assist in clinical decision making. However, individual patient factors must also be taken into account. Patients with severe obstruction initially or severe residual obstruction after treatment are at high risk (>75% probability) for relapse and will usually require admission or prolonged ED observation. Conversely, patients who exhibit only mild residual obstruction can be discharged with a high degree of confidence. It is difficult to determine the most appropriate disposition in patients who exhibit moderate residual obstruction. In these patients, an asthma risk profile should be considered (see below). The higher the risk profiles, the lower the threshold for recommending admission in this group of patients.

Asthma Risk Profile

Important risk factors that define asthma at high risk of destabilization and relapse include the following:

- hospital admission or ED visit in the previous 12 months,
- recent systemic corticosteroid use,
- use of multiple asthma medications,
- maximum use of asthma medications,
- previous severe or near death asthma attack,
- psychosocial problems,
- frequent use of inhaled β -agonists.
- environmental triggers.

The more high risk severe asthma markers in the patient's history, the more cautious the physician should be about discharge and the more closely the patient should be followed.

Corticosteroids Following Discharge

There are at least 7 trials examining asthmatics discharged from the ED after treatment for an

exacerbation, who have been given corticosteroids (oral or IM) or placebo^{23,24}. The result of the systematic review suggested that patients benefited in all outcomes from the administration of corticosteroids. First, patients experienced 65% fewer relapses in the first week. Second, the use of β -agonists was also reduced within the first week of care. Finally, the use of corticosteroids is safe, inexpensive and well tolerated by patients. No patient subgroup was identified who would benefit more from this therapy, so it is advisable that this treatment should be considered in all exacerbations in the ED.

The dose and method of delivery for corticosteroids is debatable. There is no evidence that the short-course of corticosteroids used needs to be "tapered".³⁰ Most research would suggest that patients treated with corticosteroids could be given medications for 7 to 10 days; in Canada, prednisone is the most common agent. Compliance may be highest for adults with 50 mg once daily for a 7 day routine. Intra-muscular corticosteroids are also effective in cases of poor follow-up, financial concerns, or concerns with compliance. Longer courses of corticosteroids may be required for selected patients.³¹

Inhaled Corticosteroids (ICS) Following Discharge

While the evidence for the use of systemic corticosteroids in chronic asthma is strong and consistent, the role of inhaled corticosteroids in acute asthma is poorly defined. For patients on inhaled corticosteroids at the time of presentation, maintenance of the ICS is important. The recommendations for these patients consist of enhancing compliance, avoiding side effects, and asthma education.

For those patients not receiving regular inhaled corticosteroids, a recent randomized controlled trial has demonstrated a 45% reduction in relapses over the first 3 weeks of treatment by the addition of high dose inhaled corticosteroids (1600 ug/day of budesonide).³² Other studies are being performed on different agents, doses and delivery systems, and the recommendations should be strengthened with the next year. It appears that patients should be started on ICS at discharge *in addition* to oral corticosteroids. Less is known about whether patients with mild exacerbations may be safely discharged on ICS alone, despite reports of this success.³³

Other Agents at Discharge

Currently, there is no evidence for the addition of other agents at discharge such as the leukotriene antagonists, antibiotics, longer-acting β -agonists, or anti-histamines. Short-acting β -agonists should be used for relief over the follow-up period on a 'prn' basis.

Discharge Planning

- ◆ A discharge plan and clear instructions for follow-up should be prepared for patients discharged from the ED.
 - A written action plan is recommended.

Most experts believe that asthma education is the key to optimal disease control. Optimal disease control is achieved by ensuring proper drug delivery technique, and optimizing compliance by improved understanding of pathophysiology and pharmacology. Through assessment, demonstration, education and evaluation, the patient should leave the ED with a general understanding of how to manage their asthma at home. This should include an understanding of how to use their delivery device, when to seek help, what signs and symptoms suggest early interventions, when to use each medication and where to seek education and information.

Patients should be given brief written treatment plans with clear instructions for aftercare at home including review of drug delivery technique (proper techniques and appropriate use). Spirometric results from the ED would be included in this plan.

To locate potential sources of information please refer to the Alberta Asthma Resource Catalogue

REFERENCES

1. Health Canada. Childhood Asthma in Sentinel Health Units: Findings of the Student Lung Health Survey 1995-1996. Laboratory for Disease Control, Health Canada. Ottawa 1998.
2. Hogg RS, Schechter M, Montaner J, et al. Asthma mortality in Canada, 1946-1990. Canadian Respiratory Journal, 1995; 2: 61-66
3. Krahn MD, Berka C, Langlois P, Detsky AS. Direct and indirect costs of asthma in Canada. CMAJ: 1996;154:821-31.
4. Fitzgerald J, Macklem P. Proceedings of a workshop on near fatal asthma. Canadian Respiratory Journal, 1995; 2: 113-116.
5. Fitzgerald J, Hargreave F. Acute asthma: emergency department management and prospective evaluation of outcome. CMAJ, 1990; 142:591-595.
6. Nowak R, Pensler M, Sarkar D, et al. Comparison of peak expiratory and FEV₁ admission criteria for acute bronchial asthma. Annals of Emergency medicine, 1982; 11: 64-69.
7. Corre K, Rothstein R. Assessing severity of adult asthma and need for hospitalization. Annals of Emergency Medicine, 1985; 14: 45-52.
8. Rossing T, Fanta C, Goldstein D, et al. Emergency therapy of asthma: comparison of the acute effects of parenteral and inhaled sympathomimetics and infused aminophylline. American Review of Respiratory Diseases, 1980; 122: 365-371.
9. Siegel DE, Sheppard D, gelb A, et al. Aminophylline increases the toxicity but not the efficacy of an inhaled beta-adrenergic agonist in the treatment of acute exacerbations of asthma. American Review of Respiratory Diseases, 1985; 132: 283-286.
10. McFadden E. Critical appraisal of the therapy of asthma: an idea whose time has come. American Review of Respiratory Diseases, 1986; 133: 723-724.
11. Rossing T, Fanta C, McFadden E. The effect of outpatient treatment of asthma with beta agonists on the response to sympathomimetics in an emergency room. American Journal of Medicine, 1983; 75: 781-784.
12. Anonymous. High dose inhaled versus intravenous salbutamol combined with theophylline in severe acute asthma. European Respiratory Journal, 1990; 3: 163-70.
13. Salmeron S, Brochard L, Mal H, et al. Nebulized versus intravenous albuterol in hypercapnic acute asthma: a multi centre, double blind, randomized study. American Journal Respiratory Critical Care Medicine, 1994; 149: 1466-1470.
14. Britton J, Tattersfield A. Comparison of cumulative and non-cumulative techniques to measure dose-response curves for beta agonists in patients with asthma. Thorax, 1984; 39: 597-599
15. Nelson H, Spector S, Whitsett T et al. The bronchodilator response to inhalation of increasing doses of aerosolized albuterol. Journal of Allergy Clinical Immunology, 1983; 72: 371-375
16. Robertson C, Smith F, Beck R, et al. Response to frequent low doses of nebulized salbutamol in acute asthma. Journal of Pediatrics, 1985;106: 672-674.

17. Black P, Woodhouse A, Burmeister S, et al. How frequently should nebulized salbutamol be administered in acute asthma? *American Review Respiratory Diseases*, 1993; 147: A57
18. British Thoracic Society
19. CAEP Guidelines for the Emergency management of Adult Asthma
20. Plotnick LH, Ducharme F. Efficacy and safety of combined inhaled anticholinergics and Beta-2-Agonists in the initial management of acute pediatric asthma (Cochrane Review). In: *Cochrane Collaboration*. Issue 1, 1999. Oxford: Update Software.
21. Qureshi F, Pestian J, Davis P, Zaritsky A. Effect of nebulized ipratropium on the hospitalization rates of children with asthma. *New England Journal of Medicine*. 1998;339:1030-5
22. Lanes SF, Garrett JE, Wentworth CE, FitzGerald JM, Karpel JP. The effect of adding ipratropium bromide to salbutamol in the treatment of acute asthma: a pooled analysis of three trials. *Chest*. 1998;114:365-72.
23. Rowe B, Spooner C, Ducharme F, et al. The effectiveness of corticosteroids in the treatment of acute exacerbations of asthma: a meta-analysis of their effect on relapse following acute assessment. (Cochrane Review). In: *Cochrane Collaboration*. Issue 1, 1999. Oxford: Update Software.
24. Rowe B, Keller J, Oxman A. Steroid use in the emergency department treatment of asthma exacerbations: a meta-analysis. *American Journal of Emergency Medicine*. 1992; 10: 301-310.
25. Rowe B, Bretzlaff J, Bourdon C, Bota G, Camargo C. Intravenous magnesium sulfate treatment for acute asthma in the emergency department. *Cochrane Review*; Issue 2, 1999. Oxford Update.
26. Littenburg B. Aminophylline treatment in severe, acute asthma. *JAMA* 1988; 259: 1678-1684.
27. Goodman D, Littenburg B, O'Connor G, Brooks J. Theophylline in acute childhood asthma; a meta-analysis of its efficacy. *pediatric Pulmonology*, 1996; 21: 211-218.
28. Rodrigo G, Rodrigo C. Inhaled flunisolide for acute severe asthma. *American Journal Respir Crit Care Med*. 1998; 157: 698-703.
29. Cates C. Comparison of holding chambers and nebulisers for beta-agonists in acute asthma (Cochrane Review). In: *Cochrane Collaboration*. Issue 1, 1999. Oxford: Update Software.
30. Lederle F, Pluhar R, Joseph A, et al. Tapering of corticosteroid therapy following exacerbation of asthma: a randomized double-blind, placebo-controlled trial. *Arch Internal Med*, 1987; 147: 2201-2203.
31. Chapman K, Verbeek P, White J, et al. Effect of a short course of prednisone in the prevention of early relapse after emergency room treatment of acute asthma. *NEJM*, 1991; 324: 788-794.
32. Rowe B, Bota G, Therrien S, et al. Preventing asthma relapses following discharge from the emergency department: a double-blind, randomized trial of inhaled and oral steroids (abstract). *Acad Emerg Med*, 1998; 5: 471.
33. Levy ML, Stevenson C, Maslen T. Comparison of short courses of oral prednisolone and fluticasone propionate in the treatment of adults with acute exacerbations of asthma in primary care. *Thorax*, 1996; 51:1087-1092.

THE ALBERTA CLINICAL PRACTICE GUIDELINES PROGRAM

The Alberta Clinical Practice Guidelines Program promotes appropriate, effective and quality medical care in Alberta by supporting the use of clinical practice guidelines. The program is administered by the Alberta Medical Association under the direction of a multi-stakeholder steering committee.

Alberta Clinical Practice Guidelines Steering Committee

Alberta Health
 Alberta Medical Association
 College of Family Physicians of Canada, Alberta Chapter
 College of Physicians and Surgeons of Alberta
 Physicians at Large
 Public Representative
 Regional Health Authorities
 University of Alberta
 University of Calgary

TO PROVIDE FEEDBACK

The Asthma Working Group is a multidisciplinary team composed of emergency and family physicians, pulmonary specialists, radiologists, nurses, imaging technologists, public health specialists, and members of the public.

The Working Group encourages your feedback. If you need further information or if you have difficulty applying this guideline, please contact:

The Alberta Clinical Practice Guidelines Program
 12230 - 106 Avenue NW
 EDMONTON, AB T5N 3Z1
 (780) 482-2626
 or toll free 1-800-272-9680
 Fax:(780) 482-5445
 E-mail: cpg@albertadoctors.org
 Website: <http://www.albertadoctors.org>

Wheezing

Wheezing is produced by vibration of opposing walls of an airway that is narrowed almost to the point of closure. It can originate from airways of any size, from upper airways to intrathoracic small airways. Polyphonic wheezing is more likely to originate from more central airways. Although the triad of wheezing, chronic cough and dyspnea are highly suggestive of asthma, asthma is NOT the most common cause of wheezing. Postnasal drip is the cause in almost 50% of wheezing patients. Calculation of the A-a gradient and its use in differentiating conditions with ventilation perfusion disturbances from those with normal gradient and hypoventilation.

Chronic cough

Chronic cough is the 5th most common symptom for which patients seek medical advice. The commonest causes are benign: post-nasal drip, gastro esophageal reflux disease, asthma, and some drugs such as ACE inhibitors. Patients with benign causes for their cough can often be effectively and easily managed. Following viral infections, 45% of patients will have a cough that persists up to 2 weeks, and 25% will have a cough persisting for 3 weeks. Prolonged cough alone does not merit antibiotic therapy.

Other less common causes include:

- Foreign body
- Chronic bronchitis
- Bronchiectasis
- CHF
- Lung neoplasm
- Lung abscess
- Tuberculosis
- Respiratory Irritants (smoke, fumes)
- Post-viral infection hyper-irritability

Investigations of chronic cough in a smoker should always include a chest x-ray.

Acute exacerbation of COPD and Hypercarbia versus Hypoxia

CO₂ retention in a patient with an acute exacerbation of COPD is related to rapid shallow breathing. This pattern of breathing decreases the tidal volume, increases the dead space to tidal volume ratio and thereby decreases alveolar ventilation. Impairment of the hypoxic drive to breathe accounts for only ~ 10% of the increase in PaCO₂ that occurs when COPD patients are administered oxygen. Carbon dioxide retention in this situation is primarily due to the Haldane effect (deoxyhemoglobin is a better carrier of CO₂ than oxyhemoglobin) and to relaxation of pre-existing hypoxic vasoconstriction.

Severe hypoxemia is potentially immediately life-threatening, while mild to moderate respiratory acidosis (pH > 7.25) is usually well-tolerated. The immediate goal of therapy, therefore, is rapid correction of the patient's hypoxemia, aiming for a PaO₂ of at least 60 torr and a oxyhemoglobin saturation of at least 90%. Subsequent therapeutic measures are directed at the reversing the underlying cause of the COPD exacerbation and may include inhaled bronchodilators, systemic corticosteroid therapy and antibiotics.

Noninvasive mechanical ventilatory support, such as BiPAP and CPAP, has been shown to reduce the need for intubation in the COPD patient with an acute exacerbation. Intubation with mechanical ventilation in this clinical context is reserved for those patients where hypoxemia cannot be corrected by supplemental oxygen and/or the excessive work of breathing cannot be met by BiPAP.

1. Anthonisen NR. Hypoxemia and O₂ therapy. Am Rev Respir Dis 1982; 126 (4):729-33
2. Hillberg RE, Johnson DC. Noninvasive Ventilation. NEJM 1997; 337: 1746-52

Management of Acute Bronchitis and Acute Exacerbations of Chronic Bronchitis

Summary of the Alberta Clinical Practice Guidelines, December 2000

Diagnosis

Acute

Based on acute onset of symptoms (cough +/- sputum production, fever, chest discomfort) and normal respiratory exam (other than wheezes)

- Chest X-ray, sputum cultures **ONLY** indicated for patients with evidence of consolidation
- Green/yellow sputum production is indicative of inflammatory reaction and does not necessarily imply bacterial infection

AECB

Based on history of chronic bronchitis with acute onset of: increased sputum production, increased sputum purulence, increased dyspnea.

- Physical findings of: increased respiratory rate, increased wheezing, +/- diffuse crackles without localization.
- Measure peak flow and/or FEV₁, O₂ saturation +/- ABGs
- Chest X-ray, sputum cultures **ONLY** indicated for patients with evidence of consolidation

Management

Acute

- Smoking cessation, fluids/increased humidity, analgesics/antipyretics, antitussives
 - Bronchodilators may offer modest benefit in prolonged/protracted cough but are not routinely recommended
 - Corticosteroids (inhaled or oral) and expectorants are **NOT** recommended
- Antibiotic therapy **NOT** indicated

AECB

- Smoking cessation, bronchodilators (ipratropium and short acting beta-agonists), oxygen, oral corticosteroids, rehabilitation and nutritional programs
 - Long-acting beta-agonists and inhaled corticosteroids are **NOT** recommended
- Antibiotics if at least 2 of: increased sputum production, increased sputum purulence, increased dyspnea

1st-Line

Amoxicillin

500 mg PO tid for 6 to 9 days, OR

Doxycycline

200 mg PO day 1 then 100 mg PO daily for 6 to 9 days, OR

TMP/SMX

1 DS tab PO bid for 7 to 10 days

Failure of 1st-line agents OR antibiotics in last 6 weeks and/or 4 or more episodes in past year

2nd-Line

Cefuroxime axetil

250-500 mg PO bid for 7 to 10 days, OR

Amoxicillin-clavulanate

500 mg PO tid for 7 to 10 days

Beta-lactam Allergy

Azithromycin

500 mg PO day 1 then 250 mg PO daily for 4 days, OR

Clarithromycin

250-500 mg PO bid for 7 to 10 days

Failure of 2nd-line agents

Levofloxacin

500 mg PO daily for 5 to 10 days, OR

Moxifloxacin

400 mg PO daily for 5 to 10 days, OR

Gatifloxacin

400 mg PO daily for 5 to 10 days

ANTIBIOTIC PROPHYLAXIS IS NO LONGER RECOMMENDED IN AECB

Antibiotics **NOT** Recommended

Cephalexin, cefaclor, cefixime, ceftriaxone, clindamycin, erythromycin

Follow-up

Acute

- Routine follow-up not required

AECB

- Non-responders: reassess at 72 hours
- Routine follow-up is recommended to evaluate maintenance therapy

For complete guideline refer to the Alberta Medical Association Web Site: www.albertadoctors.org
Revised November 2001

Hemoptysis

Expectoration of blood can range from blood-streaked sputum to massive hemoptysis (100-600 cc/day) that may be life-threatening. Bleeding usually stops and starts unpredictably, but under certain circumstances may require immediate airway management and control of the bleeding. If there is massive hemoptysis, establish an airway first and consult a specialist capable of controlling the bleeding.

On history and clinical examination, try to determine whether the expectorated blood represents true hemoptysis originating from below the vocal chords, or rather, upper respiratory tract bleeding (epistaxis etc) or hematemesis. Over 90% of hemoptysis originates from bleeding from the bronchial artery vascular bed, which receives only 10% of the cardiac output, rather than the pulmonary arteries

Select investigations to determine the cause of hemoptysis (chest x-ray, CT scan, bronchoscopy). If arteriography is eventually selected, select imaging of the bronchial arteries first.

Causes include:

- Acute and Chronic bronchitis
- Pneumonia
- Tb, Lung abscess, bronchiectasis
- Tumor
- Trauma
- Foreign body
- Pulmonary hemorrhagic syndromes (SLE, Goodpasture's, Wegener's, Hemosiderosis)
- Mitral stenosis
- Pulmonary embolism
- AV malformations

Pleural effusions

D. Sin 2000

The biochemical characteristics of pleural fluid exudates include raised protein, raised LDH and an elevated white cell count. Visible bacteria on Gram's stain or a pH < 7.2 suggest an empyema.

Approximately 80% of exudative pleural effusions are caused by pneumonia, pleural malignancy, or thromboembolism.

Negative pleural fluid cytology does not exclude a malignancy because cytologic studies are positive in only 50% to 60% of patients with malignant pleural effusions. Approximately 10% of patients with malignant pleural effusions have a mild elevation of pleural fluid amylase, which is the salivary rather than pancreatic isoenzyme. The differential diagnosis of an elevated pleural fluid amylase would also include pancreatitis, a pancreatic pseudocyst, or esophageal rupture.

Tuberculous pleuritis may produce large effusions. Atypical lymphocytes are often present, but this finding is nonspecific and is present in most chronic inflammatory pleuritis. The culture of the pleural fluid is only positive in 25% of cases of tuberculous pleuritis. However, pleural biopsies reveal granulomas in 80% of cases (with 3 or more specimens), and addition of culture of the pleural biopsy specimen increases the yield to 90%. Medical or "blind" pleural biopsies are less sensitive than thoroscopic guided biopsies.

Fungal infections rarely if ever produce large pleural effusions. HIV infections rarely produce large unilateral pleural effusions unless complicated by opportunistic infections such as tuberculosis.

Acute monoarthritis

- Septic arthritis
- Crystal arthropathies (gout, pseudogout)
- Associated diseases (hemarthrosis/trauma, rheumatoid arthritis, etc)
- Indications for aspiration, and interpretation of synovial fluid
- Principles of management of septic arthritis/potential organisms involved
- Precipitants of acute gouty arthritis
- Management of acute gout and prophylaxis

Chronic inflammatory polyarthritis to include Rheumatoid arthritis (RA)

- Site and pattern specific differential diagnoses (RA versus SLE versus OA etc)
- Investigations used to confirm diagnosis of RA
- Articular and extra-articular complications of RA
- Basic management of RA

Osteoarthritis: Clinical features and basic management

Autoimmune Diseases

Clinical presentation of:

- Systemic Lupus Erythematosus
- Scleroderma
- Polymyositis
- Polymyalgia Rheumatica
- Vasculitis

Clinical Skills (see clinical skills section)

- Examination of the knee for effusion
- Examination of shoulder
- Examination of the rheumatoid hand
- General screening rheumatologic examination

Acute Monoarticular arthritis

Differential Diagnosis:

Septic Arthritis:	Bacterial	Fungal	Mycobacteria
Crystal-Induced:	Gout (monosium urate)	Pseudogout (calcium pyrophosphate)	Hydroxyapatite
Inflammatory Arthritis:	Psoriatic or Rheumatoid Arthritis	Reactive Arthritis	Systemic Lupus Erythematosus (SLE)
Non-inflammatory Causes:	Fracture, hemarthrosis, internal derangement	Tumor: Benign vs malignant	Osteoarthritis

Making the Diagnosis:

- History & physical examination determines the acuity of onset, relevant past medical history, and presence of effusion
- **Gold-standard for Diagnosis: Arthrocentesis** (joint aspiration): Send for gram stain, culture, cell-count & differential, crystals. It is important to always consider the possibility of a septic joint (infection), as this is relatively common cause of acute pain and swelling in a single joint, and it can result in cartilage destruction within a few days if untreated.
- **Supportive Work-up:** Complete blood count, blood cultures

Treatment (Diagnosis-specific):

- **Crystal-arthropathy** → For gout, NSAID's, intra-articular or systemic steroids, colchicine; consider allopurinol in future once acute gouty attack has fully resolved & pt has history of > 2 – 3 attacks per year, or has history of renal stones, or tophaceous gout. Positively birefringent crystals are pathognomonic of pseudogout. A typical presentation is acute monoarthritis, often of the knee, in older patients. Anti-inflammatories are more appropriate than colchicine, which has little role in this disease.
- **Septic arthritis** → Consult orthopedics for possible surgical drainage, start intravenous antibiotics (cover the most likely agents (Staph. aureus → e.g. Ancef (cefazolin
- **Inflammatory arthritis** → Symptomatic treatment with NSAID's, possible intra-articular steroid injection. Consider disease-modifying agents (eg. Methotrexate, sulfasalazine, or plaquenil) for rheumatoid arthritis or psoriatic arthritis.

Inflammatory Polyarticular Arthritis

Differential Diagnosis:

Acute Onset	Chronic (> 6 weeks)
Crystal arthropathy (gout, pseudogout)	Rheumatoid arthritis
Infection (viral, bacterial)	Reactive arthritis
Reactive Arthritis	
Systemic Rheumatic Illness (eg. Early	Other systemic illness (sarcoidosis,

rheumatoid arthritis, ankylosing spondylitis, SLE, systemic vasculitis, polymyositis)

malignancy, palindromic rheumatism)

When crystal and septic arthritis are ruled out, the most common inflammatory arthropathies are:

Rheumatoid arthritis (see below)

Seronegative spondyloarthropathies (Ankylosing Spondylitis, psoriatic arthritis, inflammatory bowel disease-related arthritis)

- Axial skeleton, large joints (eg. Hips), sometimes peripheral, smaller joints
- Possible sacroiliitis (buttock pain)
- Variable peripheral distribution (oligoarthritis (4 or less joints), large joints, peripheral small joints)

Reactive Arthritis

- Post urinary or gastrointestinal tract infection
- Usually within several weeks of initial infection
- Most self-resolve, some linger, some cause progressive joint damage

Classic inflammatory features in addition to joint involvement:

- Morning stiffness > 30 minutes
- Gelling phenomenon (stiffness after prolonged immobility)
- Constitutional symptoms (fatigue, weight loss, anorexia)

Making the Diagnosis:

Full history and physical examination

- Assess pattern of joint involvement & pain
- Careful joint examination, spine & muscle exam → risk of cervical (C1/C2) subluxation with rheumatoid arthritis
- Skin exam (psoriasis, nodules)

Laboratory tests → non-specific but CBC & differential (anemia of chronic disease), ESR or CRP may help; rheumatoid factor & ANA may/may not be helpful

- Arthrocentesis → help rule out crystal or infectious process & confirm inflammatory white blood cell count
- Imaging → Radiography may help in chronic arthritis, less helpful acutely as will probably be normal; early arthritis may be reflected in bone scan

Treatment:

- **Symptom-relief:** NSAID's, occasionally intra-articular steroids, acetaminophen
- **Disease-modification:** Choice dependant on degree of joint involvement, other medical conditions (eg. Plaquenil, methotrexate, sulfasalazine, arava (leflunomide), newer biologics (etanercept or infliximab)

Rheumatoid arthritis

This condition affects about 1% of the population, with a female to male ratio of 2:1. It is NOT strongly familial. It is characterized by symmetric, progressive, chronic polyarthritis typically of the smaller joints. The most common joints involved early on are the MCPs, PIPs (sparing DIPs), wrists, and ankles. The initial joint involvement may be asymmetric and oligoarticular (4 or less joints involved). Later on, RA

frequently affects the feet, but not the back. Larger joint involvement may also be seen. The majority of RA cases (85%) develop insidiously over weeks to months. Initial symptoms may include general fatigue, malaise, weight loss, and diffuse poorly localized musculoskeletal stiffness. About 15% of RA develops as an abrupt onset of polyarticular joint inflammation, often associated with significant constitutional symptoms. With progression of active inflammation, it results in joint destruction, deformity and associated disability.

To be treated early, RA must be diagnosed early, and the diagnosis of RA is a clinical one. A patient may be considered to have RA if **at least 4 of the following criteria have been present for at least 6 weeks.**

American Rheumatism Association Revised Criteria for RA

Criteria	Definition
Morning stiffness	Morning stiffness in and around joints lasting at least 1 hour before maximal improvement
Arthritis in 3 or more joint areas	At least 3 joint areas out of a possible 14 (PIP, MCP, wrist, elbow, knee, ankle, MTP joints)
Arthritis of the hand joints	At least one area swollen in a wrist, MCP or PIP joint
Symmetric arthritis	Simultaneous involvement of the same joint (as defined above) on both sides of the body
Rheumatoid nodules	Subcutaneous nodules over bony prominences or extensor surfaces or in juxta-articular regions as observed by a physician
Positive Serum rheumatoid factor	See comments below
Radiographic changes	Erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints. **

See next page for footnotes

*Rheumatoid factor has a false positive rate of 1-5% in the population, and the test is not very useful for ruling RA in or out. It has some value in prognostication. High titers correlate with increased risk of extra-articular manifestations of RA.

**These findings are usually not present for a number of months in established disease, and early on in the disease x-rays are not very useful.

Extra-articular Complications of Rheumatoid Arthritis

- **Ocular:** Episcleritis / scleritis, keratoconjunctivitis sicca, cataracts (chronic glucocorticoid use)
- **Skin:** Vasculitis, rheumatoid nodules (pressure-dependent areas especially)
- **Pulmonary:** Interstitial lung disease, rheumatoid lung nodules, pleural effusions, BOOP (bronchiolitis obliterans organizing pneumonia)
- **Cardiac (rare):** Increased risk of atherosclerosis, pericarditis
- **GI:** Possible elevated liver enzymes (especially alkaline phosphatase)
- **Muscles:** Muscle atrophy secondary to joint inflammation
- **Renal:** Secondary amyloidosis (chronic inflammation), low-grade membranous nephropathy
- **Amyloidosis:** Rare with today's treatments; serum amyloid-A protein elevation due to inflammation leading to end-organ damage
- **Vasculitis:** Sensorimotor neuropathy, skin changes

Treatment

Symptomatic treatment involves NSAIDs, and acetaminophen. However, aggressive DMARD (disease modifying anti-rheumatic drugs) therapy instituted early on positively affects both short-term well being of patients, long-term outcomes of joint preservation, is more likely to result in sustained remission, and is

better tolerated. If you are unsure of the diagnosis, or unfamiliar with DMARD therapy, promptly consult a rheumatologist to avoid treatment delay.

DMARDS include gold salts, antimalarials (hydroxychloroquine), sulfasalazine, penicillamine, methotrexate, and leflunomide. The right choice of agent for each patient requires clinical judgment. Methotrexate is popular owing to its clinical effectiveness, rapid onset of action, and safety/side-effect profile. **Combination** DMARD use has improved response rates. A combination example is methotrexate, sulfasalazine and hydroxychloroquine. Although costly, biological therapies with TNF alpha receptor antagonists (Etanercept), TNF alpha monoclonal antibodies (Infliximab), and Interleukin-1 receptor binders (Kineret) show disease modifying properties and clinical results superior to previous therapies for RA, and are commonly used in combination with other standard DMARDS, especially methotrexate.

Osteoarthritis

Osteoarthritis is the most common type of arthritis in the population, with an estimate adult prevalence (U.S. figures) of 12.1%. Rheumatoid arthritis, in the same population, had a prevalence of 0.8%

Predisposing factors: age, sex, heredity, obesity, reproductive variables, osteoporosis, hyper-mobility

Biomechanical factors: Joint shape, trauma, occupation, and certain activities

General Signs and Symptoms:

Use-related pain, < 30 minutes of morning stiffness & stiffness after inactivity (gelling), loss of movement, feelings of insecurity or instability of affected joint, functional limitations, tender spots along joint, coarse crepitus, cool effusions, instability of joint

Making the Diagnosis:

- History to rule out inflammatory arthritis
- Physical exam focusing on distribution of affected joint(s), lack of involvement of other organs, looking for classic osteoarthritis changes (Heberden's (DIP's) & Bouchard's (PIP's) nodes. Should spare MCP joints

Hand OA	Hip OA	Knee OA
<p>Hand pain, aching, stiffness (3 or 4 of:)</p> <ul style="list-style-type: none"> - Hard tissue enlargement of 2 or more joints - Involvement of 2 or more DIP joints - Deformity of 1 or more of these joints - Less than 3 swollen MCPs 	<p>Hip (groin) pain (2 or more of:)</p> <ul style="list-style-type: none"> - ESR < 20 mm/hr - X-ray: femoral or acetabular osteophytes - X-ray: Joint space narrowing 	<p>Knee pain, bony tenderness or enlargement</p> <ul style="list-style-type: none"> - Cool or no effusion - Age > 50 - Stiffness < 30 minutes - Crepitus - ESR < 40 mm/hr - Negative rheumatoid factor

Treatment:

- **Symptom-relief:** Acetaminophen (up to 4 grams daily) if no hepatic compromise; NSAIDs (classic & COX-2 inhibitors): eg. Voltaren, Naproxen, Vioxx, celebrex
- **Intra-articular Steroids:** Consider for symptomatic knee; if no relief after 1 – 2 injections, do not repeat. Otherwise can safely repeat several times per year.
- **Systemic Steroids:** No role in osteoarthritis
- **DMARD's:** No disease modifying agents for OA
- **Glucosamine sulfate:** Trial of 500 mg tid for 3 months safe, limited side effects; discontinue if no improvement in joint pain after 3 months

- **Synvisc:** Injected viscous fluid similar to hyaluronic acid → requires 3 injections spaced 1 week apart; may provide symptomatic relief but is often of limited duration

Back Pain

As a first step in diagnosis, it is useful to ask the patient to point to where on the “back” the pain is felt. Do not assume the use of the term “back” pain refers to per-spinal pain. Patients may point to a buttock or a region of the shoulder!

Polymyalgia Rheumatica

Polymyalgia rheumatica is a relatively common rheumatic disorder, with a prevalence of about 7 per 1000 persons over 50 years of age. Polymyalgia is rarely diagnosed in people under the age of 50 years

Patients with PMR as the primary diagnosis may also develop Giant Cell Arteritis (GCA). Both disorders may occur in the same patient at different times. Unrecognized GCA, if not treated quickly and aggressively with steroids, may lead to painless irreversible blindness.

PMR is classically characterized by a gradual onset of bilateral, usually symmetrical aching and morning stiffness in at least two of the following areas: the shoulders or proximal regions of the arms, hip girdles or proximal aspects of the thighs, neck and torso. Stiffness worsens with rest, and lasts 1 to 2 hours first thing in the morning. Pain with movement, and night pain are common. Some patients also complain of malaise, fatigue, anorexia, weight loss, and fever, but high spiking fever is rare unless GCA is also present.

Physical examination may reveal decreased active range of motion of the shoulders, neck, and hips. Despite the name “polymyalgia”, **muscle tenderness** is not a prominent feature of this disease. What tenderness there may be about the shoulders is more likely due to synovial or bursal inflammation than muscular involvement. Some patients develop swelling and pitting edema over the hands, wrists, ankles, and top of the feet. The edema usually occurs with other signs of polymyalgia rheumatica but can be the presenting symptom. It appears to represent tenosynovitis and synovitis in regional structures.

Normocytic anemia or mild elevations in platelets may be present, but are non-specific findings. Routine x-rays of inflamed joints rarely reveal any abnormalities. The erythrocyte sedimentation rate (ESR) is typically elevated (often above 100 mm/h), but may be less than 40 mm/h in some patients, especially if they have milder disease or have been treated with corticosteroids.

The differential diagnosis of polymyalgia rheumatica includes early seronegative rheumatoid arthritis, hypothyroidism, endocarditis, polymyositis, amyloidosis, malignancies, and fibromyalgia.

Clinical Features and Diagnosis of Giant Cell Arteritis include fatigue, headaches, jaw claudication (pain with chewing), scalp tenderness (especially in temporal area), loss of vision, diplopia, or amaurosis fugax. Diagnosis confirmed with temporal artery biopsy. Biopsies may miss the affected site, as there the artery may have “skip” lesions. If patient has clinical picture of giant cell arteritis despite negative biopsy, consider repeating biopsy and treating with steroids anyway; you usually have 3 – 7 days after steroids are started before the biopsy would be affected

Treatment of PMR

With PMR, there is usually dramatic response to steroids. Slowly taper down steroids when the patient feels better. Often, patients require long durations of low dose therapy (average 1 to 2 years). Osteoporosis prophylaxis with bisphosphonates, calcium, and vitamin D is usually recommended. Treatment of Giant Cell Arteritis usually requires higher initial doses of steroids, again with a very slow taper, and similar osteoporosis prevention.

Vasculitis

A mixed group of diseases characterized by inflammatory infiltration of blood vessels. There are many different methods of classification:

The 1992 Chapel Hill Conference (CHC) classified the vasculitides by:

- Clinical and histopathologic features
- **The size of the predominant vessel involved**
- Presence of serologic markers and other immune phenomena (eg. ANCA)
- The affected tissue (eg. Immune deposits) as seen with immunohistochemistry

Large vessel	Medium sized vessel	Small vessel
Takayasu arteritis Giant cell arteritis	Polyarteritis nodosa Kawasaki disease Isolated central nervous system vasculitis	Churg-Strauss arteritis Wegener's granulomatosis Microscopic polyarteritis Henoch-Schonlein purpura Essential cryoglobulinemia vasculitis Hypersensitivity vasculitis 2ndary to connective tissue disorders Vasculitis secondary to viral infection

Consider the possibility of vasculitis in patients with systemic symptoms ,who also have evidence of single or multiorgan dysfunction. Signs and symptoms may encompass fatigue, weakness, fever, arthralgias, abdominal pain, hypertension, renal insufficiency (active urine sediment with red and white cells and/or red cell casts) and neurologic dysfunction.

AUTOIMMUNE DISEASES

Systemic Lupus Erythematosus

An inflammatory multisystem disease of unknown origin

Classification Criteria: (mnemonic = SOAPBRAIN MD)

For research purposes, 4 of 11 of these criteria must be positive to diagnose SLE.

- **Serositis** – pleuritis, pericarditis
- **Oral ulcers** – painless oral or nasopharyngeal ulceration
- **Arthritis & arthralgias** – non-erosive, 2 or more peripheral joints
- **Photosensitivity** – skin rash from unusual reaction with sunlight
- **Blood** – *Hemolytic* anemia, WBC < 4, lymphocytes < 1.55), or platelets < 100
- **Renal disorder** – persistent proteinuria > 0.5 g/day or > 3+; cellular casts (red cell, hemoglobin, granular, tubular, mixed)
- **Anti-nuclear antibody positive** – abnormal titre by immunofluorescence
- **Immunological disorder** – elevated double-stranded DNA and/or positive anti-Sm (Smith nuclear antigen) and/or positive antiphospholipid antibodies
- **Neurological disorder** (seizures, psychosis)
- **Malar rash** – fixed, erythema, flat or raised over malar eminences, sparing nasolabial folds
- **Discoid rash** – erythematous, raised patches with adherent keratotic scaling, follicular plugging; atrophic scarring

Treatment: Focus on affected organ systems:

- **Lupus nephritis:** Consult nephrology; consider combination therapy of pulse steroids & cyclophosphamide or mycophenolate mofetil (MMF)
- **Pulmonary hemorrhage/alveolitis:** Consult pulmonary; consider pulse steroids & cyclophosphamide; early intubation if signs of airway compromise
- **Lupus cerebritis:** Consider lumbar puncture to rule out infection; early CT head and/or MRI to help rule out early stroke; pulse steroids & cyclophosphamide considered
- **Antiphospholipid Syndrome:** Anticoagulation (heparin overlapping with warfarin therapy); consider ASA if full anticoagulation contraindicated
- **Immune-mediated Cytopenias:** Consider antimalarials (eg. Plaquenil (hydroxychloroquine) → eg. ITP (immune-mediated thrombocytopenia)
- **Cutaneous Lupus:** Several types; antimalarials helpful for malar rash, “subacute cutaneous lupus”; topical therapies (topical steroids) helpful; discoid lupus more difficult as often results in irreversible scarring
- **Arthritis:** May require only antimalarial therapy
- **Lupus flares:** Anti-malarial therapy is shown to prevent systemic flares of lupus

Systemic Sclerosis

Diagnosis of systemic sclerosis may be made if patient has 1 major and 2 or more minor criteria

Major criteria:

- **Proximal scleroderma:** typical involves symmetrical thickening, tightening, induration of the skin of the fingers and hand proximal to the metacarpophalangeal joints. It occasionally involves the entire extremity, face, neck and trunk (thorax & abdomen)

Minor criteria:

- **Sclerodactyly:** Skin changes described above are limited to fingers
- **Digital pitting scars or loss of substance from the finger pad:** Depressed areas at the tips of fingers or loss of digital pad tissue from ischemia
- **Bibasilar pulmonary fibrosis:** Bilateral reticular pattern most pronounced in basilar portions of lungs on standard chest x-ray; may appear as “honeycomb lung”

Treatment:

- **Skin:** No proven therapies: Steroids *may* help in the early edematous phase of skin tightening
- **Organ-specific therapy:** Treat pulmonary hypertension with vasodilators (calcium channel blockers, nitroglycerin, bosentan). Monitor for hypertension and start ACE-inhibitor with first sign of hypertension to prevent renal crisis

Polymyositis

One of a heterogeneous group of myopathies including: dermatomyositis, juvenile dermatomyositis, myositis with neoplasia or collagen vascular disease, inclusion body myositis. An immune-mediated process, of unknown etiology, polymyositis affects striated muscles, and sometimes skin (dermatomyositis).

Classic features of disease:

- Symmetric proximal muscle weakness
- Constitutional symptoms: fatigue, anorexia, morning stiffness
- Other affected organ systems: joints, lung (fibrosis), heart, gastrointestinal tract

Investigative findings:

- Elevated serum enzymes from muscles → creatine kinase (CK)
- Autoantibody associations (eg. Anti-Jo1)
- Electromyography (EMG) shows myopathic changes seen with inflammation
- Muscle biopsy shows histologic features of muscles inflammation

Treatment:

- Corticosteroids + steroid-sparing agents (eg. Methotrexate, azathioprine, antimalarials (eg. Plaquenil), IVIG (intravenous immunoglobulin)
- Physiotherapy
- Swallowing assessment (occupational therapy)

General screening rheumatologic examination

- General appearance and Vital Signs
- Start at the periphery examining the nails, hands, skin, elbows, shoulder
- Examine the heart, lungs, abdomen
- Examine hips, knees, ankles, feet
- Review the axial skeleton (examine the neck, back)
- Check the reflexes, gross motor strength and sensation
- Ask the patient to walk and observe gait
- Asking patient to squat and resume standing position from squat provides good estimate of proximal strength
- Special Tests: eg. Straight leg raise if concerned of sciatica

Suggested Readings:

- 12th Edition Primer of Rheumatic Disease, 2001, Arthritis Foundation Publication, Main editor: Klippel
- Up-to-Date On-line or CD-ROM → multiple chapters on autoimmune disease
- Kelly's Rheumatology Textbook (available on-line with MD Consult & in the library)