2
CARDIOLOGY

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Aortic Dissection

DIFFERENTIAL DIAGNOSIS

CARDIAC

- **MYOCARDIAL**—myocardial infarction, angina, myocarditis
- **VALVULAR**—aortic stenosis, aortic regurgitation
- **PERICARDIAL**—pericarditis
- **VASCULAR**—aortic dissection

RESPIRATORY

- **PARENCHYMAL**—pneumonia, cancer
- **PLEURAL**—pneumothorax, pneumomediastinum, pleural effusion, pleuritis
- **VASCULAR**—pulmonary embolism, pulmonary hypertension

GI—esophagitis, esophageal cancer, GERD, peptic ulcer disease, Boerhaave's, cholecystitis, pancreatitis

OTHERS—musculoskeletal, shingles, anxiety

PATHOPHYSIOLOGY

ANATOMY—layers of aorta include intima, media, and adventitia. Majority of tears found in ascending aorta at right lateral wall where the greatest shear force is produced

AORTIC TEAR AND EXTENSION—aortic tear may produce a tearing, ripping sudden chest pain radiating to the back. Aortic regurgitation can produce diastolic murmur. Pericardial tamponade may occur, leading to hypotension or syncope. Initial aortic tear and subsequent extension of a false lumen along the aorta may also occlude blood flow into any of the following vascular structures:

- **CORONARY**—acute myocardial infarction (usually RCA)
- **BRACHIOCEPHALIC**, **LEFT SUBCLAVIAN**, **DISTAL AORTA**—absent or asymmetric peripheral pulse, limb ischemia
- **RENAL**—anuria, renal failure
- **CAROTID**—syncope/hemiplegia/death
- **ANTERIOR SPINAL**—paraplegia/quadriplegia, anterior cord syndrome

PATHOPHYSIOLOGY (CONT'D)

CLASSIFICATION SYSTEMS

- **STANFORD**—**A** = any ascending aorta involvement, **B** = all others
- **DEBAKEY**—**I** = ascending and at least aortic arch, **II** = ascending only, **III** = originates in descending and extends proximally or distally

RISK FACTORS

- **COMMON**—hypertension, age, male
- **VASCULITIS**—Takayasu arteritis, giant cell arteritis, rheumatoid arthritis, syphilitic aortitis
- **COLLAGEN DISORDERS**—Marfan syndrome, Ehlers–Danlos syndrome, cystic medial necrosis
- **VALVULAR**—bicuspid aortic valve, aortic coarctation, Turner syndrome, aortic valve replacement
- **OTHERS**—cocaine, trauma

CLINICAL FEATURES

RATIONAL CLINICAL EXAMINATION SERIES: DOES THIS PATIENT HAVE AN ACUTE THORACIC AORTIC DISSECTION?

	LR+	LR–
History		
Hypertension	1.6	0.5
Sudden chest pain	1.6	0.3
Tearing or ripping pain	1.2–10.8	0.4–0.99
Physical		
Pulse deficit	5.7	0.7
Focal neurological deficit	6.6–33	0.71–0.87
Diastolic murmur	1.4	0.9
CXR/ECG		
Enlarged aorta or wide mediastinum	2.0	0.3
LVH on ECG	0.2–3.2	0.84–1.2

APPROACH—"presence of tearing, ripping, or migrating pain may suggest dissection. Pulse deficit or focal neurological deficits greatly increase likelihood of dissection. Absence of pain of sudden onset decreases likelihood of dissection. Normal aorta and mediastinum on CXR help to exclude diagnosis"

JAMA 2002 287:17

D. Hui et al. (eds.), *Approach to Internal Medicine: A Resource Book for Clinical Practice*,
DOI 10.1007/978-3-319-11821-5_2, © Springer International Publishing Switzerland 2016

INVESTIGATIONS

BASIC

- **LABS**—CBCD, lytes, urea, Cr, troponin/CK × 3, glucose, AST, ALT, ALP, bilirubin, albumin, lipase, INR/PTT
- **IMAGING**—CXR, echocardiogram (TEE), CT chest or MRI chest
- **ECG**

SPECIAL

- **AORTOGRAPHY**

DIAGNOSTIC AND PROGNOSTIC ISSUES

CXR FINDINGS—wide mediastinum (>6 cm [2.4 in.]), indistinct aortic knuckle, pleural cap, difference in diameter between ascending and descending aorta, blurring of aortic margin secondary to local extravasation of blood, pleural effusion or massive hemothorax, displaced calcification (separation of the intimal aortic calcification from the edge of the aortic shadow >1 cm [0.4. in.])

PROGNOSIS

- **TYPE A**—with surgery, 1-month survival 75–80%, 10-year survival 55%

DIAGNOSTIC AND PROGNOSTIC ISSUES (CONT'D)

- **TYPE B**—with aggressive hypertensive treatment, 1-month survival >90%, 10-year survival 56%

MANAGEMENT

ABC—O_2 to keep sat >95%, IV, **antihypertensive therapy** (keep HR <60 and SBP <120 mmHg. *Labetalol* 2 mg/min IV loading drip, then 2–8 mg/min (target heart rate 55–60) or 20–80 mg IV q10 min, maximum 300 mg, then 200–400 mg PO BID. If SBP still >120 mmHg, *sodium nitroprusside* 0.25–0.5 μg/kg/min IV initially, then 0.25–3 μg/kg/min, maximum 10 μg/kg/min)

TREAT UNDERLYING CAUSE—**Type A** (emergent surgical repair, endovascular stenting, long-term blood pressure control). **Type B** (medical blood pressure control). Monitor over time with serial CT/MR chest

Related Topics
Acute Coronary Syndrome (p. 28)
Stroke (p. 337)

Acute Coronary Syndrome

ACCF/AHA 2013 STEMI Guidelines
ACCF/AHA 2007 UA/NSTEMI Guidelines
ACCF/AHA UA/NSTEMI 2012 Focused Update

DIFFERENTIAL DIAGNOSIS OF CHEST PAIN

CARDIAC

- **MYOCARDIAL**—myocardial infarction, angina (atherosclerosis, vasospasm), myocarditis
- **VALVULAR**—aortic stenosis
- **PERICARDIAL**—pericarditis
- **VASCULAR**—aortic dissection

RESPIRATORY

- **PARENCHYMAL**—pneumonia, cancer

DIFFERENTIAL DIAGNOSIS OF CHEST PAIN (CONT'D)

- **PLEURAL**—pneumothorax, pneumomediastinum, pleural effusion, pleuritis
- **VASCULAR**—pulmonary embolism

GI—esophagitis, esophageal cancer, GERD, peptic ulcer disease, Boerhaave's, cholecystitis, pancreatitis

OTHERS—musculoskeletal (costochondritis), shingles, anxiety

PATHOPHYSIOLOGY

	Pathologic changes	Clinical presentation
Pre-clinical	Atherosclerosis	Asymptomatic
Angina	Luminal narrowing	Central chest discomfort; worsened by exertion, emotion, and eating; relieved by rest and nitroglycerine
Unstable angina	Plaque rupture or thrombus	Worsening pattern or rest pain; no elevation in troponin, with or without ECG changes of ischemia
NSTEMI	Partial occlusion	Non-ST elevation MI; elevation in troponin, with or without ECG changes of ischemia
STEMI	Complete occlusion	ST elevation MI; elevation in troponin, with distinct ST segment elevation in ≥2 contiguous leads, new LBBB, or posterior wall MI with reciprocal ST depression in precordial leads on ECG

PATHOPHYSIOLOGY (CONT'D)

THIRD UNIVERSAL DEFINITION OF MYOCARDIAL INFARCTION (MI)

- **TYPE 1**—spontaneous MI due to a primary coronary event (atherosclerotic plaque rupture or erosion with acute thromboembolism)
- **TYPE 2**—MI secondary to an ischemic imbalance (supply demand mismatch)
- **TYPE 3**—MI resulting in death when biomarker values are unavailable (sudden unexpected cardiac death before serum biomarkers collected for measurement)
- **TYPE 4**—MI related to PCI (4A) or stent thrombosis (4B)
- **TYPE 5**—MI related to CABG

RISK FACTORS

- **MAJOR**—diabetes, hypertension, dyslipidemia, smoking, family history of premature CAD, advanced age, male gender
- **ASSOCIATED**—obesity, metabolic syndrome, sedentary lifestyle, high-fat diet
- **EMERGING**—lipoprotein abnormalities, inflammation (↑ CRP), chronic infections, chronic kidney disease

POST–MI COMPLICATIONS—arrhythmia (VT/VF, bradycardia), sudden death, papillary muscle rupture/dysfunction, myocardial rupture (ventricular free wall, interventricular septum), ventricular aneurysm, valvular disease (especially acute mitral regurgitation), heart failure/cardiogenic shock, peri-infarction pericarditis, post-cardiac injury pericarditis (Dressler's syndrome)

CLINICAL FEATURES

CHEST PAIN EQUIVALENTS—dyspnea, syncope, fatigue, particularly in patients with diabetic neuropathy who may not experience chest pain

NEW YORK HEART ASSOCIATION (NYHA) CLASSIFICATION

- **I** = no symptoms with ordinary physical activity
- **II** = mild symptoms with normal activity (walking >2 blocks or 1 flight of stairs)
- **III** = symptoms with minimal exertion
- **IV** = symptoms at rest

CANADIAN CARDIOVASCULAR SOCIETY (CCS) CLASSIFICATION

- **I** = angina with strenuous activity
- **II** = slight limitation, angina with meals/cold/stress
- **III** = marked limitation, angina with walking <1–2 blocks or 1 flight of stairs
- **IV** = unstable angina
  - **IVA** = unstable angina resolves with medical treatment

CLINICAL FEATURES (CONT'D)

  - **IVB** = unstable angina on oral treatment, symptoms improved but angina with minimal provocation
  - **IVC** = unstable angina persists, not manageable on oral treatment or hemodynamically unstable

KILLIP CLASS CLASSIFICATION

- **I** = no evidence of heart failure
- **II** = mild to moderate heart failure (S3, lung rales less than half way up, or jugular venous distension)
- **III** = overt pulmonary edema
- **IV** = cardiogenic shock

RATIONAL CLINICAL EXAMINATION SERIES: IS THIS PATIENT HAVING A MYOCARDIAL INFARCTION?

	LR+
History	
Pain radiation to the shoulder OR both arms	*4.1*
Pain radiation to right arm	*3.8*
Radiation to left arm	2.2
Radiation to both arms	*9.7*
Vomiting	*3.5*
Ex-smoker	*2.5*
Diaphoresis	2.0
Pleuritic chest pain	0.2
Sharp or stabbing chest pain	0.3
Positional chest pain	0.3
Chest pain reproducible by palpation	0.2–0.4
Physical	
Hypotension	3.1
S3	3.2
Pulmonary crackles	2.1
ECG	
New ST elevation ≥1 mm	5.7–53.9
New Q wave	5.3–24.8
Any ST elevation	11.2
New conduction defect	6.3
New ST depression	3.0–5.2
Any Q wave	3.9
Any ST depression	3.2
T wave peaking or inversion ≥1 mm	3.1
New T wave inversion	2.4–2.8
Any conduction defect	2.7
Multivariate Prediction Models	
ACI-TIPI (Acute Cardiac Ischemia Time Insensitive Predictive Instrument)	*3.9–12*
Goldman Protocol	*2.9–3.6*

APPROACH—"radiation of chest pain, diaphoresis, hypotension, and S3 suggest acute MI. Chest pain that is pleuritic, sharp or stabbing, positional or reproduced by palpation decreases likelihood of acute MI. On ECG, any ST ↑, new Q waves, or new conduction Δ make acute MI very likely. Normal ECG is very powerful to rule out MI"

JAMA 1998 280:14

CLINICAL FEATURES (CONT'D)

UPDATE—"after clinical symptoms are used to identify patients with possible ischemia, the ECG and troponin results take precedence in making the diagnosis. The presence of diabetes, HTN, or dyslipidemia should not affect clinician's probability estimate that an episode of chest pain represents an ACI"

The Rational Clinical Examination. McGraw-Hill, 2009

INVESTIGATIONS

BASIC

- **LABS**—CBCD, lytes, urea, Cr, troponin/CK × 3 q6-8 h, BNP or NT-pro-BNP, AST, ALT, ALP, bilirubin, INR/PTT, Mg, Ca, PO_4, albumin, lipase, fasting lipid profile, random and fasting glucose, HbA1C
- **IMAGING**—CXR, echocardiogram (first 72 h), MIBI/thallium (>5 days later)
- **ECG**—q8h × 3 or with chest pain
- **STRESS TESTS**—ECG, echocardiogram, MIBI once stable (>48 h post-MI)
- **CORONARY CATHETERIZATION**

DIAGNOSTIC AND PROGNOSTIC ISSUES

RISK STRATIFICATION FOR STABLE CORONARY DISEASE

- **ECG EXERCISE STRESS TEST**
  - **ABSOLUTE CONTRAINDICATIONS**—recent myocardial infarction (<4 days), unstable angina, severe symptomatic LV dysfunction, life-threatening arrhythmia, acute pericarditis, aortic dissection, PE, severe symptomatic aortic stenosis
  - **GOAL**—keep on treadmill until subject reaches 85–90% of age-predicted heart rate (220–age)
  - **ISCHEMIA CRITERIA**— ≥ 1 mm horizontal or down-sloping ST ↓ over multiple leads, or ST ↑ → myocardial ischemia (sens 68%, spc 77%) → proceed to angiogram
  - **INCONCLUSIVE**—premature termination due to chest pain/poor exercise tolerance → proceed to pharmacological stress test
  - **DUKE TREADMILL SCORE**—(exercise time in minutes) − 5 × (maximum ST ↓ in mm) − 4 × (treadmill angina index [0 = none, 1 = non-limiting, 2 = exercise limiting]). **Low risk** ≥ +5 (4-year survival 98–99%), **moderate risk** −10 to +4, **high risk** ≤ −11 (4-year survival 71–79%)
- **DIPYRIDAMOLE/ADENOSINE MIBI**—dipyridamole (Persantine) causes vasodilation. In CAD, the coronary artery is already maximally dilated to compensate, so addition of dipyridamole will not change perfusion to diseased vessel(s) further. This results in a relative perfusion mismatch compared to areas with normal dilatory reaction. Contraindicated in asthma/COPD. Antidote is aminophylline or caffeine
- **DOBUTAMINE ECHOCARDIOGRAPHY**—assesses wall motion abnormalities. Compared to MIBI, echocardiogram is more specific and less sensitive. Contraindicated in severe hypertension and arrhythmias

APPROACH TO DIAGNOSIS OF STABLE CAD—start with history, physical, rest ECG, and CXR. If low probability, do not investigate further. If high probability, proceed with management. If intermediate probability → stress test → cardiac CT, MIBI or stress echo → angiography

DIFFERENTIAL DIAGNOSIS OF TROPONIN ELEVATION

- **CARDIAC**—myocardial infarction, myocarditis, congestive heart failure, pericarditis, vasospasm, tachycardia with supply–demand mismatch, drug/cocaine ingestion, stress (takotsubo) cardiomyopathy
- **PULMONARY**—pulmonary embolism
- **HEPATIC**—liver failure
- **RENAL**—chronic kidney disease
- **NEUROLOGIC**—stroke, intracranial hemorrhage
- **SYSTEMIC**—sepsis, prolonged strenuous exercise

SERUM MARKERS

- **TROPONIN I/T**—rises within 4–6 h, peaks at 18–24 h, remains elevated 7–10 days (sens 40% at presentation, 40–70% after 6–9 h of symptoms)
- **CK/CKMB**—rises within 4–6 h, peaks at 18–24 h, remains elevated 3–4 days (sens 35–50% at presentation, 90% after 3 h in ER)
- **MYOGLOBIN**—rises within 1–2 h, peaks in few hours

Therefore, measure markers (e.g., troponin) at least twice separated by 6–8 h with serial ECG. Despite all appropriate investigations, missed MI rate is 2–5%

ECG CHANGES IN ACUTE MI—see APPROACH TO ECG p. 73

TIMI SCORE FOR PATIENTS WITH UNSTABLE ANGINA/NSTEMI

- **SCORING** (out of 7)—age ≥65, ≥3 CAD risk factors, known CAD (stenosis >50%), ASA use within prior 7 days, ≥2 angina episodes within 24 h, ↑ cardiac markers, ST deviation ≥0.5 mm

DIAGNOSTIC AND PROGNOSTIC ISSUES (CONT'D)

- **RISK GROUPS**—**low** = 0–2, **intermediate** = 3–4, **high** = 5–7. Consider GPIIb/IIIa and early angiography with revascularization in intermediate or high-risk groups
- **RISK OF DEATH, MI OR REVASCULARIZATION IN 14 DAYS**—0/1 = 4.7%, 2 = 8.3%, 3 = 13.2%, 4 = 19.9%, 5 = 26.2%, 6/7 = 40.9%

GRACE RISK SCORE FOR PATIENTS WITH UNSTABLE ANGINA/NSTEMI

- **SCORING** (based on regression model)—age, SBP, HR, creatinine, Killip class, cardiac arrest at admission, presence of ST segment deviation, elevation in serum cardiac enzymes/markers. Risk score calculated using online software: www.outcomes-umassmed.org/grace/acs_risk/acs_risk_content.html

Risk category	GRACE risk score	In-hospital death (%)
Low	≤108	<1
Intermediate	109–140	1–3
High	>140	>3

Risk category	GRACE risk score	6-month death
Low	≤88	<3
Intermediate	89–118	3–8
High	>118	>8

TIMI SCORE FOR PATIENTS WITH STEMI

- **SCORING** (out of 14)—age (3 points = ≥75, 2 points = 65–74), any of diabetes, hypertension, or angina (1 point), systolic BP ≤100 mmHg (3 points), HR >100 (2 points), Killip class II–IV (2 points), weight <67 kg (1 point), anterior ST elevation or LBBB (1 point), time to reperfusion >4 h (1 point)
- **RISK OF DEATH IN 30 DAYS**—0 = 0.8%, 1 = 1.6%, 2 = 2.2%, 3 = 4.4%, 4 = 7.3%, 5 = 12.4%, 6 = 16.1%, 7 = 23.4%, 8 = 26.8%, >8 = 35.9%

IN-HOSPITAL OUTCOMES

	NSTEMI (%)	STEMI (%)
Death	4	6
Reinfarction	0.9	1.1
Cardiogenic shock	2.8	6.4
Stroke	0.7	0.8
Major bleeding	10	12

ACTION registry 2008/2009 data

ACUTE MANAGEMENT

ABC—O_2 to keep sat >95%, IVs, inotropes, consider balloon pump if hemodynamically unstable

PAIN CONTROL—**nitroglycerin** (*nitro drip* 25 mg in 250 mL D5W, start at 5 μg/min IV, then ↑ by 5–10 μg/min every 3–5 min to 20 μg/min, then ↑ by 10 μg/min every 3–5 min up to 200 μg/min, or until relief of pain, stop titration if SBP is <100 mmHg. *Nitro patch* 0.4 mg/h daily. *Nitro spray* 0.4 mg SL q5min × 3. Beware if suspect right ventricular infarction or if patients on sildenafil). ***Morphine*** 2–4 mg IV every 5–15 min PRN

CLOT CONTROL

- **ANTIPLATELET**—***ASA*** 162–325 mg PO chew × 1 dose, then 75–100 mg PO daily indefinitely. $P2Y_{12}$ receptor blockade with ***clopidogrel*** 300–600 mg × 1 dose then 75 mg PO daily for 1 year; or ***ticagrelor*** 180 mg × 1 dose, then 90 mg PO BID for 1 year; or ***prasugrel*** (with PCI only; do not give if history of CVA or TIA, or age ≥75 years) 60 mg × 1 dose then 10 mg daily for 1 year. Combination ASA plus clopidogrel for minimum of 1 month (ideally 1 year)-post PCI with bare-metal stent, or minimum 12 months (possibly indefinitely) for drug-eluting stents. Consider **GPIIb/IIIa inhibitor** if intermediate/high-risk NSTEMI, treated with PCI, and pain unresponsive to nitroglycerin (*tirofiban* 0.4 μg/kg/min × 30 min IV, then continue 0.1 μg/kg/min × 18–24 h; *eptifibatide* 180 μg/kg IV bolus, then 2 μg/kg/min × 18–24 h; or, *abciximab* 0.25 mg/kg IV bolus, then 0.125 μg/kg/min × 12 h)
- **ANTICOAGULATION**—options include **LMWH** (*enoxaparin* 30 mg IV bolus, then 1 mg/kg SC BID for STEMI [no IV bolus for NSTEMI], caution if renal failure or age >75) or **unfractionated heparin** (*unfractionated heparin* 70 U/kg [up to 4,000 U] IV bolus, then 18 U/kg/h [up to 1,000 U/h] and adjust to 1.5–2.5× normal PTT for 72 h). **Factor Xa inhibitors** (*fondaparinux* 2.5 mg SC daily until discharge or 8 days, caution if renal failure). **Direct thrombin inhibitors** (*bivalirudin* 0.1 mg/kg IV bolus then 0.25 mg/kg/h initially, followed by second 0.5 mg/kg bolus before PCI and 1.75 mg/kg/h during PCI, then continue infusion for up to 4 h post-PCI, if needed)
- **REPERFUSION THERAPY**—see **PCI** for details. **Fibrinolytics** for STEMI (*alteplase* 15 mg IV over 2 min, then 0.75 mg/kg over 30 min [maximum 50 mg], then 0.5 mg/kg over 60 min

ACUTE MANAGEMENT (CONT'D)

[overall maximum 100 mg]; or *tenecteplase* IV bolus over 5 s, weight-based dosing: 30 mg for weight <60 kg, 35 mg for 60–69 kg, 40 mg for 70–79 kg, 45 mg for 80–89 kg, 50 mg for ≥90 kg])

RATE CONTROL—start with *metoprolol tartrate* [immediate release] 25 mg PO q6-12 h. Titrate as tolerated up to maximum dose of *metoprolol tartrate* [immediate release] 100 mg PO q12h or *metoprolol succinate* [extended release] 200 mg PO daily. Alternatively, *carvedilol* 6.25 mg PO BID and titrate as tolerated up to 25 mg PO BID. The goal heart rate is 50–55 with normal activity. If ongoing ischemia or refractory hypertension at the time of presentation, may also consider *metoprolol tartrate* 5 mg IV q5min, up to 3 doses. Avoid if HF, low-output state, presence of prolonged first-degree or high-grade AV block, history of reactive airways disease, or MI precipitated by cocaine use. If β-blocker contraindicated, consider non-dihydropyridine calcium channel blockers (*diltiazem* 30–120 mg PO QID or *verapamil* 80–120 mg PO TID [contraindicated if LV dysfunction])

LIPID CONTROL—high-intensity statin such as *atorvastatin* 80 mg PO daily or *rosuvastatin* 40 mg PO daily

BLOOD PRESSURE SUPPORT—for patients with cardiogenic shock, consider IV fluids, inotropes (dobutamine/dopamine), balloon pump, and early revascularization

OVERALL APPROACH

	Stable angina	Unstable angina or NSTEMI	STEMI
ASA	✓	✓	✓
Nitrates	✓	✓	✓
Morphine	±	✓	✓
β-blockers	✓	✓	✓
ACE inhibitors or ARBs	✓	✓	✓
HMG-CoA inhibitors	✓	✓	✓
Heparin or antithrombin	NO	✓	✓
$P2Y_{12}$ inhibitors	NO	✓	✓
GPIIb/IIIa inhibitors	NO	✓ (consider)	NO
Fibrinolytics or PCI[a]	NO	NO	✓
Cardiology consult	Outpatient[b]	CCU[c]	CCU[c]

[a]If initial presentation is to a PCI-capable hospital, then primary PCI should be performed within 90 min from time of first medical contact (FMC). If initial presentation is to a non-PCI-capable hospital, then arrange urgent transfer to PCI-capable hospital if primary PCI can be performed within 120 min from time of FMC. If timely PCI cannot be provided, administer fibrinolytic within 30 min of FMC. Urgent CABG is also an option post-catheterization

[b]Outpatient cardiology for stress test

[c]CCU consult for risk stratification, monitoring, PCI, and/or CABG

ACUTE MANAGEMENT (CONT'D)

CAUTIONS IN TREATMENT OF ACUTE MYOCARDIAL INFARCTION—avoid negative inotropic agents such as β-blockers and non-dihydropyridine calcium channel blockers if clinical heart failure. Avoid administration of nitroglycerin, morphine, and diuretics to patients with right ventricular infarction as these medications can cause venodilation and decrease preload, leading to hypotension

LONG-TERM MANAGEMENT OF CORONARY ARTERY DISEASE

ANTIANGINAL—nitroglycerin (*nitro patch* 0.4–0.8 mg/h daily; nitro spray 0.4 mg SL q5 min × 3; *isosorbide mononitrate* 30 mg PO daily, maximum 240 mg), **β-blocker** (*metoprolol tartrate* [immediate release] 25–100 mg PO BID, *metoprolol succinate* [extended release] *50–200 mg PO daily*, carvedilol 6.25–25 mg PO BID, *bisoprolol* 5–10 mg PO daily), **calcium channel blocker** (*amlodipine* 5–10 mg PO daily)

LONG-TERM MANAGEMENT OF CORONARY ARTERY DISEASE (CONT'D)

ACE INHIBITOR—*ramipril* 2.5–10 mg PO BID, lisinopril 2.5–10 mg PO daily, trandolapril 0.5–4 mg PO daily, perindopril 2–8 mg PO daily. If ACE inhibitor not tolerated, use ARB

ANTIPLATELET—***ECASA*** 81 mg PO daily indefinitely. P2Y12 receptor blockade (***clopidogrel*** 75 mg PO daily; ***ticagrelor*** 90 mg PO BID, or ***prasugrel*** 10 mg PO daily) generally for 1 year after ACS. Combination ASA plus clopidogrel for minimum of 1 month (ideally 1 year)-post PCI with bare-metal stent, or minimum 12 months (possibly indefinitely) for drug-eluting stents. Consider ticagrelor or prasugrel if received PCI

ANTICOAGULATION—controversial especially in combination with ASA and/or $P2Y_{12}$ inhibitor. May be considered for patients post-STEMI or NSTEMI with one of the following criteria: (1) atrial fibrillation, (2) left ventricular thrombus, (3) significant left ventricular dysfunction with extensive regional wall motion abnormalities. Start *warfarin* 5 mg daily within 72 h and continue heparin/LMWH until INR is between 2 and 3 (unless planning angioplasty). Beware bleeding risk. If possible, minimize duration of "triple therapy" (i.e., ASA, $P2Y_{12}$ inhibitor, and warfarin), consider GI protection with proton-pump inhibitor, and target lower INR (e.g., 2.0-2.5)

RISK REDUCTION ★ABCDEFG★

- **ASA/ACE INHIBITOR/ARB**
- **BLOOD PRESSURE CONTROL** (see HYPERTENSION p. 65)
- **CHOLESTEROL CONTROL** (see DYSLIPIDEMIA p. 70)
- **DIABETIC CONTROL** (see DIABETES p. 381)
- **EXERCISE** (30 min of moderate-intensity exercise 3–4×/week)
- **FAT REDUCTION** (see OBESITY ISSUES p. 457)
- **GET GOING TO QUIT SMOKING!** (see SMOKING ISSUES p. 480)

DRIVING POST-MYOCARDIAL INFARCTION—see p. 490 for details

TREATMENT ISSUES

RIGHT VENTRICULAR INFARCTION—evidence of inferior MI should automatically trigger one to check right-sided leads (V4R) to assess for the possibility of RV infarction, which occurs in about 50% of patients with inferior MI. May see increased JVP, Kussmaul sign, and clear lungs clinically. ST elevation in V4R is diagnostic and prognostic. Hypotension should be treated with fluid bolus to ensure good preload

TREATMENT ISSUES (CONT'D)

POSTERIOR INFARCTION—ST depression in V1–V2 in a regular ECG should automatically trigger one to request for posterior (V7–V9) leads to check for posterior MI. Posterior infarct may be associated with inferior infarcts (90%) and lateral infarcts (10%) as the PDA may be supplied by the right or left circumflex coronary artery

POST-MI RISK STRATIFICATION

- **EXTENT OF INFARCT/RESIDUAL FUNCTION**—assessment is based on clinical factors (↑ HR, ↓ BP, Killip class, diabetes, renal failure, ↑ WBC, GRACE risk score, TIMI risk score), ECG, biomarkers (CK, troponin), imaging (echocardiogram, MIBI, cardiac MRI), and angiography. Early measurement of LV function, although of prognostic importance, is misleading as myocardium function may improve in first 2 weeks. Medical management according to risk
- **EXTENT OF MYOCARDIUM AT RISK**—assessment is based on exercise stress test, stress echocardiogram, stress sestamibi (ischemic tissue), thallium scan (viable tissue), PET scan, cardiac MRI, angiography. Angioplasty or CABG should be considered
- **RISK OF ARRHYTHMIA**—high risk of VF/VT within the first 48 h, therefore monitor with telemetry. If it occurs after 48 h, consider antiarrhythmics and early ICD

BALLOON PUMP—a long balloon in the descending aorta that deflates during systole and inflates during diastole to augment coronary perfusion and cardiac output as well as decrease afterload. Reasonable for severe refractory ischemia and hemodynamic instability. May be used in conjunction with inotropes. Contraindicated in aortic regurgitation, AAA, aortic dissection, uncontrolled sepsis bleeding disorder, and severe PVD

FIBRINOLYTICS USE

- **INDICATIONS**—>120 min anticipated delay from first medical contact to primary PCI, ≥30 min of chest pain, patient presentation within 12 h (ideal door to needle time <30 min), ECG criteria (>1 mm ST ↑ in ≥2 contiguous leads, or new LBBB with suggestive history, age <75)
- **ABSOLUTE CONTRAINDICATIONS**—any intracranial hemorrhage; ischemic stroke within 3 months (except acute ischemic stroke within first 4.5 h); structural cerebral vascular lesion; malignant

TREATMENT ISSUES (CONT'D)

intracranial neoplasm; closed-head or facial trauma within 3 months; intracranial or intra spinal surgery within 2 months); severe uncontrolled hypertension (unresponsive to emergency therapy); suspected aortic dissection; bleeding diathesis or active bleeding (excluding menses)

- **RELATIVE CONTRAINDICATIONS**—chronic, poorly-controlled, severe hypertension; severe hypertension on presentation (>180/110 mmHg); ischemic stroke >3 months; dementia; other intracranial pathology (not already specified above); internal bleeding within 2–4 weeks; active peptic ulcer; major surgery within 3 weeks; non-compressible vascular punctures; use of anticoagulation therapy; pregnancy; traumatic CPR >10 min; prior exposure to streptokinase (if planning to use this fibrinolytic again)
- **RISK OF BLEEDING**—average risk of severe bleed is 1.8%. Increased risk with women, BP >165/95 mmHg, age >65, weight <70 kg [<154 lbs], and lysis with TPA (+0.5% absolute risk/factor)
- **PERSISTENT ST ELEVATION**—look for resolution of symptoms and ST elevation to decrease by >50% within 90 min of fibrinolytic therapy. Persistent ST elevation may suggest failed fibrinolytic therapy, and requires urgent rescue catheterization. Other causes of ST elevation include pericarditis, ventricular aneurysm, hyperkalemia, LBBB, and early repolarization abnormality

Related Topics
Aortic Dissection (p. 27)
Asystole (p. 495)
Diabetes Mellitus (p. 381)
ECG (p. 73)
Hyperlipidemia (p. 70)
Hypertension (p. 65)
Pericarditis (p. 35)
Shock (p. 108)
Smoking Cessation (p. 480)

TREATMENT ISSUES (CONT'D)

PERCUTANEOUS CORONARY INTERVENTION (PCI, PTCA)

- **INDICATIONS FOR ACUTE STEMI**—patient presents within 12 h of chest pain (at a PCI-capable hospital, ideal time from first medical contact to device or "FMC-to-device time" ≤90 min; if at a non-PCI-capable hospital requiring transfer for primary PCI, then ideal "FMC-to-device time" ≤120 min), ECG criteria (>1 mm ST ↑ in ≥2 contiguous leads, new or presumed new left bundle branch block), contraindications to fibrinolysis, or in patients in cardiogenic shock irrespective of time of MI onset
- **INDICATIONS FOR CHRONIC STABLE CAD**—single/double vessel disease refractory to medical therapy. Decision for revascularization (PCI vs. CABG) should follow assessment by heart team (interventional cardiology and cardiac surgery)
- **ADVERSE EVENTS**—access site (bleeding, hematomas, arteriovenous fistulae, pseudoaneurysms), contrast nephropathy, arrhythmia (VT, VF), stroke, dissection, myocardial infarction, death
- **BARE METAL STENTS VS. DRUG-ELUTING STENTS**—in-stent restenosis is due to fibrosis of coronary vasculature and usually happens 3 months post-procedure. Drug-eluting stents (sirolimus, paclitaxel, everolimus, or zotarolimus) are designed to inhibit cell proliferation and decrease the risk of in-stent restenosis. There has been some controversy regarding higher adverse events in patients with first generation drug-eluting stents (sirolimus or paclitaxel). The most recent outcomes research analysis suggests that newer-generation drug-eluting stents (everolimus or zotarolimus) are associated with a decreased rate of repeat revascularization, stent thrombosis, and no significant difference in mortality
- **BENEFITS**—primary PCI is generally preferred given the superior outcomes compared to fibrinolysis, particularly if (1) fibrinolysis contraindicated, (2) previous history of CABG, or (3) cardiogenic shock. However, patients who are able to seek medical attention within 1 h of chest pain onset, have allergy to contrast dye, or do not have access to PCI in a timely fashion should consider fibrinolytics

TREATMENT ISSUES (CONT'D)

OUTCOMES FOR FIBRINOLYTICS VS. PRIMARY PCI

	Fibrinolytics (%)	Primary PCI (%)
Non-fatal reinfarction	7	3
Stroke	2	1
Death (4–6 weeks)	7–9	5–7
Combined endpoint of death–fatal reinfarction and stroke	14	8

NEJM 2007 356:1; NEJM 2007 356:10; NEJM 2007 357:16

CORONARY ARTERY BYPASS GRAFT SURGERY

- **CORONARY ANATOMY**
  - **RIGHT CORONARY** (RCA)—gives rise to right marginal (RMA), right posterior descending (RPDA), and right posterolateral branches (RPL 1, 2, 3)
  - **LEFT MAIN** (LM)—gives rise to left anterior descending (LAD) → diagonal (D1, 2 3) and septals; ramus intermediate (Ram Int); and left circumflex (LCX) → obtuse marginal (OM 1, 2, 3)
  - **DOMINANT ARTERY**—defined as the artery that supplies PDA and at least one posterolateral (PL) artery
- **INDICATIONS**—studies suggest CABG provides mortality benefit for specific subgroups, including patients with (1) left main disease >50% occlusion, (2) two vessel disease with

TREATMENT ISSUES (CONT'D)

significant involvement of proximal left anterior descending, and (3) diffuse triple vessel disease. Diabetic patients and those with reduced left ventricular function derive more benefit from bypass surgery. Angiographic disease severity should be assessed using the SYNTAX score. Decision for revascularization (PCI vs. CABG) should follow assessment by heart team (interventional cardiology and cardiac surgery)

- **MORBIDITY BENEFIT**—95% have improvement of symptoms immediately after surgery, 75% symptom free at 5 years. Recurrent disease more common in vein grafts than artery grafts
- **GRAFTS**—saphenous veins from calf or thigh (SVG), internal mammary arteries (LIMA/RIMA), radial arteries (RA), and gastroepiploic artery from stomach (GA). A total of 90% of arterial graft and 50% of vein graft remain patent by 10 years
- **COMPLICATIONS**
  - **CARDIAC**—MI 2–4%, arrhythmia (AF 40%, sustained VT/VF 2–3%), AV block requiring pacemaker 0.8–4%, pericarditis/tamponade, aortic dissection
  - **NEUROLOGICAL**—stroke, postoperative delirium, cognitive impairment, depression, phrenic nerve damage, intercostal nerve damage
  - **OTHERS**—renal failure, bleeding, infection, pleural effusions, death
- **MEDICATIONS**—hold clopidogrel or ticagrelor 5–7 days prior to CABG. Continue ASA before and after surgery

Pericardial Diseases: Pericarditis and Tamponade

DIFFERENTIAL DIAGNOSIS

★MINT★

METABOLIC—uremia, dialysis, hypothyroidism
MEDICATIONS—procainamide, hydralazine, INH, phenytoin, penicillin
INFARCTION—MI (early, late)
INFECTIOUS—HIV, Coxsackie, echovirus, adenovirus, TB

DIFFERENTIAL DIAGNOSIS (CONT'D)

INFLAMMATORY—psoriatic arthritis, enteric arthritis, rheumatoid arthritis, SLE, mixed connective tissue disease

IDIOPATHIC

NEOPLASTIC—primary (mesothelioma), metastasis (breast, lung, melanoma), leukemia, lymphoma
TRAUMA—stab, gunshot wound, blunt, CPR, postpericardiotomy

CLINICAL FEATURES

RATIONAL CLINICAL EXAMINATION SERIES: DOES THIS PATIENT WITH A PERICARDIAL EFFUSION HAVE CARDIAC TAMPONADE?

	Sens (%)
History	
Dyspnea	87–89
Fever	25
Chest pain	20
Cough	7–10
Physical	
Tachycardia	77
Pulsus paradoxus >10 mmHg[a]	82
Elevated JVP	76
↓ heart sounds	28
Hypotension	26
Hypertension	33
Tachypnea	80
Peripheral edema	21–28
Pericardial rub	19–29
Hepatomegaly	28–55
Kussmaul sign	26
ECG	
Low voltage	42
Atrial arrhythmia	6
Electrical alternans	16–21
ST elevation	18–30
PR depression	18

[a]Pulsus paradoxus LR+ 3.3, LR– 0.03

APPROACH—"among patients with cardiac tamponade, a minority will not have dyspnea, tachycardia, elevated JVP, or cardiomegaly on chest radiograph. A pulsus paradoxus >10 mmHg among patients with a pericardial effusion helps distinguish those with cardiac tamponade from those without. Diagnostic certainty of the presence of tamponade requires additional testing"

JAMA 2007 297:16

DISTINGUISHING FEATURES OF ACUTE TAMPONADE AND CHRONIC CONSTRICTIVE PERICARDITIS

	Acute tamponade	Constrictive pericarditis
Vitals	Tachycardia, hypotension +++, **pulsus paradoxus**	Hypotension, pulsus paradoxus (rare)
JVP	Elevated, Kussmaul (rare) Prominent *x*′ descent but blunted *y* descent	Elevated, **Kussmaul** Prominent *x*′ and *y* descent (Friedrich's sign)
Apex beat	Impalpable	Impalpable
Heart sounds	Distant	Distant, early S3/knock
Other features	Dullness and bronchial breath sounds over left base (Ewart sign)	Hepatosplenomegaly, edema

INVESTIGATIONS

BASIC

- **LABS**—CBCD, lytes, urea, Cr, troponin, CK
- **IMAGING**—CXR (calcification if constrictive disease), echocardiogram
- **ECG**—may have sinus tachycardia, low voltages, and electrical alternans in tamponade/effusion; diffuse ST elevation (concave up) and PR depression may be seen in pericarditis

SPECIAL

- **PERICARDIOCENTESIS**—diagnostic or therapeutic (for tamponade, TB/bacterial pericarditis, or large persistent effusion)
- **PERICARDIOSCOPY**
- **CT/MRI CHEST**—if suspect constrictive pericarditis

MANAGEMENT

ACUTE PERICARDITIS—NSAIDs (*indomethacin* 25–50 mg PO TID, *ibuprofen* 600–800 mg PO TID×2–4 weeks, or until resolution of pain) for most cases of idiopathic or viral pericarditis, but avoid after acute MI. If post-MI, ***ASA*** 650 mg PO TID×3–4 weeks. Adjuvant ***colchicine*** 0.6 mg PO BID×3 months in addition to NSAID/ASA to reduce risk of recurrence. ***Prednisone*** 0.25–0.5 mg/kg PO daily×2 weeks (followed by taper) may be considered for connective tissue-mediated disease, although symptoms may recur upon withdrawal

RECURRENT PERICARDITIS—*ASA* 650 mg PO TID×4–8 weeks or **NSAIDs** (*indomethacin* 25–50 mg PO TID, *ibuprofen* 600–800 mg PO TID×4–8 weeks). Add ***colchicine*** (0.6 mg PO BID×3–6 months) for longterm prophylaxis. Avoid anticoagulation as risk of hemopericardium. ***Prednisone*** 0.25–0.5 mg/kg PO daily may also be useful, although symptoms may recur upon withdrawal

MANAGEMENT (CONT'D)

TAMPONADE—ABC, $\mathbf{O_2}$, IV's, bolus IV fluids, **pericardiocentesis** (subxyphoid blind approach, echocardiogram-guided parasternal or apical approach), **pericardiectomy**, **pericardial window** if recurrent/malignant effusion. Avoid nitroglycerin and morphine if tamponade as they may decrease preload, leading to worsening of cardiac output

CONSTRICTIVE PERICARDITIS—complete pericardiectomy

SPECIFIC ENTITIES

ACUTE PERICARDITIS—may be preceded by upper respiratory tract infection. Diagnosis is based on any two of the following inflammatory signs (LR+ 5.4): fever, pericardial friction rub (three components), characteristic chest pain (better with upright position and leaning forward, or pleuritic), PR depression, and diffuse ST elevation. Large effusion without inflammatory signs or tamponade suggests chronic idiopathic pericardial effusion (LR+ 20)

RECURRENT PERICARDITIS—returns in days to weeks upon stopping medications. Likely causes include rheumatologic disorders, Dressler's syndrome, and post-pericardiotomy syndrome

TAMPONADE—a *clinical* diagnosis based on dyspnea, tachycardia, hypotension, pulsus paradoxus, and elevated JVP. Tamponade causes restriction in left or right ventricular diastolic filling. Tamponade with inflammatory signs suggests malignant effusion (LR+ 2.9)

CONSTRICTIVE PERICARDITIS—contraction of pericardium due to chronic inflammation, leading to left and/or right heart failure. May follow pericarditis or radiation. May be difficult to distinguish from restrictive cardiomyopathy clinically

Heart Failure

NEJM 2003 348:20
Canadian Heart Failure Guidelines 2006
Canadian Heart Failure Guidelines Updates 2017–2013

DIFFERENTIAL DIAGNOSIS OF HF EXACERBATION/DYSPNEA

CARDIAC

- **MYOCARDIAL**—HF exacerbation, myocardial infarction
- **VALVULAR**—aortic stenosis, acute aortic regurgitation, mitral regurgitation/stenosis, endocarditis
- **PERICARDIAL**—tamponade
- **DYSRHYTHMIA**

DIFFERENTIAL DIAGNOSIS OF HF EXACERBATION/DYSPNEA (CONT'D)

RESPIRATORY

- **AIRWAY**—COPD exacerbation, asthma exacerbation, acute bronchitis, bronchiectasis, foreign body obstruction
- **PARENCHYMA**—pneumonia, cryptogenic organizing pneumonia, ARDS, interstitial lung disease exacerbation

DIFFERENTIAL DIAGNOSIS OF HF EXACERBATION/DYSPNEA (CONT'D)

- **VASCULAR**—pulmonary embolism, pulmonary hypertension
- **PLEURAL**—pneumothorax, pleural effusion

SYSTEMIC—sepsis, ARDS, metabolic acidosis, anemia, neuromuscular, psychogenic, anxiety

PATHOPHYSIOLOGY

ANATOMIC/PHYSIOLOGIC CLASSIFICATION OF CARDIOMYOPATHY

- **DILATED** (dilatation and impaired contraction of one or both ventricles)—idiopathic, ischemic, valvular, viral, genetic, late manifestation of hypertrophic heart disease, tachycardia induced, alcohol induced, peripartum
- **HYPERTROPHIC** (disorder with disproportionate hypertrophy of the left ventricle and occasionally right ventricle)—**idiopathic** (autosomal dominant inheritance with incomplete penetrance), **storage disease** (Fabry's disease, Pompe disease, Hurler's syndrome, Noonan's syndrome), athlete's heart, obesity, amyloid
- **RESTRICTIVE** (non-dilated ventricles with impaired ventricular filling)—idiopathic familial, **infiltrative** (amyloidosis, hemochromatosis, sarcoidosis), drugs, radiation, endomyocardial fibrosis
- **ARRHYTHMOGENIC RIGHT VENTRICULAR** (replacement of right ventricular free wall with fatty tissue)—arrhythmogenic right ventricular dysplasia
- **UNCLASSIFIABLE**—endocardial fibroelastosis, left ventricular non-compaction

ETIOLOGIC CLASSIFICATION OF CARDIOMYOPATHY

- **ISCHEMIC CARDIOMYOPATHY** (mostly dilated)—varying degrees of persistent ischemia, infarction, and left ventricular remodeling
- **VALVULAR CARDIOMYOPATHY** (mostly dilated)—abnormal loading conditions and secondary left ventricular remodeling and dysfunction
- **HYPERTENSIVE CARDIOMYOPATHY** (dilated, restrictive)—left ventricular hypertrophy and dysfunction
- **DIABETIC CARDIOMYOPATHY** (dilated)—left ventricular dysfunction in the absence of atherosclerosis or hypertension
- **INFLAMMATORY CARDIOMYOPATHY** (mostly dilated)—**infectious** (diphtheria, rheumatic fever, scarlet fever, typhoid fever, meningococcal, TB, Lyme disease, Leptospirosis, RMSF, poliomyelitis, influenza, mumps, rubella, rubeola, variola, varicella, EBV, Coxsackie virus, echovirus, CMV, hepatitis, rabies, mycoplasma, psittacosis, arboviruses, histoplasmosis, cryptococcosis, Chagas disease), **autoimmune**, **idiopathic** myocardial inflammatory diseases

PATHOPHYSIOLOGY (CONT'D)

- **METABOLIC CARDIOMYOPATHY** (dilated, restrictive, and/or hypertrophic)—**endocrine** (thyrotoxicosis, hypothyroidism, acromegaly, pheochromocytoma), **storage diseases** (glycogen storage disease, Fabry's disease, Gaucher's disease, Niemann–Pick disease), **nutritional deficiencies** (Beriberi, Kwashiorkor, pellagra), **deposition** (amyloidosis, hemochromatosis, sarcoidosis)
- **MUSCULAR DYSTROPHIES** (mostly dilated)—Duchenne, Becker's, myotonic dystrophy
- **NEUROMUSCULAR**—Friedreich's ataxia (hypertrophic), Noonan's syndrome, lentiginosis
- **GENERAL SYSTEMIC DISEASE** (mostly dilated)—**connective tissue diseases** (rheumatoid heart disease, ankylosing spondylitis, SLE, scleroderma, dermatomyositis), granulomatous (sarcoidosis, Wegener's granulomatosis, granulomatous myocarditis), **other inflammatory** (giant cell myocarditis, hypersensitivity myocarditis), **neoplasm** (primary, secondary, restrictive pattern)
- **SENSITIVITY AND TOXIC REACTIONS** (mostly dilated)—alcohol, amphetamine, arsenic, catecholamines, cocaine, anthracyclines, zidovudine, radiation (restrictive as well)
- **PERIPARTUM** (dilated)—see p. 471

FUNCTIONAL CLASSIFICATION OF HEART FAILURE

- **SYSTOLIC DYSFUNCTION** (↓ LVEF <45%)—S3 (dilated ventricle with volume overload). Mechanisms include decreased contractility and increased afterload. Causes include MI, cardiomyopathy (dilated, infiltrative), valvular (aortic regurgitation, mitral regurgitation, "burned out" aortic stenosis), "burned out" hypertension and myocarditis
- **DIASTOLIC DYSFUNCTION** (normal LVEF)—S4 (stiff ventricle), LVH, ↓ ventricular relaxation, normal LVEF, ↑ chamber pressures. Mechanisms include decreased active relaxation and passive relaxation (stiff ventricle). Causes include ischemia, hypertension, valvular (aortic stenosis), cardiomyopathy (restrictive, hypertrophic), and pericardial disease
- **MIXED DYSFUNCTION**—in many cases, diastolic dysfunction is present with systolic heart failure

PATHOPHYSIOLOGY (CONT'D)

PRECIPITANTS OF HF ★FAILURE★

- **F**orget to take medications (non-adherence)
- **A**rrhythmia, anemia
- **I**nfection, ischemia, infarction
- **L**ifestyle change

PATHOPHYSIOLOGY (CONT'D)

- **U**pregulators (thyroid, pregnancy)
- **R**heumatic heart disease, acute valvular disease
- **E**mbolism

CLINICAL FEATURES

DISTINGUISHING FEATURES BETWEEN COPD AND HEART FAILURE

	COPD	Heart Failure
History	Previous COPD Medications	Previous HF Medications
Inspect	Nicotine stain, barrel chest Laryngeal height <4 cm	
Cardiac exam	Subxyphoid cardiac pulse	Elevated JVP, S3, S4
Resp. exam	Hyperresonance Prolonged expiratory time	Bilateral crackles
Investigations	CXR shows hypeinflation ABG shows hypercapnia and hypoxemia	CXR shows redistribution and cardiomegaly ABG shows hypoxemia Elevated BNP

CLINICAL FEATURES (CONT'D)

LEFT HEART FAILURE—left-sided S3, rales, wheezes, tachypnea. Causes include previous MI, aortic stenosis, and left-sided endocarditis

RIGHT HEART FAILURE—right-sided S3, ↑ JVP, ascites, hepatomegaly, peripheral edema. Causes include left heart failure, pulmonary hypertension, right ventricular MI, mitral stenosis, and right-sided endocarditis

CLINICAL FEATURES (CONT'D)

GRADING OF PITTING EDEMA—**0** = no edema, **1** = trace edema, **2** = moderate edema disappears in 10–15 s, **3** = stretched skin, deep edema disappears in 1–2 min, **4** = stretched skin, fluid leaking, very deep edema present after 5 min

RATIONAL CLINICAL EXAMINATION SERIES: DOES THIS DYSPNEIC PATIENT IN THE EMERGENCY DEPARTMENT HAVE CONGESTIVE HEART FAILURE?

	Sens (%)	Spc (%)	LR+	LR–
History				
Initial clinical judgment	61	80	4.4	0.45
Hx heart failure	60	90	5.8	0.45
Myocardial infarction disease	40	87	3.1	0.69
Coronary artery	52	70	1.8	0.68
Dyslipidemia	23	87	1.7	0.89
Diabetes	28	83	1.7	0.86
Hypertension	60	56	1.4	0.71
Smoker	62	27	0.84	1.4
COPD	34	57	0.81	1.1
PND	41	83	2.6	0.70
Orthopnea	50	77	2.2	0.65
Edema	51	76	2.1	0.64
Dyspnea on exertion	84	34	1.3	0.48
Fatigue and weight gain	31	70	1.0	0.99
Cough	36	61	0.93	1.0

CLINICAL FEATURES (CONT'D)

	Sens (%)	Spc (%)	LR+	LR–
Physical				
S3	13	99	11	0.88
AJR	24	96	6.4	0.79
JVD	39	92	5.1	0.66
Rales	60	78	2.8	0.51
Any murmur	27	90	2.6	0.81
Lower extremity edema	50	78	2.3	0.64
Valsalva maneuver	73	65	2.1	0.41
SBP <100 mmHg	6	97	2.0	0.97
S4	5	97	1.6	0.98
SBP ≥150 mmHg	28	73	1.0	0.99
Wheezing	22	58	0.52	1.3
Ascites	1	97	0.33	1.0
CXR				
Pulmonary venous congestion	54	96	12	0.48
Interstitial edema	34	97	12	0.68
Alveolar edema	6	99	6.0	0.95
Cardiomegaly	74	78	3.3	0.33
Pleural effusions	26	92	3.2	0.81
Any edema	70	77	3.1	0.38
Pneumonia	4	92	0.50	1.0
Hyperinflation	3	92	0.38	1.1
ECG				
Atrial fibrillation	26	93	3.8	0.79
New T wave changes	24	92	3.0	0.83
Any abnormal finding	50	78	2.2	0.64
ST elevation	5	97	1.8	0.98
ST depression	11	94	1.7	0.95
BNP				
BNP ≥ 250 pg/mL			*4.6*	
BNP ≥ 100 pg/mL[a]			*2.7*	
BNP ≥ 50 pg/mL			*1.7*	*0.06*

[a]For patients with an estimated GFR of 15–60 mL/min/1.73 m^2, a threshold of 201 pg/mL can be used

APPROACH—"the features evaluated in more than one study with the highest LRs (>3.5) for diagnosing heart failure were the following: the overall clinical judgment, history of heart failure, S3, jugular venous distension, pulmonary venous congestion or interstitial edema on CXR, and atrial fibrillation on ECG. The features evaluated in more than one study with the lowest LRs (<0.60) for diagnosing of heart failure were the following: the overall clinical judgment, no prior history of heart failure, no dyspnea on exertion, the absence of rales, and the absence of radiographic pulmonary venous congestion, or cardiomegaly. The single finding that decreased the likelihood of heart failure the most was a BNP <100 pg/mL. While the findings of this study are useful when assessing dyspneic patients suspected of having heart failure, no individual feature is sufficiently powerful in isolation to rule heart failure in or out. Therefore, an overall clinical impression based on all available information is best. If the appropriate constellation of findings with high LRs for heart failure are present, that may be sufficient to warrant empirical treatment without further urgent investigations"

JAMA 2005 294:15

The Rational Clinical Examination. McGraw-Hill, 2009

CLINICAL FEATURES (CONT'D)

RATIONAL CLINICAL EXAMINATION SERIES: DOES THIS PATIENT HAVE ABNORMAL CENTRAL VENOUS PRESSURE?

JVP VS. CAROTID—JVP has biphasic waveforms, is non-palpable, is occludable, decreases with inspiration, changes with position, and increases with abdominojugular reflux (AJR). To perform the AJR, the blood pressure cuff is pumped 6× and then pressed against the abdomen at 20–35 mmHg for 15–30 s. Normal = no change in JVP, or transient increase of >4 cm that returns to baseline before 10 s, or sustained increase <3 cm throughout. Positive AJR occurs when abdominal compression causes a sustained increase in JVP >4 cm (sens 24%, spc 96%, LR+ *4.4*)

JAMA 1996 275:8

UPDATE—a JVP height ≥3 cm above the sternal angle in any position indicates an abnormal CVP. Clinical assessment of high JVP has a LR+ for high CVP of 3.1. An assessment of low JVP has a LR+ for low CVP of 3.4

The Rational Clinical Examination. McGraw-Hill, 2009

RATIONAL CLINICAL EXAMINATION SERIES: CAN THE CLINICAL EXAMINATION DIAGNOSE LEFT-SIDED HEART FAILURE IN ADULTS?

INCREASED FILLING PRESSURE—very helpful findings are **radiographic redistribution** and **jugular venous distension**. Somewhat helpful findings are dyspnea, orthopnea, tachycardia, decreased systolic or pulse pressure, S3, rales, and abdominojugular reflux. Edema is helpful only when present

SYSTOLIC DYSFUNCTION—very helpful findings are **radiograph** (cardiomegaly, redistribution), **anterior Q waves**, **LBBB**, and **abnormal apical impulse** (especially if sustained). Somewhat helpful findings are tachycardia, decreased blood pressure or pulse pressure, S3, rales, dyspnea, previous infarction other than anterior, and high peak CK (post-infarct). Edema and increased jugular venous pressure are helpful if present

DIASTOLIC DYSFUNCTION—very helpful finding is **elevated blood pressure** during the episode of increased filling pressure. Somewhat helpful findings are obesity, lack of tachycardia, older age, and absence of smoking or CAD. Normal radiographic heart size is helpful if present

CLINICAL FEATURES (CONT'D)

APPROACH—"in patients without known systolic dysfunction, ≤1 finding of increased filling pressure can exclude diagnosis, ≥3 findings suggests increased filling pressure. In patients with known systolic dysfunction, absence of finding of increased filling pressure can exclude diagnosis, ≥1 finding suggests increased filling pressure. For systolic dysfunction, can exclude diagnosis if no abnormal findings, including no sign of increased filling pressure are present (LR– 0.1). ≥3 findings are needed to confirm the diagnosis (LR+ 14)"

JAMA 1997 277:21

INVESTIGATIONS

BASIC

- **LABS**—CBCD, lytes, urea, Cr, troponin/CK × 3, BNP or NT-pro-BNP, D-dimer, TSH, albumin
- **IMAGING**—CXR, echocardiogram (check E/A ratio if diastolic dysfunction)
- **ECG**

SPECIAL

- **FURTHER IMAGING**—MIBI, MUGA
- **STRESS TEST**—to assess ischemic heart disease
- **CARDIAC CATHETERIZATION**
- **ABG**—if severe dyspnea

DIAGNOSTIC AND PROGNOSTIC ISSUES

B-TYPE NATRIURETIC PEPTIDE/N-TERMINAL PROHORMONE OF BRAIN NATRIURETIC PEPTIDE

- **DIAGNOSIS**—BNP and NT-proBNP levels are elevated with HF, PE, pulmonary hypertension, LVH, ACS, AF, renal failure, overload, and sepsis. Generally, can rule-out HF if BNP <100 pg/mL or NT-proBNP <300 pg/mL; may rule-in if BNP >500 pg/mL, NT-proBNP >900 pg/mL (if age 50–75 years), or NT-proBNP >1,800 pg/mL (if age >75 years). Best used in combination with clinical scoring system when diagnosis is uncertain
- **BAGGISH CLINICAL SCORING SYSTEM**—elevated NT-proBNP [>450 pg/mL if age <50 years, or >900 pg/mL if age ≥50 years] (+4), interstitial edema on CXR (+2), orthopnea (+2), lack of fever (+2), age >75 years (+1), lack of cough (+1), use of loop diuretic prior to presentation (+1), rales (+1). If score 0–5, low likelihood of

DIAGNOSTIC AND PROGNOSTIC ISSUES (CONT'D)

HF; if 6–8, intermediate likelihood of HF; if 9–14, high likelihood of HF

- **PROGNOSIS**—BNP >80th percentile is associated with a >50% increase in long-term mortality

HF PROGNOSIS—33% 1-year mortality, 75% 6-year mortality

ACUTE MANAGEMENT

ABC—O_2 to keep sat >95%, IV's

SYMPTOM CONTROL—★**LMNOP**★ ***L****asix/furosemide* 20–120 mg IV PRN, ***M****orphine* 2–5 mg IV PRN, ***N****itroglycerin* 0.4 mg SL PRN, **O_2**, **P**osition (upright)

LONG-TERM MANAGEMENT

★**DDDD**★

DIET—**low salt** (<100 mmol/day, 1.5–2 g/day), **fluid restriction** (1.5–2 L/day)

DIURETICS—***furosemide*** 20–120 IV/PO daily-BID with daily adjustments (try to use smallest dose possible to allow ACE inhibitor) ± ***metolazone*** 2.5–5 mg PO 30 min before furosemide, ***spironolactone*** 12.5–50 mg PO daily or ***eplerenone*** 25–50 mg PO daily **VASODILATORS**—**ACE inhibitor** (*captopril* 6.25–50 mg PO TID, *enalapril* 1.25–10 mg PO BID, *ramipril* 2.5–10 mg PO BID, *lisinopril* 2.5–20 mg PO daily, *perindopril* 2–8 mg PO daily). **ARB** (*valsartan* 40–160 mg PO BID, *candesartan* 8–32 mg PO daily). ***Hydralazine*** 10–50 mg PO QID and **nitrates** (*nitropatch* 0.4 mg topical daily or *isosorbide mononitrate* 30–90 mg PO daily). β-**blockers** (*metoprolol tartrate* 50–100 mg PO BID, *carvedilol* 3.125–25 mg PO BID, *bisoprolol* 2.5–10 mg PO daily)

DIGITALIS—***digoxin*** 0.0625–0.25 mg PO daily

TREAT UNDERLYING CAUSE—**CAD** (PCI/CABG), **aortic stenosis** (AV replacement), **sleep apnea** (CPAP)

DEVICES—if ejection fraction <30–35%, consider **cardiac resynchronization therapy** (CRT/biventricular pacing) ± **implantable cardioverter defibrillators** (ICD). **Ventricular assist devices** may also be considered in selected cases of refractory HF

TREATMENT ISSUES

ACE INHIBITOR (Garg, JAMA 1995)—hazard ratios for total mortality 0.77 and mortality/hospitalization 0.65 for any patients with LVEF <40%. Target dose = maximum tolerated. Contraindications include SBP <80 mmHg, bilateral renal artery stenosis, severe renal failure, and hyperkalemia

TREATMENT ISSUES (CONT'D)

ARB (CHARM)—consider substitution with ARB if ACE inhibitor *not tolerated* (e.g., cough). May also be used as adjunct to ACE inhibitor if β-blocker not tolerated. Contraindications similar to ACE inhibitor

HYDRALAZINE/NITRATES (VHEFT I and II, A-HeFT)—less effective than ACE inhibitor. Particularly useful for pregnant patients, African Americans, or those who developed renal insufficiency while on ACE inhibitor, or as add-on therapy

ANGIOTENSIN RECEPTOR–NEPRILYSIN INHIBITOR (McMurray, NEJM 2014, PARADIGM-HF)—combination sacubitril-valsartan demonstrated 16% reduction in all-cause mortality, 20% reduction in death from cardiovascular causes, and 21% reduction heart failure hospitalizations compared to enalapril

β-BLOCKERS (Foody JAMA 2002)—hazard ratios for total mortality 0.65 and mortality/hospitalization 0.64. May worsen symptoms in first few weeks and may take up to 1 year to see full effect in LVEF. Useful for patients with NYHA II–III (and stable IV) and LVEF <40%, also NYHA I, LVEF <40%, and post-MI. Contraindications include fluid overload and severe asthma. Start only when patient euvolemic

SPIRONOLACTONE (RALES 1999, EPHESUS 2003, EMPHASIS-HF 2011)—hazard ratios for all-cause mortality 0.7 and hospitalization for HF, 0.65 for patients with NYHA III–IV, LVEF <35%, and already on maximum medical therapy. Hazard ratios for cardiovascular death/HF hospitalization 0.63 and cardiovascular mortality 0.76 for patients with NYHA II and LVEF ≤30% (or LVEF 31–35% *plus* QRS duration >130 msec), and already on maximum medical therapy. Caution in elderly and renal failure patients as higher risk of hyperkalemia

DIGOXIN (DIG 1997)—hazard ratios for total mortality 0.99 and mortality/hospitalization 0.92. Particularly useful for patients with both HF and atrial fibrillation, or symptomatic HF despite maximum medical therapy

TREATMENT ISSUES (CONT'D)

OVERALL APPROACH—treat underlying cause if possible. Non-pharmacological treatments (diet, exercise, smoking cessation) → add ACE inhibitor if LVEF ≤40% (or hydralazine/nitrates if renal failure, ARB if cough secondary to ACE inhibitor) → add β-blocker when euvolemic if LVEF ≤40% → add spironolactone/eplerenone if NYHA II-IV if LVEF ≤30% (or ≤35% and QRS duration >130 msec) → add digoxin ± ARB if still symptomatic. If ejection fraction is <30–35% despite optimal medical therapy, consider revascularization, implantable cardioverter defibrillator, cardiac resynchronization (if QRS is wide), and ventricular-assist device/heart transplant

SPECIFIC ENTITIES

CAUSES OF FLASH PULMONARY EDEMA—**cardiac** (ischemic heart disease, acute aortic regurgitation, acute mitral regurgitation, mitral stenosis/obstruction, arrhythmia), **pulmonary** (pulmonary embolism, pneumonia), **renal** (bilateral renal artery stenosis), **systemic** (hypertension crisis, fever, sepsis, anemia, thyrotoxicosis)

HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY (HOCM)

- **PATHOPHYSIOLOGY**—autosomal dominant condition with mutated cardiac sarcomere, leading to massive ventricular hypertrophy (particularly septum). This results in left ventricular outflow tract obstruction, mitral regurgitation, diastolic dysfunction, and subsequently myocardial ischemia and overt heart failure. Cardiac arrhythmias may lead to sudden death (<1%/year). Other complications include atrial fibrillation and infective endocarditis
- **RISK FACTORS FOR SUDDEN DEATH**—major risk factors include history of cardiac arrest (VF), sustained VT, unexplained syncope, nonsustained VT on Holter, abnormal BP response on exercise test, left ventricular wall thickness >30 mm, and family history of sudden death. Minor risk factors include left ventricular outflow obstruction (gradient ≥30 mmHg), diastolic dysfunction, microvascular obstruction, late gadolinium enhancement on cardiac MRI, and high-risk genetic defect
- **CLINICAL FEATURES**—most are asymptomatic although dyspnea, chest pain, syncope, and sudden death may develop. Family history should be obtained. Physical findings include brisk carotid upstroke, bifid carotid pulse, double apical impulse, systolic ejection murmur (LLSB, louder with standing and Valsalva) ± mitral regurgitation murmur
- **DIAGNOSIS**—echocardiogram (septal thickening, systolic-anterior motion of mitral valve). Further workup includes 48 h Holter monitor and exercise testing annually
- **TREATMENTS**—**avoidance** (dehydration and strenuous exercise), **medical** (β-blockers and non-dihydropyridine calcium channel blockers as first line, disopyramide as second line), **interventional/surgical** (septal myomectomy, alcohol septal ablation, dual-chamber pacing), **prophylaxis** (implantable cardioverter defibrillator for high-risk patients to prevent sudden cardiac death, anticoagulation if atrial fibrillation)

NEJM 2004 350:13

Digoxin Intoxication — Circulation 2004 109:24

CAUSES

OVERDOSE—intentional, accidental (digoxin, foxglove, yellow oleander)

DRUG INTERACTIONS—quinidine, amiodarone, verapamil, diltiazem, tetracycline, erythromycin, rifampin, cyclosporine, SSRIs

PHARMACOKINETICS (see precipitants below)

CAUSES (CONT'D)

- **OLD AGE, RENAL FAILURE**
- **CARDIAC**—ischemia, myocarditis, cardiomyopathy, amyloidosis, cor pulmonale
- **METABOLIC**—hypokalemia, hypomagnesemia, hypernatremia, hypercalcemia, hypoxemia, acid–base imbalance

PATHOPHYSIOLOGY

DIGOXIN LEVEL—measurement of serum levels is not routinely necessary as dosing can usually be titrated according to clinical and hemodynamic effects. When measured, serum level should be collected at 12–24 h after the last dose (post-distribution phase). While the upper normal limit is 2.6 nmol/L [2.0 ng/mL], higher digoxin levels may be seen in asymptomatic patients. Low-dose digoxin, resulting in serum levels 0.5–0.9 nmol/L [0.4–0.7 ng/mL] is associated with possible survival benefit compared to ≥1 nmol/L [≥0.78 ng/mL] in HF patients

MECHANISM—digitalis acts by inhibiting the membrane-bound Na/K ATPase transport system. This leads to intracellular loss of K and gain of Na. Increase in intracellular Ca leads to ↑ cardiac contractility. Digoxin also exerts a vagotonic action, which slows conduction through the SA and AV node and helps to control heart rate

PRECIPITANTS OF DIGOXIN TOXICITY—toxicity is not merely related to serum levels, but also digoxin dosing (e.g., acute overdose), other medications (e.g., non-potassium sparing diuretics), and conditions (e.g., renal insufficiency, acute coronary syndromes, cardiac amyloidosis, hypothyroidism). For instance, hypokalemia, hypernatremia, hypomagnesemia and acidosis predispose to toxicity even at low-serum digoxin levels because of their depressive effects on the Na/K ATPase pump. In contrast, hyperkalemia occurs in acute toxicity and is directly related to prognosis

CLINICAL FEATURES

SIGNS AND SYMPTOMS

- **NEUROLOGICAL**—delirium, hallucination, blurred vision with altered color perception, headaches, dizziness
- **CARDIAC**—bradycardia, high-degree AV block, paroxysmal atrial tachycardia (often 2:1 AV conduction), unifocal or multifocal PVCs, bidirectional ventricular tachycardia, accelerated junctional tachycardia
- **GI**—anorexia, N&V, diarrhea, abdominal pain
- **METABOLIC**—hyperkalemia

INVESTIGATIONS

BASIC

- **LABS**—CBCD, lytes, urea, Cr, Ca, Mg, albumin, serum digoxin level
- **ECG**
- **ABG**

DIAGNOSTIC ISSUES

ECG CHANGES ASSOCIATED WITH DIGOXIN

- **THERAPEUTIC LEVELS**—sagging of ST segments, flattened T waves, U waves, and shortened QT. Not to be confused with digoxin toxicity
- **TOXIC LEVELS**—first degree heart block, paroxysmal atrial tachycardia (often 2:1 AV conduction), regularized atrial fibrillation (i.e., with complete heart block), unifocal or multifocal PVCs, ventricular bigeminy, bidirectional VT

MANAGEMENT

ACUTE—ABC, **O_2**, IV, **treat arrhythmia**

TREAT UNDERLYING CAUSE—**observe**, **cardiac monitoring**, **activated charcoal** (if ingestion within 4 h). **Correct** electrolyte disturbances and reverse acidosis. **Atropine** for bradycardia. **Digibind**/**purified antidigoxin FAB fragments** (if acute ingestion of 10 mg or more in adults, or digoxin level >13 nmol/L [10 ng/mL], K >5 mM and life-threatening arrhythmia, hemodynamic instability, unstable arrhythmia [e.g., symptomatic bradycardia], or end-organ hypoperfusion [e.g., acute renal failure]). May see response in 20 min and complete response up to 4 h. Monitor potassium levels after treatment with Digibind)

TREATMENT ISSUES

AVOID

- **IV CALCIUM**—indicated for other causes of severe hyperkalemia, calcium may precipitate VT/sudden death and should **NOT** be given for hyperkalemia of digoxin toxicity
- **CARDIOVERSION**—relatively contraindicated because asystole or ventricular fibrillation may be precipitated
- **TRANSVENOUS PACING**—can precipitate arrhythmias and deterioration

HALF-LIVES—plasma $t_{½}$ for digoxin 1.6 days, digitoxin 5 days

INDICATIONS FOR DIGOXIN THERAPY—in patients with **symptomatic systolic HF and sinus rhythm** (digoxin may be especially useful in patients with severe symptoms despite standard medical therapy, LVEF <25%, or cardiomegaly), **diastolic HF** (with rapid atrial fibrillation or severe symptoms despite standard medical therapy), and **rapid atrial fibrillation** (with or without heart failure). Use with extreme caution or avoid in the elderly, patients with severe conduction abnormalities, acute coronary syndromes, or renal failure

Atrial Fibrillation

NEJM 2001 344:14; NEJM 2004 351:23
AHA/ACC/HRS 2014 Atrial Fibrillation Guidelines
Canadian Cardiovascular Society 2014 Atrial Fibrillation Guidelines

DIFFERENTIAL DIAGNOSIS OF PALPITATIONS

★PPP★

PHYSIOLOGIC (high output states)—anemia, pregnancy, fever, exercise, stress

PATHOLOGIC★CDE★

- **CARDIAC**—**arrhythmia** (see tachycardia below), **myocardial** (cardiomyopathy, atrial myxoma, shunts), valvular, transplanted heart
- **DRUGS**—sympathomimetic agents, vasodilators, anticholinergic agents, β-blocker withdrawal, illicit (cocaine, amphetamines)
- **ENDOCRINE**—hypoglycemia, hyperthyroidism, pheochromocytoma

PSYCHIATRIC—panic attack/disorder, generalized anxiety disorder, somatization disorder

DIFFERENTIAL DIAGNOSIS OF NARROW COMPLEX TACHYCARDIA

REGULAR NARROW COMPLEX TACHYCARDIA —sinus tachycardia, atrial flutter with fixed block (rate 300, 150, 100), supraventricular tachycardia (atrial tachycardia, AV nodal reentry, orthodromic AV reentrant/WPW), accelerated junctional tachycardia

IRREGULAR NARROW COMPLEX TACHYCARDIA—sinus tachycardia/arrhythmia, premature atrial contractions, multifocal atrial tachycardia, atrial flutter with variable block, atrial tachycardia with variable block, atrial fibrillation

DIFFERENTIAL DIAGNOSIS OF IRREGULARLY IRREGULAR RHYTHM

ATRIAL—sinus arrhythmia (rate 60–100), wandering pacemaker (rate 60–100), premature atrial rhythm/beat, multifocal atrial tachycardia (rate >100), ectopic atrial tachyarrhythmia with variable block, atrial flutter with variable block, atrial fibrillation

VENTRICULAR—premature ventricular contraction, polymorphic ventricular tachycardia, ventricular fibrillation

PATHOPHYSIOLOGY

CAUSES OF ATRIAL FIBRILLATION

- **CARDIOVASCULAR**—**myocardial** (hypertension, CAD, HF, hypertrophic cardiomyopathy, dilated cardiomyopathy, myocarditis, infiltration [amyloidosis, sarcoidosis, hemochromatosis], ASD), **valvular** (rheumatic, acquired, endocarditis), **arrhythmia** (WPW, SSS), **pericardial** (pericarditis), cardiac surgery
- **PULMONARY**—COPD, pulmonary embolism, pleural effusion
- **METABOLIC**—thyrotoxicosis, obesity
- **DRUGS**—theophylline, adenosine, digitalis, β-agonists, alcohol
- **IDIOPATHIC** (10%)

CLASSIFICATION OF ATRIAL FIBRILLATION

- **PAROXYSMAL ATRIAL FIBRILLATION**—episodes of AF last <7 days (usually <24 h). Terminates spontaneously or with intervention. May variably recur
- **PERSISTENT ATRIAL FIBRILLATION**—continuous AF sustained >7 days
- **LONG-STANDING PERSISTENT ATRIAL FIBRILLATION**—continuous AF >12 months
- **PERMANENT ATRIAL FIBRILLATION**—a classification determined by clinician and patient to stop further attempts to restore and/or maintain sinus rhythm. A therapeutic attitude rather than inherent pathophysiological attribute of AF
- **NONVALVULAR ATRIAL FIBRILLATION**—AF in the absence of rheumatic mitral stenosis, mechanical or bioprosthetic heart valve, or mitral valve repair
- **LONE ATRIAL FIBRILLATION**—AF in patients <60 years, no structural heart disease or risk factors, including hypertension

CLINICAL FEATURES OF NARROW COMPLEX TACHYCARDIA

HISTORY—palpitations, chest pain, dyspnea, dizziness, syncope, past medical history (AF, SVT, WPW, CAD, HF, hypertension, diabetes, stroke, TIA, thyroid dysfunction), medications (antihypertensives, antiarrhythmics), DVT/PE risk factors

PHYSICAL—vitals (pulse rate and rhythm, BP), cardiac and pulmonary examination for heart failure

CAROTID SINUS MASSAGE, VALSALVA, OR ADENOSINE—SVT may spontaneously terminate, while AF or atrial flutter may slow down. Avoid adenosine if suspect pre-excitation syndrome (atrial fibrillation or atrial flutter with WPW)

CLINICAL FEATURES

RATIONAL CLINICAL EXAMINATION SERIES: DOES THIS PATIENT WITH PALPITATIONS HAVE A CARDIAC ARRHYTHMIA?

	Any arrhythmia		Significant arrhythmia	
	LR+	LR–	LR+	LR–
History				
Cardiac disease	2.03	0.71	0.42	1.07
Male sex	1.63	0.76	1.20	0.90
Age >60	1.70	0.83	1.89	0.77
Smoking >11/day	0.78	1.03	0.77	1.03
Anxiety disorder	0.98	1.01	0.92	1.04
FH of palpitations	0.86	1.04	1.07	0.98
EtOH >10 days/week	0.76	1.05	1.02	1.00
Panic disorder	0.26	1.30	–	–
Any psychiatric disorders	–	–	0.67	1.12
Palpitations				
Regular	1.66	–	1.38	0.55
Irregular	1.65	0.62	–	1.23
Duration >5 min	1.52	0.38	0.79	0.95
Duration >60 s	1.15	0.69	1.17	0.63
Continuous symptoms	1.06	–	0.93	1.20
HR >100/min	0.91	–	1.08	0.86
Precipitating factors				
Affected by sleep	2.29	0.70	2.44	0.63
Occurring at work	2.17	0.76	1.54	0.86
Caffeine	1.84	0.91	2.06	0.89
Occurs holiday	1.56	0.92	0.79	1.04
Occurs weekend	1.43	0.90	0.72	1.08
Alcohol	1.36	0.96	1.94	0.90
Lying in bed	1.30	0.61	1.02	0.97
Exercise	0.74	1.09	0.78	1.07
Breathing	0.52	1.23	0.52	1.20
While resting	–	–	1.02	0.97
Associated symptoms				
Regular rapid pounding sensation in neck	–	–	177	0.07
Neck fullness	–	–	0.85	1.04
Visible neck pulsations	–	–	2.68	0.87
Dizzy spells	0.93	1.08	1.34	0.67
Chest pain	0.81	1.07	0.92	1.02
Dyspnea	0.31	–	0.27	1.12
Vasovagal symptoms	–	–	1.72	0.63
Presyncope	–	–	1.04	0.95
Physical examination				
HR <60 or >100	–	–	3.00	0.78
Obesity	–	–	1.55	0.93
Hypertension	–	–	1.01	1.00

APPROACH—"while the presence of a regular rapid-pounding sensation in the neck or visible neck pulsations associated with palpitations makes the diagnosis of atrioventricular nodal reentry tachycardia likely, the reviewed studies suggest that the clinical examination is not sufficiently accurate to exclude clinically significant arrhythmias in most patients. Thus, prolonged electrocardiographic monitoring with demonstration of symptom-rhythm correlation is required to make the diagnosis of a cardiac arrhythmia for most patients with recurrent palpitations"

JAMA 2009 302:19

INVESTIGATIONS

BASIC

- **LABS**—CBCD, lytes, urea, Cr, Mg, TSH, INR, PTT, D-dimer, troponin
- **IMAGING**—CXR, echocardiogram (enlarged left atrium)
- **ECG**
- **24-H HOLTER**
- **EXERCISE STRESS TEST**

SPECIAL

- **ELECTROPHYSIOLOGY STUDIES**

ACUTE MANAGEMENT

ABC—O_2 to keep sat >95%, IV

SYNCHRONIZED CARDIOVERSION—premedicate if possible with *midazolam* 1–2 mg IV q2–3 min, *fentanyl* 50–150 μg IV × 1, shock 50, 100, 200, 300, 360 J, prepare to intubate and give IV anti-arrhythmics PRN

AV NODAL BLOCKING AGENTS ★ABCD★

- **AMIODARONE**—*amiodarone* 150 mg IV bolus over 10 min, q10–15 min. Alternatively, infusion 60 mg/h over 6 h, then 30 mg/h over 18 h. Maximum 2.2 g/day
- **β-BLOCKERS**—*metoprolol* 5 mg IV over 1 min q5min × 3 PRN, *esmolol* 500 μg/kg IV over 1 min, maintenance dose 50–200 μg/kg/min IV
- **CALCIUM CHANNEL BLOCKERS**—*diltiazem* 15–20 mg IV over 2 min, repeat in 15 min at 20–25 mg PRN, maintenance dose 5–20 mg/h IV; *verapamil* 2.5–5.0 mg IV over 1–2 min, followed by 5–10 mg in 15–30 min PRN with maximum of 30 mg, maintenance dose 0.05–0.2 mg/min IV
- **DIGITALIS**—*digoxin* 0.25–0.5 mg IV q6h to a total dose of 1 mg, maintenance dose 0.125–0.25 mg PO/IV daily

OVERALL APPROACH

- **UNSTABLE ATRIAL FIBRILLATION**—perform cardioversion immediately
- **STABLE ATRIAL FIBRILLATION <48 H—rate control** (β-blockers, calcium channel blockers, digoxin) and consider **rhythm control** (DC cardioversion, amiodarone, propafenone, flecainide). Anticoagulate at least × 4 weeks post-cardioversion
- **STABLE ATRIAL FIBRILLATION >48 H OR UNKNOWN DURATION—rate control** (β-blockers, calcium channel blockers, digoxin) and consider **rhythm control** (IV unfractionated heparin → TEE to exclude atrial thrombus → cardioversion within 24 h → anticoagulate × 4 weeks; ALTERNATIVELY anticoagulate × 3 weeks → cardioversion → anticoagulate at least × 4 weeks)
- **TREAT UNDERLYING CAUSE/PRECIPITANT**—infection, myocardial infarction, ischemia, drugs, pulmonary embolism, thyrotoxicosis

LONG-TERM MANAGEMENT

RATE CONTROL—target resting HR <80 and exercise HR <110 in patients with significant symptoms. (Consider target resting HR <110 in asymptomatic patients with preserved LVEF). **β-blocker** (*metoprolol tartrate* [immediate release] 50–100 mg PO BID, *metoprolol succinate* [extended release] 100–200 mg PO daily, *carvedilol* 6.25–50 mg PO BID, *bisoprolol* 5–10 mg PO daily). **Calcium channel blockers** (*diltiazem CD* 120–480 mg PO daily). **Digitalis** (*digoxin* 0.5 mg PO × 1 dose, then 0.25 mg × 2 doses q6–12 h, then 0.0625–0.25 mg daily)

RHYTHM CONTROL—elective cardioversion (only after a 3-week course of therapeutic anticoagulation or atrial thrombus excluded by TEE. Cardioversion should be followed by 4 weeks of anticoagulation). **Antiarrhythmics** (*amiodarone* 200–400 mg PO daily, *sotalol* 40–160 mg PO BID, especially if CAD; *flecainide* 50 mg PO q12h, especially if no structural heart disease; *propafenone* 150 mg PO q8h, especially if no structural heart disease)

CLOT CONTROL—***ASA*** 81 mg daily if low-risk (nonvalvular disease and $CHADS_2 = 0$). Otherwise, **anticoagulation** (*warfarin* 5 mg PO daily to target INR between 2–3, *dabigatran* 110–150 mg PO BID, *rivaroxaban* 15–20 mg PO daily, *apixaban* 2.5–5 mg PO daily). Warfarin for AF with valvular disease. Novel anticoagulants (dabigatran, rivaroxaban, and apixaban) should not be used in patients with severe renal impairment, prosthetic heart valves, mitral stenosis, or valvular lesions associated with moderate to severe heart failure. Patients at higher risk of bleeding may require lower doses. Bridging anticoagulation (for initiation/interruption of warfarin therapy) not routinely required but should be considered in those at high risk for acute thrombosis (e.g., mechanical heart valves)

PROCEDURES—radiofrequency ablation of the pulmonary veins (PVI). Radiofrequency ablation of AV node with insertion of a permanent pacemaker and long-term anticoagulation as last resort. **Surgical** (corridor and maze procedures)

NEJM 2002 347:23; NEJM 2009 361:12; NEJM 2010 362:15; NEJM 2011 365:10; NEJM 2011 365:11

TREATMENT ISSUES

STROKE RISK FACTORS IN PATIENTS WITH ATRIAL FIBRILLATION

★CHADS2★

- **CHF** (any history, 1 point)
- **HYPERTENSION** (any history, 1 point)
- **AGE** ≥75 (1 point)
- **DIABETES** (1 point)
- **STROKE OR TIA** (2 points)

- **RISK OF STROKE (IF UNTREATED)**—0 points = 1.9%/year, 1 = 2.8%, 2 = 4.0%, 3 = 5.9%, 4 = 8.5%, 5 = 12.5%, 6 = 18.2%

★CHA2DS2-VASC★

- **CHF** (any history, 1 point)
- **HYPERTENSION** (any history, 1 point)
- **AGE** ≥75 (2 point)
- **DIABETES** (1 point)
- **STROKE OR TIA** (2 points)
- **VASCULAR DISEASE** (**coronary**, **aortic**, **or peripheral**) (1 point)
- **AGE 65–74** (1 point)
- **SEX, FEMALE** (1 point)

- **RISK OF STROKE (IF UNTREATED)**—0 points = 0%/year, 1 = 1.3%, 2 = 2.2%, 3 = 3.2%, 4 = 4.0%, 5 = 6.7%, 6 = 9.8%, 7 = 9.6%, 8 = 6.7%, 9 = 15.2%
- **OTHER RISK FACTORS**—CAD, echocardiography abnormalities (atrial size >5 cm, LV dysfunction), thyrotoxicosis, rheumatic valvular disease (RR 17). *All* mitral stenosis and HOCM patients with AF should have chronic anticoagulation (regardless of $CHADS_2$ or CHA_2DS_2-VASc score)
- **RISK REDUCTION**—ASA decreases risk by ~30%. Anticoagulation decreases risk of stroke by ~60%
- **FACTORS INCREASING RISK OF BLEEDING WITH WARFARIN USE**—advanced age, female sex, diabetes, prior hemorrhage, uncontrolled hypertension, alcoholism or liver disease, cancer, bleeding disorder, chronic kidney disease, ASA/clopidogrel/NSAIDs (including COX-2 inhibitors). Note that risk of fall by itself is not a contraindication to warfarin use
- **RISK OF BLEEDING ON ANTICOAGULATION**—as $CHADS_2$ score increases so does risk of major bleeding (but risk of stroke usually remains higher than risk of bleeding). Benefit-to-risk ratio for anticoagulation generally becomes even more favorable as risk factors for stroke accumulate. Risk calculation for bleeding usually unnecessary. Existing risk models do not reliably predict individual risk. Use clinical judgment

TREATMENT ISSUES (CONT'D)

★HASBLED★

- Hypertension, SBP >160 mmHg (1 point)
- Abnormal liver function (1 point)
- Abnormal renal function (1 point)
- Stroke (1 point)
- Bleeding tendency/predisposition (1 point)
- Labile INR on warfarin (1 point)
- Elderly, age >65 (1 point)
- Drugs (ASA, clopidogrel, NSAIDS) (1 point)
- Drugs (alcohol abuse) (1 point)

- **RISK OF BLEEDING**—0 = 1.13 bleeds/100 patient-years, 1 = 1.02, 2 = 1.88, 3 = 3.74, 4 = 8.70, 5 = 12.50, insufficient data for scores ≥6

IMPORTANT TOXICITIES OF AMIODARONE

- **CARDIAC** (5%)—sinus bradycardia and AV nodal block. QT prolongation leading to torsades de pointes may rarely occur
- **THYROID**—amiodarone-induced thyrotoxicosis (3%). Type 1 from increased thyroid hormone synthesis from excess iodine (usually with underlying multinodular goiter or Graves' disease). Type 2 from destructive thyroiditis and thyroid hormone release. Doppler US showing goiter and ↑ vascularity favors type 1 (hyperthyroidism), but normal sized gland and normal/↓ vascularity favor type 2 (thyroiditis). Presence of (any) radioiodine uptake favors hyperthyroidism (type 1), but absence of uptake does not reliably differentiate between type 1 or type 2. Patients on amiodarone may not develop classic symptoms of thyrotoxicosis; however, recurrence of AF should prompt investigation. Discontinuing amiodarone MAY paradoxically worsen thyrotoxicosis; treatment includes anti-thyroid drugs and steroids (for type 2). Hypothyroidism also common (20%)
- **PULMONARY** (<3%)—chronic interstitial pneumonitis (most common), cryptogenic organizing pneumonia, ARDS, and solitary pulmonary nodule. Histologically characterized by foamy macrophages in the air space. DLCO is often decreased. CT chest may show diffuse/localized interstitial or alveolar opacities. Treat with steroids and stop amiodarone

TREATMENT ISSUES (CONT'D)

- **HEPATIC** (15%)—non-alcoholic steatohepatitis which in severe cases may lead to cirrhosis
- **NEUROLOGIC** (30%)—ataxia, tremor, peripheral polyneuropathy, insomnia, and impaired memory
- **VISION** (100%)—corneal microdeposits may result in halo vision, photophobia, and blurred vision. Optic nerve injury (1–2%) may cause blindness
- **DERMATOLOGIC** (25–75%)—photosensitivity, gray-bluish discoloration (blue man syndrome), and alopecia. This is reversible upon discontinuation of amiodarone, but may take a few years

TREATMENT ISSUES (CONT'D)

- **MONITORING**—baseline TSH, LFTs, PFT and CXR. TSH and LFTs every 6 months, CXR yearly, and PFT as needed

NEJM 2007 356:9

Related Topics
ACLS (p. 495)
Digoxin (p. 43)
ECG (p. 73)
Wolff–Parkinson–White Syndrome (p. 76)

Syncope

See SYNCOPE (p. 353)

Cardiac Examination

PULSE

PULSUS TARDUS ET PARVUS (low carotid upstroke and amplitude)—aortic stenosis
BRISK PULSE (rapid carotid upstroke)—hypertrophic cardiomyopathy
BOUNDING PULSE (rapid carotid upstroke and descent)—↑ left ventricular volume (aortic regurgitation, mitral regurgitation, VSD, PDA, severe bradycardia), ↓ peripheral resistance (fever, anemia, thyrotoxicosis, rigid arteries, pregnancy)
PULSUS BISFERIENS (double-peaked)—combination aortic stenosis and regurgitation
REGULARLY IRREGULAR PULSE—sinus arrhythmia, pulsus bigeminus (PVC, PAC)
IRREGULARLY IRREGULAR PULSE—atrial fibrillation, premature atrial or ventricular contractions

BLOOD PRESSURE

CORRECT CUFF SIZE—width of bladder ≥40% of arm circumference and length of bladder ≥80% of arm circumference
AUSCULTATORY GAP—defined as the gap between the first Korotkoff sound (which may disappear briefly) and its reappearance. Missing the higher reading can lead to an underestimation of systolic blood pressure. Thus, the systolic blood pressure should always be palpated first before auscultation

BLOOD PRESSURE (CONT'D)

WIDE PULSE PRESSURE—isolated systolic hypertension, aortic regurgitation, hyperdynamic states (sympathetic hyperactivity, fever/sepsis, anemia, thyrotoxicosis, large AV fistula, PDA, beriberi, pregnancy)
PSEUDOHYPERTENSION—false elevation of systolic blood pressure secondary to rigid arteries. The Osler's maneuver may be useful for determining the presence of pseudohypertension
PULSUS ALTERNANS (alternating fluctuation in pulse pressure)—initially hear only the more prominent beats. As cuff pressure decreases, start to hear the less intense beats (1:1 ratio). This may be detected in severe LV dysfunction and aortic stenosis
PULSUS PARADOXUS—inspiratory drop in systolic blood pressure >10 mmHg. Causes include asthma, COPD, **tamponade**, restrictive cardiomyopathy, constrictive pericarditis, hypovolemic shock, and rarely pulmonary embolism, SVC obstruction, and morbid obesity

JUGULAR VENOUS PRESSURE

A WAVE—atrial contraction

- **PROMINENT A WAVE**—tricuspid stenosis, pulmonary stenosis, pulmonary hypertension, hypertrophic cardiomyopathy, and Ebstein's anomaly
- **CANNON A WAVE**—AV dissociation (complete heart block, ventricular tachycardia) (right atrium contracts against closed tricuspid valve)
- **DECREASED A WAVE**—dilated right atrium
- **ABSENT A WAVE**—atrial fibrillation

X DESCENT—atrial relaxation. S1 starts

- **DECREASED X DESCENT**—atrial fibrillation
- **X DESCENT DEEPER THAN Y DESCENT**—tamponade

C WAVE—bulging of tricuspid valve into right atrium during ventricular isometric contraction

X' DESCENT—descent of the base of the heart during systole

V WAVE—atrial filling. S2 just before peak of v

- **DOMINANT V WAVE**—tricuspid regurgitation (cv wave), right heart failure, atrial septal defect

Y DESCENT—opening of tricuspid valve/atrial emptying

- **RAPID STEEP Y DESCENT**—constrictive pericarditis (square root sign), severe right heart failure
- **DECREASED Y DESCENT**—tricuspid stenosis
- **BLUNTED/ABSENT Y DESCENT**—tamponade

ABDOMINOJUGULAR REFLUX (AJR)—blood pressure cuff pumped 6×, then pressed against abdomen at 20–35 mmHg for 15–30 s. Positive AJR occurs when abdominal compression causes a sustained increase in JVP >4 cm [>1.6 in.] and predicts elevated left atrial pressure (≥15 mmHg, LR+ 8.0, LR– 0.3)

KUSSMAUL SIGN—paradoxical increase in JVP during inspiration. Causes include right ventricular failure, restrictive cardiomyopathy, constrictive pericarditis, SVC obstruction, and pulmonary embolism

PRECORDIAL EXAMINATION

INSPECTION—apex, right ventricular heave

PALPATION—apex, heaves, thrills, palpable heart sounds

- **DISPLACED APICAL BEAT** (lateral to mid-clavicular line)—left ventricular dilatation, LR+ 8.0
- **ENLARGED APICAL BEAT** (≥2.5 cm)—left ventricular dilatation, LR+ 4.7

PRECORDIAL EXAMINATION (CONT'D)

- **SUSTAINED APICAL BEAT** (outward impulse extends to, or past, S2)—left ventricular pressure overload (aortic stenosis), volume overload (aortic regurgitation, VSD), severe cardiomyopathy, or ventricular aneurysm
- **RETRACTING APICAL BEAT** (retraction during systole; inward motion begins at S1, outward impuse after S2)—constrictive pericarditis (up to 90%), tricuspid regurgitation
- **SUSTAINED LEFT PARASTERNAL MOVEMENT** ("lift/heave")—tricuspid regurgitation, mitral regurgitation
- **PALPABLE P2**—pulmonary hypertension in mitral stenosis, LR+ 3.6

HEART SOUNDS

TECHNIQUE—S1, S2, and physiological splitting of S2 are best heard over the base. Identification of S3 and S4 requires conscious effort listening for low pitched sounds over the apex (using the bell)

DISTINGUISHING S1 FROM S2—time with carotid pulse, diastole longer than systole, S2 louder than S1 at the base, S1 is low pitched and longer while S2 is high pitched and shorter, S2 often split

INTENSITY OF S1 AND S2

- **LOUD P2 >A2 AT PULMONIC AREA**—increased pulmonary pressure (left ventricular failure, mitral stenosis, pulmonary hypertension), increased pulmonary flow (atrial septal defect)
- **LOUD S2 AT AORTIC AREA**—hypertension, hyperdynamic states (fever, hyperthyroidism, anemia)
- **SOFT S2 OVER AORTIC AREA**—severe aortic stenosis
- **LOUD S1 AT MITRAL AREA**—mitral stenosis
- **SOFT S1**—mitral regurgitation, left bundle branch block, short PR interval

SPLITTING OF S2

- **FIXED SPLITTING** (splitting same degree during both inspiration and expiration)—atrial septal defect, right ventricular failure
- **WIDE SPLITTING** (splitting greater during inspiration than expiration)—right bundle branch block, pulmonary stenosis, pulmonary hypertension
- **PARADOXICAL (REVERSED) SPLITTING** (splitting only during expiration)—left bundle branch block, severe aortic stenosis, RV pacing

NORMAL AND EXTRA HEART SOUNDS

Sound	Heard	Pitch	Others
S1	LUSB	High	
Early systolic click	RUSB	High	Aortic stenosis
Mid-systolic click	Apex	High	MVP, louder standing
S2	LUSB	High	Splitting

HEART SOUNDS (CONT'D)

Sound	Heard	Pitch	Others
Opening snap (early diastolic)	Apex	High	Mitral stenosis
S3 (early diastolic)	Apex	Low	Heart failure
S4 (late diastolic)	Apex	Low	HTN, aortic stenosis

HEART SOUNDS (CONT'D)

High pitch sounds are best heard with the diaphragm, while low pitch sounds are best heard with the bell

DISTINGUISHING FEATURES BETWEEN P2 AND OPENING SNAP

1. P2 is best heard at LUSB while opening snap is best heard at the apex
2. P2 separates from A2 on inspiration, while opening snap tends to move closer to S2 on inspiration

DISTINGUISHING FEATURES BETWEEN S4 AND S1

1. S4 is usually best heart at apex with the bell while S1 is best heard at base
2. S4 is usually more widely separated from S1 than splitting of S1
3. S4 is loudest at the start of expiration, softest at mid-inspiration
4. S4 may be accentuated by lying down, exercise, or forced inspiration with closed glottis
5. S4 has a lower pitch than S1

DISTINGUISHING FEATURES BETWEEN S3 AND OPENING SNAP

1. S3 has a lower pitch than opening snap
2. S3 occurs later than opening snap

DISTINGUISHING FEATURES BETWEEN S3 AND S4

1. S3 has a lower pitch than S4
2. S3 is closer to S2 while S4 is closer to S1
3. Left ventricular S3 is louder at the apex while right ventricular S3 or S4 is usually best heart at left sternal border or at the base

MURMURS

TIMING

- **MID-SYSTOLIC**—aortic stenosis, aortic sclerosis, pulmonary stenosis, hypertrophic obstructive cardiomyopathy, atrial septal defect, flow murmurs (fever, pregnancy, hyperthyroidism, anemia, aortic regurgitation due to high flow)
- **PANSYSTOLIC**—mitral regurgitation, tricuspid regurgitation, ventricular septal defect, aortopulmonary shunts
- **LATE SYSTOLIC**—mitral valve prolapse, papillary muscle dysfunction
- **EARLY DIASTOLIC**—aortic regurgitation, pulmonary regurgitation

MURMURS (CONT'D)

- **MID-DIASTOLIC**—mitral stenosis, tricuspid stenosis, atrial myxoma, Austin Flint murmur of aortic regurgitation, Carey Coombs murmur during acute phase of rheumatic fever
- **PRE-SYSTOLIC**—mitral stenosis, tricuspid stenosis, atrial myxoma
- **CONTINUOUS MURMURS**—patent ductus arteriosus, arteriovenous fistula, aortopulmonary connection, venous hum, mammary souffle

INTENSITY—grade I (barely audible), grade II (faint but can be heard immediately), grade III (easily heard), grade IV (loud AND associated with palpable thrill), grade V (very loud, can be heard with the stethoscope half off chest), grade VI (very loud, can be heard with stethoscope off chest wall)

QUALITY—depends on the pitch, may be musical, harsh, blowing, rumbling, scratchy, grunting, or squeaky

CONFIGURATION—crescendo, decrescendo, crescendo–decrescendo, plateau, holosystolic

LOCATION—aortic valve (RUSB), pulmonary valve (LUSB), tricuspid valve (LLSB), mitral valve (apex)

RADIATION—aortic valve (carotids), pulmonary valve (left shoulder), tricuspid valve (xyphoid, right of sternum), mitral valve (axilla)

MANEUVERS

- **RESPIRATION**—**right-sided** murmurs typically increase with inspiration (except pulmonic click) or sustained abdominal pressure (↑ venous return), while **left-sided** murmurs are generally louder during expiration
- **VALSALVA MANEUVER** (↓ venous return and ↑ systemic arterial resistance)—most murmurs decrease in length and intensity during the Valsalva maneuver. Two exceptions are the systolic murmur of **hypertrophic cardiomyopathy**, which usually becomes much louder, and the systolic murmur of **mitral valve prolapse**, which becomes longer and often louder (click moves closer to S1)
- **POSITIONAL CHANGES**—most murmurs diminish with standing due to reduced preload. However, the murmur of **hypertrophic cardiomyopathy** becomes louder and the murmur of **mitral valve prolapse** lengthens and often is intensified. Squatting (or usually passive leg raising, both ↑ venous return and ↑ systemic arterial resistance) produces opposite effect

MURMURS (CONT'D)

- **ISOMETRIC EXERCISE** (↑ systemic arterial resistance)—murmurs caused by blood flow across normal or obstructed valves (e.g., **mitral or pulmonic stenosis**) become louder. Murmurs of **mitral and aortic regurgitation** and **ventricular septal defect** also increase with handgrip exercise

MURMURS (CONT'D)

- **TRANSIENT ARTERIAL OCCLUSION** (↑ systemic arterial resistance)—transient external compression of both arms by bilateral cuff inflation to 20 mmHg greater than peak systolic pressure augments the murmurs of **mitral regurgitation**, **aortic regurgitation**, **and ventricular septal defect**, but not murmurs due to other causes

DISTINGUISHING FEATURES AMONG COMMON SYSTOLIC AND DIASTOLIC MURMURS

	Systolic murmurs						**Diastolic murmurs**			
Findings[a]	**Tricuspid regurgitation**	**Mitral valve prolapse**	**Mitral regurgitation**	**Aortic sclerosis**	**Aortic stenosis**	**Hypertrophic cardiomyopathy**	**Tricuspid stenosis**	**Pulmonary regurgitation**	**Mitral stenosis**	**Aortic regurgitation**
Inspection	Dyspnea Cyanosis Cachexia Jaundice	Pectus excavatum Marfan's scoliosis	Dyspnea	Normal	Dyspnea Sustained apex	Dyspnea Double apex	Normal	Dyspnea	**Mitral facies** Cyanosis Dyspnea	Argyll Robertson Marfan's Ank. Spond
Radial pulse	Irregular (AF)	Normal	Irregular (AF)	Normal	**Brachio-radial delay**	Brisk	Irregular (AF)	Normal	**Irregular** (AF)	**Water-hammer**
BP	Normal	Normal	Normal	Normal	Narrow PP	Normal	Normal	Normal	**Narrow PP**	**Wide PP**
Carotid	Normal	Normal	Bounding Irregular (AF)	Normal	**Pulsus parvus et tardus**	**Brisk bifid**	Irregular (AF)	Normal	**Irregular** (**AF**)	**Bounding/ collapsing pulse**
JVP	Increased **V wave** Prominent a wave (pul. HTN), no a wave (AF)	Normal	Absent a wave (AF)	Normal	Normal	Prominent a wave	**Prominent a wave**, **slow y descent**, absent a wave (AF)	Prominent a wave (pul. HTN)	Absent a wave (AF) Prominent a wave (pul. HTN), cv wave (TR)	Normal
Palpation	Palpable P2 (pul. HTN), thrill RV heave	Normal	Enlarged, displaced apex, thrill RV heave	Normal	Sustained apex, thrill LV heave	**Double apical impulse** Thrill LV heave	Normal	Palpable P2 (pul. HTN), thrill RV heave	RV heave Palpable P2 (pul. HTN)	Sustained, displaced apex, thrill LV heave
S1[b]	Soft	Normal	Soft	Normal	Normal	Normal	Wide splitting S1	Normal	**Loud S1**	Split (chronic) Absent (acute)
S2[b]	Loud (pul. HTN)	Normal	Normal	Normal	**Paradoxical split**, **soft**	Paradoxical split	Normal	Loud (pul. HTN)	**Palpable P2** (**pul. HTN**)	Soft
S3	R sided	Normal	L sided	Normal	Normal	**L sided**	Normal	R sided	**Absent**	L sided
S4	None	Normal	Normal	Normal	**L sided**	**L sided**	Normal	R sided	Normal	L sided
Clicks or snaps	None	**Mid-systolic click**	None	None	Early systolic click	None	Opening snap (LSB)	None	**Opening snap** (apex)	None
Murmur[c]	LLSB High pitch Holosystolic	Apex High pitch **Late** systolic	Apex High pitch **Holo**systolic	RUSB High pitch Mid-systolic	RUSB High pitch Mid-systolic	**LLSB**, apex High pitch Mid-systolic	LLSB **Low pitch** Mid-diastolic	LUSB High pitch Early diastolic	Apex **Low pitch** Mid-diastolic[e]	RUSB High pitch Early diastolic
Radiation	Xyphoid	None	Axilla	None	Clavicle Carotids	Base of heart	None	None	None	Apex Sternum
Maneuvers	↑ **inspiration**, **sustained Abdominal pressure**	↑ **standing**, **Valsalva**[d] ↓ **squatting**	↑ isometric, transient art. occlusion	None	↑ squatting, leg raise ↓ standing, Valsalva, isometric	↑ **standing**, **Valsalva** ↓ **squatting**	↑ inspiration	↑ inspiration	↑ isometric ↓ standing, Valsalva	↑ isometric, transient art. occlusion, Best heard sitting up in end expiration
Other associated murmurs/ clinical features	**Graham Steell murmur** (pul. HTN) Ascites, pulsatile liver, edema	Mitral regurgitation (holosystolic at apex)	Pulmonary edema	None	**Gallavardin phenomenon** (mid-systolic murmur at apex)	Mitral regurgitation (mid-systolic at apex)	Mitral stenosis may also be present	PR murmur called **Graham Steell m**. if secondary to pul. HTN	**Pulmonary and tricuspid regurg. Murmurs** (pul. HTN)	**Austin Flint Murmur** (mid-diastolic over apex) Mid-systolic **flow** m. Other signs[f]

[a]Not all findings listed for each condition may be present on examination

[b]Loud heart sounds are usually due to mild-moderate stenotic lesions, while light heart sounds are usually due to regurgitant or severe stenotic lesions

[c]Regurgitant murmurs usually start early, while stenotic murmurs tend to start mid-way

[d]For mitral valve prolapse, maneuvers that increase murmur intensity also move both the click and murmur closer to S1

[e]For mitral stenosis, the murmur is classically described as mid-diastolic with presystolic accentuation

[f]All the following special signs for aortic regurgitation are related to increased pulse pressure. These include Quincke's sign (pulsatile refill in capillary bed of finger nails), Becker's sign (pulsatile retinal artery), deMusset's sign (head bob), Mueller's sign (pulsatile uvula), Mayne's sign (DBP ↓ 15 mmHg with arm raised), Gerhardt's sign (pulsatile spleen), Rosenbach's sign (pulsatile liver), Traube's sign (pistol shot sound over femoral arteries), Duroziez's sign (femoral artery bruit with compression), Hill's sign (popliteal SBP > brachial SBP by 60 mmHg)

MURMURS (CONT'D)

RATIONAL CLINICAL EXAMINATION SERIES: DOES THIS PATIENT HAVE AN ABNORMAL SYSTOLIC MURMUR?

AORTIC STENOSIS—"presence of any of following significantly increases the likelihood of aortic stenosis: effort syncope, slow carotid upstroke, late or mid peaking systolic murmur, decreased or absent S2, apical-carotid delay, brachioradial delay." "The presence of AS requires detection of a systolic murmur, generally radiating to the right clavicle."

Update for Clinical Signs for Detecting Aortic Stenosis

	LR+	LR–
Slow carotid upstroke	9.2	0.56
Murmur radiating to right carotid	8.1	0.29
Reduced or absent S2	7.5	0.50
Murmur over the right clavicle	3.0	0.10
Reduced carotid volume	2.0	0.64

The Rational Clinical Examination. Mcgraw-Hill, 2009

MITRAL REGURGITATION—"for cardiologists, absence of a mitral area murmur or a late systolic/holosystolic murmur significantly reduces the likelihood of mitral regurgitation, except in the setting of acute MI. Cardiologists can accurately distinguish left-sided regurgitant murmurs, such as mitral regurgitation and ventricular septal defect, using transient arterial occlusion"

TRICUSPID REGURGITATION—"cardiologists can accurately detect the murmur of tricuspid regurgitation. Cardiologists can accurately rule in and rule out tricuspid regurgitation using the quiet inspiration and sustained abdominal pressure maneuvers"

HYPERTROPHIC CARDIOMYOPATHY—"cardiologists can rule in or rule out hypertrophic cardiomyopathy by evaluating for decreased murmur intensity with passive leg elevation or increased murmur intensity when the patient goes from a **squatting to standing position**"

MITRAL VALVE PROLAPSE—"a **systolic click, with or without systolic murmur**, is sufficient for the diagnosis of mitral valve prolapse. The absence of both a systolic click and murmur significantly reduces the likelihood of echocardiographic mitral valve prolapse. In patients with echocardiographic mitral valve prolapse, a holosystolic murmur without a systolic click significantly increases the likelihood of long term complications, whereas absence of both a systolic click and murmur significantly reduces the likelihood of long term complications"

JAMA 1997 277:7

MURMURS (CONT'D)

INNOCENT MURMURS—in otherwise healthy younger patients. Systolic murmurs tend to be mid-systolic, grade 1 or 2 (possibly 3), loudest over LUSB, and do not radiate. Murmurs that are associated with systolic thrill (LR+ 12), holosystolic (LR+ 8.7), loud (LR+ 6.5), or plateau-shaped (LR+ 4.1) are more likely to be significant. Diastolic murmurs are always abnormal

RATIONAL CLINICAL EXAMINATION SERIES: DOES THIS PATIENT HAVE AORTIC REGURGITATION?

AORTIC REGURGITATION—"when a cardiologist hears the typical murmur of aortic regurgitation, the likelihood of mild or greater aortic regurgitation is increased significantly. The absence of a typical **diastolic murmur** significantly reduces the likelihood of aortic regurgitation"

MITRAL STENOSIS—"presence of a **mid-diastolic murmur** significantly increases the likelihood of mitral stenosis, while absence of a mid-diastolic murmur significantly reduces the likelihood of mitral stenosis"

PULMONARY REGURGITATION—"when a cardiologist hears a typical pulmonary regurgitation murmur, the likelihood of pulmonary regurgitation increases significantly. Absence of a typical murmur does not alter the likelihood of pulmonary regurgitation"

JAMA 1999 281:23

INVESTIGATIONS

ECHOCARDIOGRAM—if cardiac symptoms, murmur grade ≥3, diastolic murmur, or when other cardiac findings are present

Aortic Stenosis

AHA/ACC Valvular Heart Disease 2014 Guidelines
Lancet 2009 373:9667; NEJM 2002 346:9

DIFFERENTIAL DIAGNOSIS

VALVULAR

- **CONGENITAL MALFORMATIONS**—unicuspid, bicuspid
- **CALCIFICATION**—degenerative or senile, atherosclerosis, Paget's disease, chronic renal failure
- **INFECTIONS**—rheumatic fever, *Chlamydia pneumoniae*
- **RHEUMATOID ARTHRITIS**

SUBVALVULAR

- **DISCRETE LESIONS**—membranous diaphragm, fibromuscular ring
- **OBSTRUCTIVE**—hypertrophic cardiomyopathy

SUPRAVALVULAR—localized or discrete narrowing of the ascending aorta (Williams' syndrome)

LOW GRADIENT AORTIC STENOSIS—resulting from low cardiac output

PATHOPHYSIOLOGY

COMPLICATIONS ★BEE★

- **B**leeding (angiodysplasia + aortic stenosis + acquired vWD type IIa = Heyde's syndrome)
- **E**ndocarditis
- **E**mbolic events (cerebral, systemic)

CLINICAL FEATURES

PHYSICAL—tachypnea, decreased pulse pressure, brachioradial delay, pulsus parvus et tardus (slow rise and low amplitude), apical-carotid delay, hyperdynamic apical beat, systolic thrill at the base of heart, narrowly split or paradoxical splitting of S2 or absent S2, harsh mid-systolic ejection murmur (radiation to carotids), Gallavardin phenomenon

GALLAVARDIN PHENOMENON—aortic stenosis murmur is usually harsh and loudest over the right upper sternal border, whereas a Gallavardin murmur is musical and may be heard over apex. It is due to radiation of the high-frequency components of the aortic stenosis murmur to the apex

DISTINGUISHING FEATURES BETWEEN AORTIC SCLEROSIS AND AORTIC STENOSIS MURMUR

	Aortic sclerosis	Aortic stenosis
Pathophysiology	Abnormally thickened valve leaflets but minimal outflow obstruction	Decreased functional area of valve to cause decreased outflow
Carotid pulse	Normal	Pulsus parvus et tardus
S2	Normal	Soft single S2 (P2)
Murmur	Mid-systolic murmur	Late peaking of systolic murmur

DISTINGUISHING FEATURES BETWEEN AORTIC STENOSIS, MITRAL REGURGITATION, AND HYPERTROPHIC CARDIOMYOPATHY

	Aortic stenosis	Mitral regurgitation	HOCM
Carotid upstroke	Slow, low amplitude	Normal or low amplitude	Brisk
S1	Normal	Soft	Normal
S2	Single if severe	Normal	Often reversed
S3	No	Loud	No
S4	If severe	No	Yes
Loudest murmur	RUSB	Apex	LLSB and apex
Maneuvers			
Standing	↓	↓	↑
Squatting	↑	↑	↓
Valsalva	↓	↓	↑

INVESTIGATIONS

BASIC

- **CXR**
- **ECHOCARDIOGRAM**—transthoracic
- **ECG**—left ventricular hypertrophy
- **EXERCISE TESTING**

SPECIAL

- **CARDIAC CATHETERIZATION**

DIAGNOSTIC AND PROGNOSTIC ISSUES

AORTIC VALVE AREA AND SEVERITY

- **NORMAL** = peak velocity <2 m/s, area = 3–4 cm^2
- **MILD** = peak velocity 2.0–2.9 m/s, mean gradient <20 mmHg, area = 1.5–2 cm^2
- **MODERATE** = peak velocity 3.0–3.9 m/s, mean gradient 20–39 mmHg, area = 1–1.5 cm^2
- **SEVERE** = peak velocity ≥4 m/s, mean gradient >40 mmHg, area = ≤1 cm^2 (or indexed area ≤ 0.6 cm^2/m^2)
- **SYMPTOMS**—usually do not appear until valve ≤1 cm^2. The significance of valve area depends on patient size (larger patient = more severe for same valve area)
- **PROGRESSION**—valve area decreases by ~0.1 cm^2/year and the mean gradient increases by 7 mmHg/year (particularly if cardiac risk factors)

PROGNOSIS OF AORTIC STENOSIS ★ASH★
(**A**ngina, **S**yncope, **H**eart failure)

- **SEVERE AORTIC STENOSIS WITH NO SYMPTOMS**—1–2% DIE IN SHORT PERIOD
- **SEVERE AORTIC STENOSIS WITH ANGINA PRESENTATION**—50% DIE IN 5 YEARS
- **SEVERE AORTIC STENOSIS WITH SYNCOPE PRESENTATION**—50% DIE IN 3 YEARS
- **SEVERE AORTIC STENOSIS WITH HEART FAILURE PRESENTATION**—50% DIE IN 2 YEARS
- **SEVERE AORTIC STENOSIS AFTER VALVE REPLACEMENT**—survival similar to normal individuals

MANAGEMENT

MILD OR MODERATE AORTIC STENOSIS—follow clinically and with echocardiogram (every 3–5 years for mild, every 1–2 years for moderate, every year for severe)

SEVERE OR SYMPTOMATIC AORTIC STENOSIS—**aortic valve replacement** (transcatheter or surgical, see criteria below), balloon valvuloplasty (offers no survival benefit and is only a temporizing measure until surgical or percutaneous aortic valve replacement can be performed)

VASODILATORS—use with caution in the setting of hypertension or HF. ACE inhibitors

MANAGEMENT (CONT'D)

preferred over β-blockers because of risk of reduced inotropy; start low dose and titrate slowly; risk of hypotension and syncope

TREATMENT ISSUES

AORTIC VALVE REPLACEMENT (AVR)

- **RECOMMENDED INDICATIONS** (**CLASS I**)—if severe AS with symptoms of HF, syncope, exertional dyspnea, angina, or presyncope (by history or on exercise testing); asymptomatic severe AS and LVEF <50%; or severe AS and undergoing cardiac surgery for other reasons
- **REASONABLE INDICATIONS** (**CLASS IIa**)—if asymptomatic but *very* severe AS (i.e., peak velocity ≥5 m/s or mean gradient ≥60 mmHg); severe AS and exercise test with ↓ exercise tolerance or ↓ in SBP; symptomatic low-flow/low-gradient severe AS (i.e., valve area ≤1 cm^2) with LVEF <50%, and severe/high gradients on dobutamine stress test; symptomatic low-flow/low-gradient severe AS (i.e., valve area ≤1 cm^2) with normal LVEF ≥50% and valve obstruction as most likely cause of symptoms (based on clinical, hemodynamic, and anatomic data); or moderate AS and undergoing cardiac surgery for other reasons
- **POSSIBLE INDICATIONS** (**CLASS IIb**)—if severe AS and rapid disease progression and low surgical risk
- **PREOPERATIVE CONSULT**—AVR should be done before elective non-cardiac surgeries in symptomatic patients
- **RISK OF AVR**—mortality 1–2%, morbidity 1%/year (venous thromboembolic disease, bleeding, deterioration of prosthetic valve, endocarditis)

SURGICAL VS. TRANSCATHETER VALVE—transcatheter aortic valve replacement (TAVR) should be considered for patients with an indication for AVR who have high or prohibitive surgical risk for surgical AVR. A multidisciplinary heart valve team should collaborate in the decision making process

MECHANICAL VS. BIOPROSTHETIC VALVE—compared to human tissue valves, mechanical valves have prolonged durability, but higher chance of thromboembolism and bleeding from chronic anticoagulation. Overall, long-term outcomes are better with a mechanical valve. Main indications for bioprosthesis valve include patients who cannot or will not tolerate warfarin or for whom compliance is uncertain, patients ≥65 years of age who do not have risk factors for thromboembolism, and women of childbearing age

Aortic Regurgitation AHA/ACC Valvular Heart Disease 2014 Guidelines

DIFFERENTIAL DIAGNOSIS

VALVE ABNORMALITY—rheumatic heart disease, infective endocarditis, SLE, calcifications, congenital (bicuspid or unicuspid aortic valve), flail leaflet, osteogenesis imperfecta, drugs (fenfluramine)

AORTIC DILATION—aortic dissection, ankylosing spondylitis, syphilis, Marfan's, Ehlers Danlos, hypertension, bicuspid aortic valve, cystic medial necrosis

PATHOPHYSIOLOGY

PATHOPHYSIOLOGY—leaky aortic valve → initial compensation with left ventricular dilatation and eccentric hypertrophy (palpitations, atypical chest pain), wide pulse pressure (due to increased stroke volume with elevation in SBP and regurgitation with rapid collapse of the arteries and a low diastolic blood pressure) → eventually decompensation leading to left ventricular dysfunction (heart failure)

CLINICAL FEATURES

PHYSICAL

- **GENERAL APPEARANCE**—Marfan's syndrome, ankylosing spondylitis, Argyll Robertson pupils, **Quincke's sign** (pulsatile refill in capillary bed of finger nails), digital throb, **Becker's sign** (visible pulsations of the retinal arteries and pupils), **deMusset's sign** (head bob occurring with each heart beat), **Mueller's sign** (systolic pulsations of the uvula)
- **VITALS**—wide pulse pressure, **water hammer** (tapping impulse in forearm, especially when arm is raised vertically), **Corrigan's pulse**, **Mayne's sign** (>15 mmHg decrease in diastolic blood pressure with arm elevation)
- **CARDIAC**—soft S1, left-sided S3 (heart failure), **diastolic murmur** (early diastolic or holodiastolic, blowing, over left upper sternal border), **Austin Flint murmur** (mid/late diastolic rumble, over apex) and **mid-systolic flow murmur**
- **OTHERS**—**Gerhardt's sign** (systolic pulsations of the spleen), **Rosenbach's sign** (systolic pulsations of the liver), **Traube's sign** (pistol shot pulse with systolic and diastolic sounds heard over the femoral arteries), **Duroziez's sign** (systolic and diastolic bruit heard when the femoral artery is partially compressed), **Hill's sign** (popliteal cuff systolic pressure exceeding brachial pressure by >60 mmHg). Note that all the special signs are due to increased pulse pressure

DISTINGUISHING FEATURES BETWEEN AORTIC REGURGITATION AND PULMONARY REGURGITATION MURMUR

- **PULMONARY REGURGITATION MURMUR**—high pitch decrescendo diastolic murmur (Graham Steell murmur) loudest over **left upper sternal border. Increases with inspiration**. May be associated with signs of pulmonary hypertension
- **AORTIC REGURGITATION MURMUR**—early diastolic decrescendo murmur loudest over **right and/or left upper sternal border**. No change or decreases with inspiration. May be associated with **Austin Flint murmur** and the other signs of aortic regurgitation

DISTINGUISHING FEATURES BETWEEN AUSTIN FLINT AND MITRAL STENOSIS MURMUR

	Austin Flint	Mitral stenosis
Gender	M > F	F > M
Hemoptysis	Almost never	Likely mitral stenosis
Rhythm	Sinus	Atrial fibrillation
M1	Usually faint	Usually loud
P2	Normal or ↑	Usually loud
Ventricular gallop/S3	Always present	Absent
Diastolic murmur	Usually early or mid-diastolic	Often presystolic accentuation (if in sinus rhythm)
Opening snap	Absent	Present
CXR	Boot shaped	LAE
ECG	Sinus, LVH, prolonged PR	Atrial fibrillation, P mitrale

INVESTIGATIONS

BASIC

- **CXR**—cardiomegaly
- **ECHOCARDIOGRAM**
- **ECG**—LVH
- **EXERCISE TESTING**

SPECIAL

- **CARDIAC CATHETERIZATION**

PROGNOSTIC ISSUES

ASYMPTOMATIC WITH NORMAL LV SYSTOLIC FUNCTION

- **PROGNOSIS**—development of symptoms and/or LV dysfunction <6%/year; asymptomatic LV dysfunction <3.5%/year; sudden death <0.2%/year

ASYMPTOMATIC WITH LV DYSFUNCTION

- **PROGNOSIS**—progression to cardiac symptoms >25%/year

SYMPTOMATIC

- **PROGNOSIS**—mortality >10%/year

MANAGEMENT

LIFESTYLE CHANGES—salt restriction/diuretics

MEDICATIONS—afterload reduction with vasodilators (nifedipine, ACE inhibitors, ARBs) indicated for severe AR with symptoms, LV dysfunction, or LV dilatation, but not for long-term management of asymptomatic mild to moderate AR and normal LV function

FOLLOW-UP—asymptomatic mild AR with normal LV function and little/no LV dilatation can be followed annually with clinical exam and echocardiogram every 2–3 years (sooner if symptoms emerge). Asymptomatic severe AR with normal LV function and LV dilatation (>60 mm) should be seen every 6 months with echocardiogram every 2–3 years

PROCEDURES—intraaortic balloon pumps should be avoided

AORTIC VALVE REPLACEMENT (AVR)

- **RECOMMENDED INDICATIONS** (**CLASS I**)—if symptomatic severe AR; asymptomatic chronic severe AR (regurgitant fraction ≥50%, regurgitant volume ≥60 mL/beat, Doppler jet width ≥65% of LVOT) and LVEF <50%; or severe AR and undergoing cardiac surgery for other reasons
- **REASONABLE INDICATIONS** (**CLASS IIa**)—if asymptomatic severe AR with normal LVEF ≥50% but severe LV dilatation (LVESD >50 mm); or moderate AR and undergoing other cardiac surgery
- **POSSIBLE INDICATIONS** (**CLASS IIb**)—if asymptomatic severe AR and normal LVEF ≥50% but with progressive severe LV dilatation (LVEDD >65 mm) and low surgical risk

Mitral Stenosis

Circulation 2009 119:11
AHA/ACC Valvular Heart Disease 2014 Guidelines

DIFFERENTIAL DIAGNOSIS

RHEUMATIC HEART DISEASE
MITRAL ANNULAR CALCIFICATION
CONGENITAL
ENDOCARDITIS
ATRIAL MYXOMA
PROSTHETIC VALVE DYSFUNCTION
COR TRIATRIATUM

PATHOPHYSIOLOGY

STENOTIC MITRAL VALVE—left ventricular inlet obstruction → left atrial overload and left ventricle output failure → atrial fibrillation, pulmonary hypertension and eventually right heart failure

CLINICAL FEATURES

HISTORY—symptoms related to pulmonary hypertension (dyspnea, hemoptysis, chest pain), symptoms related to right heart failure (hepatomegaly, ascites, edema), hoarseness (Ortner's syndrome, due to enlarged left atrium compressing on recurrent laryngeal nerve), complications (endocarditis, thromboembolism), past medical history (rheumatic fever), medications

PHYSICAL

- **GENERAL APPEARANCE**—tachypnea, peripheral cyanosis, mitral facies (purple patches on cheeks secondary to vasoconstriction)
- **VITALS**—decreased pulse volume
- **JVP**—prominent a wave (pulmonary hypertension), absent a wave (atrial fibrillation), cv wave (tricuspid regurgitation)
- **CARDIAC**—right ventricular heave, palpable P2 (pulmonary hypertension), loud S1 (valve cusps widely apart at the onset of systole) in early disease, soft S1 in severe disease (valves rigid), loud S2, absent S3, opening snap (over apex and left lower sternal border; the earlier the opening snap, the more severe the stenosis), low pitch diastolic rumble (over

CLINICAL FEATURES (CONT'D)

apex, left decubitus position in expiration) ± pre-systolic accentuation, tricuspid regurgitation

- **ABDOMINAL**—hepatomegaly, ascites, edema

INVESTIGATIONS

BASIC

- **CXR**—left atrial enlargement, splaying of carina
- **ECHOCARDIOGRAM**—TEE to exclude left atrial thrombus before treatment
- **ECG**—P mitrale, RVH

SPECIAL

- **CARDIAC CATHETERIZATION**

DIAGNOSTIC AND PROGNOSTIC ISSUES

MITRAL STENOSIS AND SEVERITY

- **PROGRESSIVE**—mitral valve area (MVA) >1.5 cm^2, diastolic pressure half-time <150 ms
- **SEVERE**—MVA ≤1.5 cm^2 (MVA ≤1.0 cm^2 with very severe MS), diastolic pressure half-time ≥150 ms (diastolic pressure half-time ≥220 ms with very severe MS); associated with severe left atrial enlargement and pulmonary artery systolic pressure >30 mmHg. Note, transmitral mean gradient often >5–10 mmHg but mean pressure gradient varies greatly according to heart rate
- **SYMPTOMS**—often present when MVA ≤1.5 cm^2 (i.e., with severe MS). Onset of symptoms may be precipitated by exercise, emotional stress, infection, pregnancy, or rapid atrial fibrillation

PROGRESSION—approximately 0.1–0.3 cm^2/year. Initially slow stable course (latent period) of 20–40 years between rheumatic fever and symptoms. From onset of symptoms (accelerated period), around 10 years until disability. Overall 10-year survival is 50–60% in untreated symptomatic MS, >80% in asymptomatic. Median survival <3 years with severe pulmonary hypertension

MANAGEMENT

LIFESTYLE CHANGES—salt restriction/diuretics

MEDICATIONS—**negative chronotropic agents** and HR control to prolong diastolic filling (β-blockers, non-dihydropyridine calcium channel blockers). **Anticoagulation** for patients with concomitant atrial fibrillation (irrespective of $CHADS_2$ score), left atrial thrombus, or prior

MANAGEMENT (CONT'D)

embolic event (even if in sinus rhythm). **Prophylaxis for rheumatic fever** (secondary prevention)

FOLLOW-UP—any change in symptoms warrant reevaluation and echocardiogram. Otherwise, yearly evaluation in asymptomatic patients including CXR and ECG. Yearly echocardiogram for severe MS

PROCEDURES—indicated when symptomatic severe mitral stenosis. **Percutaneous balloon mitral valvuloplasty** (particularly for patients with non-calcified mitral valve, no left atrial thrombus, mild mitral regurgitation, and no other cardiac interventions) is equivalent to **surgical valvuloplasty** in terms of success. Average increase in valve area is 1.0 cm^2

SPECIFIC ENTITIES

ACUTE RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE

- **PATHOPHYSIOLOGY**—group A *Streptococcus* infection → non-suppurative inflammation with cardiac, joints, and CNS manifestations 2–4 weeks later. Post-*Streptococcus* glomerulonephritis and scarlet fever may also occur separately as complications of group A *Streptococcus* infection
- **JONES CRITERIA FOR ACUTE RHEUMATIC FEVER**
  - **MAJOR CRITERIA ★J♥NES★**
    - **JOINT-MIGRATORY POLYARTHRITIS**
    - **♥CARDITIS** (pericarditis, myocarditis, valvulitis)
    - **NODULES** (subcutaneous)
    - **ERYTHEMA MARGINATUM**
    - **SYDENHAM CHOREA**
  - **MINOR CRITERIA**—clinical (fever, polyarthralgias), laboratory (↑ ESR, prolonged PR interval)
  - **DIAGNOSIS**—either two major criteria or one major criterion and two minor criteria, **plus** evidence of antecedent streptococcal infection (e.g., positive throat culture or rapid antigen detection test or elevated streptococcal antibody test)
- **INVESTIGATIONS**—anti-Streptolysin O antibodies, anti-DNase B, antihyaluronidase, positive throat culture, echocardiogram
- **TREATMENTS**—patients with rheumatic disease are at high risk of recurrent rheumatic fever. Recurrent disease causes additional valve damage, and thus these patients should receive **secondary prophylaxis** for rheumatic fever (*benzathine penicillin G* 1.2 M U IM

SPECIFIC ENTITIES (CONT'D)

q4weeks, *penicillin V* 250 mg PO BID, or *azithryomycin* 250 mg PO daily if allergic to penicillin). For patients with valvular involvement, therapy should continue for at least 10 years, or until age 40 (whichever is longer). With a history of carditis in the absence of persistent valvular disease, treat for 10 years, or until age 21 (whichever is longer)

Mitral Regurgitation AHA/ACC Valvular Heart Disease 2014 Guidelines

DIFFERENTIAL DIAGNOSIS

PRIMARY MR (VALVE ABNORMALITY)—rheumatic heart disease, infective endocarditis, mitral valve prolapse, myxomatous degeneration (Barlow's valve), fibroelastic deficiency disease, mitral annular calcification, ruptured chordae tendineae, drugs (fenfluramine)

SECONDARY MR (LEFT VENTRICULAR DILATATION)—myocardial infarction, dilated cardiomyopathy

PATHOPHYSIOLOGY

LEAKY MITRAL VALVE—left atrial and ventricle volume overload → atrial fibrillation and left heart failure

CLINICAL FEATURES

CLINICAL FEATURES—exertional dyspnea, fatigue, decreased S1, widely split S2, S3, holosystolic murmur (over apex), displaced and enlarged apex

INVESTIGATIONS

BASIC

- **CXR**—cardiomegaly, LAE
- **ECHOCARDIOGRAM**
- **ECG**—P mitrale, LVH

SPECIAL

- **CARDIAC CATHETERIZATION**

MANAGEMENT

MEDICATIONS—no specific therapy for MR. Treat concomitant atrial fibrillation if present

FOLLOW-UP—asymptomatic mild MR with normal LV function and no LV dilatation can be followed annually. Asymptomatic severe MR should be seen every 6–12 months with echocardiogram at the time of assessment

PROCEDURES—**mitral valve repair** (generally better outcome if technically possible) or **replacement** if symptomatic, atrial fibrillation, pulmonary hypertension, end-systolic dimension ≥40 mm, or LVEF 30–60%. Transcatheter mitral valve repair may be considered for severely symptomatic, severe primary MR with prohibitive surgical risk

MANAGEMENT (CONT'D)

SPECIFIC ENTITIES

TRICUSPID REGURGITATION

- **PATHOPHYSIOLOGY**—leaky tricuspid valve → right atrium and ventricle volume overload → eventually decompensation leading to right heart failure (hepatosplenomegaly, ascites, peripheral edema)
- **CAUSES**—right ventricular dilatation (left heart failure, pulmonary hypertension, Eisenmenger syndrome, pulmonic stenosis), valve abnormality (rheumatic heart disease, infective endocarditis, Ebstein's anomaly). Rarely is it due to isolated tricuspid valve abnormality
- **CLINICAL FEATURES**—cachexia, jaundice (congestive hepatomegaly), JVP cv wave, RV heave, S3 (with dilated RV), S4 (with stiff RV), holosystolic murmur (over left lower sternal border), edema
- **INVESTIGATIONS**—ECG (P pulmonale, RVH), CXR (cardiomegaly), echocardiogram, cardiac catheterization, rule out intracardiac shunts
- **TREATMENTS**—valve repair or replacement if severe symptoms

MITRAL VALVE PROLAPSE

- **PATHOPHYSIOLOGY**—prevalence 0.6–2.5% of population. May be sporadic or familial connective tissue disorder with morphologic abnormalities of the mitral valve (increased leaflet thickness and redundancy, chordal elongation, and sagging of the leaflets into the left atrium in systole)
- **TREATMENTS**—*ASA* 75–325 mg PO daily for history of transient ischemic attacks, atrial fibrillation (age <65 years, no MR, no HTN, no HF). Anticoagulation with warfarin for atrial fibrillation (if age >65, MR, HTN, or HF), history of stroke/TIA, or left atrial thrombus

SPECIFIC ENTITIES (CONT'D)

TWO SUBTYPES OF MITRAL VALUE PROLAPSE

	Mild subtype	Severe subtype
Demographics	Mainly women (age 20–50)	Mainly men (age 40–70)
Pathology	Mild leaflet abnormalities Minimal MR	Myxomatous disease Considerable leaflet thickening and MR
Symptoms	Orthostatic hypotension Palpitations	Atrial fibrillation
Physical findings	Mid-systolic click with or without a late systolic murmur	MR murmur Chordal rupture may lead to sudden worsening of MR
Prognosis	Few patients have progressive MR	Progressive MR requiring surgery Increased risk of sudden death

Endocarditis

ACC/AHA Infective Endocarditis 2008 Focused Update
AHA Infective Endocarditis 2005 Guidelines
NEJM 2001 345:18

DIFFERENTIAL DIAGNOSIS

INFECTIVE ENDOCARDITIS

- **COMMON**—*Streptococcus viridans* (*S. sanguis*, *S. mutans*, *S. mitis*), *Streptococcus pneumoniae*, *Streptococcus bovis*, *Enterococcus* (*E. faecalis*, *E. faecium*), *Staphylococcus aureus*, Gram-negative bacilli
- **LONG INCUBATION TIME (7–21) DAYS ★HACEK★**
  - ***H****aemophilus*
  - ***A****ctinobacillus*
  - ***C****ardiobacterium*
  - ***E****ikenella*
  - ***K****ingella*
- **SPECIAL MEDIA**—*Mycoplasma*, *Chlamydia*, *Legionella*, *Brucella*, *Bartonella*, *Coxiella burnetii* (Q fever), *Histoplasma*, *Tropheryma whippelii*

MARANTIC ENDOCARDITIS—non-bacterial thrombotic endocarditis secondary to malignancy (usually adenocarcinoma) or SLE (Libman–Sacks endocarditis)

PATHOPHYSIOLOGY

SUBTYPES—classified as acute vs. subacute, native valve vs. prosthetic valve, and right sided vs. left sided

- **NATIVE HEART VALVE**—usually *S. viridans*, *S. bovis*, enterococci
- **PROSTHETIC HEART VALVE**—<**2 months** (usually coagulase negative staphylococci, may need to treat surgically), >**1 year** (usually *S. viridans*, *S. bovis*, enterococci)
- **INJECTION DRUG USE**—usually *S. aureus* and Gram negative rods. Tricuspid valve most commonly affected

PATHOPHYSIOLOGY (CONT'D)

- **CANCER**—about 50% of patients with *S. bovis* endocarditis also have neoplasms of the GI tract

RISK FACTORS FOR ENDOCARDITIS

- **HIGH RISK**—complex cyanotic congenital heart disease (unrepaired or incompletely repaired cyanotic congenital heart disease, including palliative shunts and conduits; completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure; repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device), surgically constructed systemic pulmonary shunts, previous infective endocarditis, prosthetic heart valve, cardiac transplantation recipients who develop cardiac valvulopathy
- **MODERATE RISK**—most other congenital heart diseases, acquired valvular disease (rheumatic heart disease, mitral/aortic/pulmonary/tricuspid stenosis or regurgitation), mitral valve prolapse with valvular regurgitation or leaflet thickening, hypertrophic cardiomyopathy
- **LOW OR NO RISK**—secundum ASD or surgically repaired ASD, VSD, PDA, mitral valve prolapse with thin leaflets in the absence of regurgitation, ischemic heart disease, previous CABG
- **NON-CARDIAC**—IDU, poor dental hygiene, long-term hemodialysis, long-term indwelling catheter, procedures (GU, GI, surgical wound infection), diabetes, HIV

CLINICAL FEATURES

HISTORY—fever, murmur, dyspnea, chest pain, anorexia, weight loss, malaise, night sweats, complications (painful nodules, rash, stroke, myocardial infarction, any infections), past medical history (structural heart disease, recent procedures [dental, GI, GU], IDU, SLE, malignancy), medications

PHYSICAL—fever, splinter hemorrhages, clubbing, Osler nodes (tender, subcutaneous nodules in pulp of digits or thenar eminence), Janeway lesions (nontender, erythematous, hemorrhagic pustular lesions on palms or soles), needle track marks, petechiae over conjunctivae and oral mucosa, Roth spots (pale areas surrounded by hemorrhage on fundoscopic examination), lymphadenopathy, respiratory examination (HF), murmur (regurgitant), splenomegaly, petechiae over legs

HIGH INDEX OF SUSPICION—always consider endocarditis in the differential when dealing with fever of unknown origin, persistent bacteremia, HF, MI, myocarditis, pericarditis, stroke, pneumonia, pulmonary embolism, splenic infarction, glomerulonephritis, septic arthritis, and osteomyelitis. All patients with *S. aureus* bacteremia should undergo echocardiography (25% have IE)

INVESTIGATIONS

BASIC

- **LABS**—CBCD, lytes, urea, Cr, AST, ALT, ALP, bilirubin, LDH, ESR, ANA, serology (HBV, HCV, HIV), urinalysis
- **MICROBIOLOGY**—blood C&S × 3 (endocarditis protocol and blood C&S × 2 daily until culture negative), sputum Gram stain/AFB/C&S, urine C&S, stool C&S, O&P, C. diff toxin A/B
- **IMAGING**—CXR, echocardiogram (TEE >TTE), CT chest/abd
- **ECG**—heart block

DIAGNOSTIC AND PROGNOSTIC ISSUES

MODIFIED DUKE'S CRITERIA

- **MAJOR**—positive blood culture × 2 (or positive blood culture × 1 for *C. burnetii*), echocardiographic evidence (oscillating intracardiac mass, abscess, new partial dehiscence of a prosthetic valve), new murmur
- **MINOR**—**fever** (>38 °C [100.4 °F]), **risk factor** (cardiac conditions, IDU), **vascular phenomena** (major arterial emboli, septic pulmonary infarct, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions), **immunologic phenomena** (glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor), **positive blood culture** not meeting major criteria
- **DIAGNOSIS**—likely endocarditis if 2 major, 1 major plus 2 minor, or 5 minor criteria

DIAGNOSTIC AND PROGNOSTIC ISSUES (CONT'D)

ECHOCARDIOGRAM—transesophageal echocardiogram (TEE sens 90–100%, spc 95–100%) preferred over transthoracic echocardiogram (TTE sens 50–80%, spc 90%) for detecting vegetations, perivalvular extension of infection and abscesses, diagnosing prosthetic valve endocarditis, and for differentiating between uncomplicated *Staphylococcus aureus* bacteremia and endocarditis

PROGNOSIS—mortality of 25–50% for prosthetic valve endocarditis, 35% for Staphylococcal endocarditis and 10% for Streptococcal endocarditis

Related Topics
Aortic Regurgitation (p. 56)
Mitral Regurgitation (p. 59)
Tricuspid Regurgitation (p. 59)

MANAGEMENT

EMPIRIC ANTIBIOTIC THERAPY—**native valve and non-IDU** (*ampicillin* 2 g IV q4h or *cloxacillin* 2 g IV q4h plus *gentamicin* 1 mg/kg IV q8h, or *vancomycin* 1 g IV q12h plus *gentamicin* 1 mg/kg IV q8h), **native valve and IDU** (*cloxacillin* 2 g IV q4h plus *gentamicin* 1 mg/kg IV q8h or *vancomycin* 1 g IV q12h plus *gentamicin* 1 mg/kg IV q8h), **prosthetic valve** (*vancomycin* 1 g IV q12h plus *gentamicin* 1 mg/kg IV q8h plus *rifampin* 600 mg PO daily)

TARGETED ANTIBIOTIC THERAPY (please refer to the Sanford Guide to Antimicrobial Therapy for up to date recommendations)—**Streptococci** (*penicillin G* 2–3MU IV q4h or *ceftriaxone* 2 g IV/IM q24h × 4 weeks. *Gentamicin* 1 mg/kg IV q24h × 2 weeks may be added in certain circumstances to shorten the course by 2 weeks). **Penicillin-sensitive Enterococci** (*ampicillin* 2 g IV q4h or *vancomycin* 1 g IV q12h × 4–6 weeks, plus *gentamicin* 1 mg/kg IV q8h × 4–6 weeks for native valve). **Penicillin-resistant Enterococci** (*vancomycin* 1 g IV q12h × 6 weeks, plus *gentamicin* 1 mg/kg IV q8h × 6 weeks for native valve). ***S. aureus*** (*cloxacillin* 2 g IV q6h or *nafcillin* or *oxacillin* 3 g IV q6h or *cefazolin* 2 g IV q8h × 2–6 weeks [depending on right- or left-sided valve] ± *gentamicin* 1 mg/kg IV q8h × 3–5 days: for native valve).

MANAGEMENT (CONT'D)

MRSA (*vancomycin* 1 g IV q12h×6 weeks for native valve). **HACEK** (*ceftriaxone* 2 g IV/IM q24h or *ampicillin-sulbactam* 3 g IV q6h or *ciprofloxacin* 500 mg PO BID×4 weeks). For prosthetic valve infection, therapy is usually longer (by 2–4 weeks) with gentamicin

SURGERY—valvular replacement (<10% reinfection rate. See indications below)

TREATMENT ISSUES

INDICATIONS FOR SURGERY—in the acute period, refractory congestive heart failure is the most important indication. Other indications include perivalvular extension of infection with abscess, fistula, or heart block; failure of antibiotic therapy with persistent bacteremia; infection with fungi or untreatable pathogens; Staphylococci on a prosthetic valve; or recurrent embolic events with persistent vegetation(s) despite appropriate antibiotic therapy. Consider early surgical consult for mobile vegetation(s) >10 mm with or without emboli

OVERALL RECOMMENDATIONS FOR ENDOCARDITIS PROPHYLAXIS—only given to patients with the highest risk of developing endocarditis, which include the following:

TREATMENT ISSUES (CONT'D)

- **HIGH-RISK CONDITIONS**—prosthetic valve, prosthetic material used for valve repair, unrepaired cyanotic congenital heart defect, repaired cyanotic congenital heart defect with residual defects at the site or adjacent to the site of the prosthetic device, completely repaired cyanotic congenital heart defect with prosthetic material or device during first 6 months after procedure, cardiac transplant recipients with valvulopathy, previous endocarditis
- **PROCEDURES**
  - **ORAL CAVITY**—dental procedures that involve manipulation of gingival or peripical region of teeth, perforation of oral mucosa
  - **RESPIRATORY TRACT**—tonsillectomy, adenoidectomy, bronchoscopy with a rigid bronchoscope, or flexible bronchoscopy if biopsied
  - **GI/GU TRACT**—prophylaxis generally not recommended
- **PROPHYLAXIS REGIMENS**—give one of the following 30–60 min prior to procedure: *amoxicillin* 2 g PO, *ampicillin* 2 g IM/IV, *cefazolin* 1 g IV/IM, *ceftriaxone* 1 g IV/IM, *cephalexin* 2 g PO, *clindamycin* 600 mg PO/IM/IV, *azithromycin* 500 mg PO, *clarithromycin* 500 mg PO

Peripheral Vascular Disease

NEJM 2007 356:12

ACCF/AHA Peripheral Artery Disease 2005 and 2013 Guidelines

DIFFERENTIAL DIAGNOSIS OF CLAUDICATION

ARTERIAL

- **ATHEROSCLEROSIS**
- **INTRALUMINAL OCCLUSION**—embolism, thrombosis, dissection, adventitial cystic disease, arterial fibrodysplasia, arterial tumor, occluded limb aneurysm
- **VASCULITIS**—Takayasu's arteritis, temporal arteritis, thromboangiitis obliterans
- **VASOSPASM**
- **DRUGS**—ergot
- **FIBROSIS**—iliac endofibrosis, radiation fibrosis, retroperitoneal fibrosis
- **TRAUMA**

VENOUS—DVT, thrombophlebitis, venous congestion

NEUROPATHIC—spinal stenosis, peripheral neuropathy

OTHERS—arthritis (hips, knees), compartment syndrome

CLINICAL FEATURES

HISTORY—pain, discomfort, or fatigue that occurs in leg muscle with exercise and improves with resting (ischemic intermittent claudication is NOT sensitive for peripheral vascular disease), maximum walking distance, non-healing wounds, trauma, DVT risk factors, past medical history (CAD, HF, AF, stroke, TIA, renal disease, hypertension, cholesterol), medications

PHYSICAL—comprehensive pulse examination of lower extremity

- **ANKLE BRACHIAL INDEX** (ABI)—abnormally high measurement >1.40 associated with noncompressible calcified vessel (and unreliable), 1.00–1.40 normal, 0.91–0.99 borderline, and ≤0.90 abnormal. If ≤0.90 significant narrowing of one or more blood vessels in the legs likely present, <0.8 intermittent claudication, <0.4 resting claudication, <0.25 critical limb ischemia. An ABI that ↓ by 20% following exercise

CLINICAL FEATURES (CONT'D)

is diagnostic of peripheral vascular disease, while a normal ABI following exercise eliminates the diagnosis

- **BUERGER'S TEST**—raise legs to 90° with patient in supine position. Check for return of rubor as the legs are lowered. Abnormal if angle of circulation <0° i.e., legs below table)
- **DEWEESE'S TEST**—disappearance of previously palpable distal pulses after walking exercise

VENOUS INSUFFICIENCY EXAMINATION—hemosiderin deposit, pitting edema, dermatitis, cellulitis, ulcer (with prominent granulation tissue over medial malleolus), superficial venous collaterals (DVT), varicose vein (palpate for tenderness or hardness that may suggest thrombophlebitis), Trendelenburg test (helps to determine whether venous reflux is related to the superficial or deep venous system. Occlude a collapsed superficial vein just below the site of suspected reflux from deep to superficial system. With patient standing, observe refilling of vein. Rapid refilling despite occlusion suggests incompetence of valves in the deep venous system, while slow refilling with occlusion and rapid refilling after occlusion is removed suggests incompetence of valves in the superficial venous system)

RATIONAL CLINICAL EXAMINATION SERIES: DOES THE CLINICAL EXAMINATION PREDICT LOWER EXTREMITY PERIPHERAL ARTERIAL DISEASE?

	LR+	LR–
History		
Claudication	3.3	0.89
Inspection		
Wounds (ischemic ulcers and gangrene over lateral malleolus, tips of toes, metatarsal heads, bunion)	5.9	0.98
Discolouration	2.8	0.74
Atrophy	–	–
Absence of hair	–	–
Palpation		
Any palpable pulse abnormality (femoral, popliteal, posterior tibial, dorsalis pedis)	4.7	0.38
Coolness	5.9	0.92
Capillary refill time (firm pressure to planter aspect of great toe for 5 s. Abnormal if >5 s for normal skin)	1.9	–
Auscultation		
Any bruit (iliac, femoral, popliteal)	5.6	0.39

SPECIAL TESTS—**ankle brachial index** (ankle SBP by palpation/Doppler of posterior tibial or dorsalis pedis pulse divided by brachial SBP), **venous filling time** (raise leg to 45° for 1 min with patient supine position for vein to collapse. With patient then sitting up and legs dangling, determine the time for vein to refill. Abnormal if >20 s) (LR+ 3.6, LR– 0.8)

APPROACH—"for screening patients who require further testing to diagnose peripheral arterial disease, the most useful individual symptoms and signs are: claudication, femoral bruit and a pulse abnormality on palpation. The absence of claudication and the presence of normal pulses decrease the likelihood of moderate to severe disease. When considering patients who are symptomatic with leg complaints, the most useful individual findings are the presence of cool skin, the presence of at least 1 bruit and any palpable pulse abnormality. The absence of any bruit (iliac, femoral and popliteal) and the presence of normal peripheral pulses reduce the likelihood of peripheral arterial disease"

JAMA 2006 295:5

DISTINGUISHING FEATURES OF COMMON CAUSES OF LEG PAIN

	Claudication	Spinal stenosis	Venous congestion
Pain	Cramp, tiredness	Cramp, tiredness, tingling	Tightness, bursting
Sites	Buttock, hip, thigh, calf, foot	Buttock, hip, thigh	Groin, thigh
Worse	Walking	Walking, standing	Walking
Better	Rest	Sitting or change in position	Leg elevation
Others	Vascular dx, ↓ pulse	Lower back pain	History of DVT

INVESTIGATIONS

BASIC

- **LABS**—CBC, lytes, urea, Cr, fasting glucose, fasting lipids, HbA1C
- **ANKLE BRACHIAL INDEX**—with or without exercise
- **DUPLEX ULTRASOUND**
- **ECG**

SPECIAL

- **CT/MR angiography**
- **ANGIOGRAPHY**

DIAGNOSTIC ISSUES

DIAGNOSTIC APPROACH—ABI <0.90 is sufficient for the diagnosis of peripheral arterial disease as it suggests >50% stenosis of peripheral vasculature (sens 90%, spc 98%). Patients with large vessel disease (distal aorta or iliac arteries) may only have abnormal ABI after exercise. Patients with non-compressible vessels (as suggested by ABI >1.30–1.40) should have toe-brachial index done. Perform duplex US or CT/MR angiogram if the diagnosis is uncertain or if revascularization is being considered. Digital-subtraction angiograph remains the gold standard

MANAGEMENT

RISK REDUCTION ★ABCDEFG★

- **ASA**
- **BLOOD PRESSURE CONTROL** (see HYPERTENSION p. 65)
- **CHOLESTEROL CONTROL** (see DYSLIPIDEMIA p. 70)
- **DIABETIC CONTROL** (see DIABETES p. 381)
- **EXERCISE** (30 min of moderate-intensity exercise 3–4×/week)
- **FAT REDUCTION** (see OBESITY ISSUES p. 457)
- **GET GOING TO QUIT SMOKING**! (see SMOKING ISSUES p. 480)

MEDICAL—antiplatelet (*ASA* 75–325 mg PO daily, *clopidogrel* 75 mg PO daily), high-intensity **statin** (*atorvastatin* 80 mg PO daily, *rosuvastatin* 40 mg PO daily). Consider *cilostazol* 100 mg PO BID for life-limiting claudication (in the absence of heart failure), but treatment with *pentoxifylline* 400 mg PO TID is of dubious benefit

SURGICAL—revascularization (surgery or percutaneous transluminal angioplasty)

TREATMENT ISSUES

REVASCULARIZATION—indicated for patients with significant functional limitations (lifestyle or jobs) despite maximal lifestyle and medical treatment. Not optimal for patients <40 with atherosclerosis obliterans, with non-disabling symptoms, diabetes, significant coronary risk factors, or other diseases associated with high mortality

SPECIFIC ENTITIES

VASCULAR DISEASE FAMILY—CAD, CVD, PVD, AAA, renal artery stenosis, chronic mesenteric ischemia

ABDOMINAL AORTIC ANEURYSM—U.S. Preventative Services Task Force recommends one-time screening with abdominal US for men 65–75 who have ever smoked. Repair is controversial for 4–5 cm [1.6–2 in.]; >5 cm [>2 in.] warrants surgical intervention (risk of spontaneous rupture is 22%/year). Monitor lesions ≤5 cm [≤2 in.] with ultrasound regularly (every 6 months if lesions 4 cm [1.6 in.], more frequent for bigger lesions). Operative mortality is 4–6% for elective repair, 19% for urgent repair, and 50% for repair of a ruptured aneurysm. No driving if AAA >6 cm [2.4 in.] in men, >5.5 cm [2.2 in.] in women

RATIONAL CLINICAL EXAMINATION SERIES: DOES THIS PATIENT HAVE ABDOMINAL AORTIC ANEURYSM?

PALPATION—to detect abnormal widening of the aortic pulsation (sens 50% for AAA 4–4.9 cm [1.6–1.9 in.], sens 76% for AAA ≥5 cm [≥2 in.], LR+ 12 and LR– 0.72 for AAA ≥3 cm [≥1.2 in.], LR+ 15.6 and LR– 0.51 for AAA ≥4 cm [≥1.6 in.])

APPROACH—"abdominal palpation will detect most AAAs large enough to warrant surgery, but it cannot be relied on to exclude the diagnosis. The sensitivity of palpation appears to be reduced by abdominal obesity. When a ruptured AAA is suspected, imaging studies such as ultrasound or computed tomography should be performed regardless of physical findings"

UPDATE—sensitivity for palpation of AAA improved among thinner patients, especially if abdominal girth is <100 cm

JAMA 1999 281:1
The Rational Clinical Examination. McGraw-Hill, 2009

Hypertension

CHEP Hypertension 2014 Guidelines
JNC8 Hypertension 2014 Guidelines
JNC7 Hypertension 2003 Guidelines
NEJM 2003 348:7; NEJM 2006 355:4; NEJM 2007 357:8

DIFFERENTIAL DIAGNOSIS

★0–1–2–3-4★

0 **ESSENTIAL HYPERTENSION**
1 **ANATOMIC**—aorta (coarctation, aortic dissection)
2 **RENAL**—renal parenchymal disease (chronic renal failure, polycystic kidney disease), renal artery stenosis
3 **ADRENAL**—pheochromocytoma, Conn's syndrome, Cushing's syndrome
4 **SCENTS**
- **SUPER GROWTH**—acromegaly
- **CALCIUM**—hypercalcemia (hyperparathyroidism)
- **ESTROGEN OR OTHER DRUGS**—NSAIDs, corticosteroids, anabolic steroids, oral contraceptives, cocaine, amphetamines, MAO inhibitors, SNRIs, SSRIs, erythropoietin, cyclosporine, tacrolimus, midodrine, alcohol excess, licorice root
- **NEUROLOGIC**—Cushing's triad (hypertension, bradycardia, and respiratory depression associated with increased intracranial pressure)
- **THYROID**—hyperthyroidism, hypothyroidism
- **SLEEP APNEA**

PATHOPHYSIOLOGY

CLASSIFICATION OF HYPERTENSION

- **NORMAL**—SBP <120 mmHg *and* DBP <80 mmHg
- "**PREHYPERTENSION**"—SBP 120–139 mmHg *or* DBP 80–89 mmHg
- **STAGE 1 HYPERTENSION**—SBP 140–159 mmHg *or* DBP 90–99 mmHg
- **STAGE 2 HYPERTENSION**—SBP ≥160 mmHg *or* DBP ≥100 mmHg
- **MASKED HYPERTENSION**—BP consistently elevated with out-of-office measurements, but normotensive when measured in office; associated with ↑ cardiovascular risk
- **WHITE COAT HYPERTENSION**—BP consistently elevated with office measurements, but normotensive when out-of-office; possible slight ↑ cardiovascular risk (but still less than in masked or sustained hypertension)

PATHOPHYSIOLOGY (CONT'D)

- **HYPERTENSIVE EMERGENCY**—severe hypertension (usually SBP ≥220 and/or DBP ≥120 mmHg) with end organ damage such as pulmonary edema, aortic dissection, myocardial infarction, cerebrovascular hemorrhage, papilledema, fundoscopic hemorrhages or exudates, acute renal failure, eclampsia of pregnancy, and hypertensive encephalopathy
- **HYPERTENSIVE URGENCY**—severe hypertension (usually SBP ≥220 and/or DBP ≥120 mmHg) without findings of hypertensive emergency

ISOLATED SYSTOLIC HYPERTENSION—younger people tend to have isolated diastolic hypertension (50–60% of patients under 40). With age, large arteries tend to stiffen with decreased elasticity secondary to a combination of atherosclerosis, calcification, and elastin degradation. Thus, isolated systolic hypertension predominates with age (over 90% of patients over 70)

HYPERTENSIVE END ORGAN DAMAGE—ischemic heart disease, peripheral arterial disease, left ventricular hypertrophy, stroke, TIA, microalbuminuria or proteinuria, and chronic kidney disease

HYPERTENSIVE RETINOPATHY

- **MILD**—**focal arteriolar narrowing** (vasospasm), **generalized arteriolar narrowing** (increased vascular tone due to autoregulation, mild intimal hyperplasia, and hyaline degeneration in sclerotic stage). Subsequently, **arteriovenous nicking** (venous compression by a thickened arteriole, leading to dilation of vein around intersection) and **opacity of arteriolar wall** (widening and accentuation of the central light reflex leading to so-called copper wiring appearance)
- **MODERATE**—**hemorrhages** (blot, dot, or flame shaped due to disruption of the blood–retina barrier), **microaneurysms** (necrosis of the smooth muscles and endothelial cells), **hard exudates** (exudation of blood and lipids), and **soft exudates** (cotton wool spots, retinal ischemia)
- **MALIGNANT**—signs of moderate retinopathy plus swelling of the optic disc
- **UTILITY**—the retina provides a window of cerebral circulation. Risk of stroke (and death) increases with degree of retinopathy. Note that the stages may not be sequential

CLINICAL FEATURES

HISTORY—blood pressure levels, ambulatory/home monitoring, complications and hypertensive end organ damage, other cardiac risk factors (smoking, diabetes, dyslipidemia, obesity), past medical history (thyroid, renal, or adrenal disorders), medications (antihypertensives, steroids, illicit drugs)

PHYSICAL—vitals (heart rate, blood pressure), obesity (sleep apnea), moon facies and thoracocervical fat pad (Cushing's), low-pitched voice and acral enlargement (acromegaly), upper body better developed and continuous murmur over precordium/back (coarctation), narrowed oropharynx and ↑ neck circumference (OSA), goiter (hyperthyroidism), aortic regurgitation (aortic dissection), striae, renal bruits (renal artery stenosis), abdominal masses (polycystic kidney disease, adrenal tumors), radiofemoral delay and weak femoral pulses (coarctation). Assess complications including retinopathy, stroke, HF, AAA, and PVD

MEASURING BLOOD PRESSURE—NEJM 2009 360:e6

INVESTIGATIONS

BASIC

- **LABS**—lytes, urea, creatinine, fasting glucose, HbA1C, fasting lipid profile, urinalysis, urine microalbumin
- **24-H AMBULATORY BLOOD PRESSURE MONITOR**
- **ECG**

SECONDARY CAUSES WORKUP

- **HYPERALDOSTERONISM WORKUP**—if clinical features present (i.e., spontaneous hypokalemia <3.5 mmol/L; diuretic-induced hypokalemia <3.0 mmol/L; resistance to ≥3 antihypertensive drugs; adrenal incidentaloma with hypertension) then consider serum renin/aldosterone, saline infusion test, oral sodium loading test, adrenal vein sampling. Plasma renin activity is difficult to interpret in patients taking mineralocorticoid receptor antagonists (e.g., spironolactone)
- **PHEOCHROMOCYTOMA WORKUP**—if clinical features present (i.e., paroxysmal and/or severe hypertension refractory to usual antihypertensive drugs; symptoms of catecholamine excess; hypertension triggered by β-blockers, MAO inhibitors, micturition, or Valsalva maneuver; adrenal incidentaloma with hypertension; genetic syndrome [MEN2A, MEN2B, von Hippel-Lindau, neurofibromatosis]) then consider 24-h urine metanephrine, plasma fractionated metanephrines
- **OTHER ENDOCRINE WORKUP** (guided by clinical suspicion)—Ca, albumin, PTH, TSH, free T4, 24-h urine cortisol, 1 mg dexamethasone suppression test, late night salivary cortisol, IGF-1
- **RENOVASCULAR WORKUP**—if ≥2 clinical features present (i.e., sudden-onset or worsening hypertension and age >55 or <30 years; presence of abdominal bruit; resistance to ≥3 antihypertensive drugs; ↑ serum Cr ≥30% with ACEi or ARB; other atherosclerotic disease; or recurrent flash pulmonary edema), then consider renal Doppler US, CT/MR angiogram, renal angiogram
- **SLEEP OXIMETRY TEST**—if suspect sleep apnea

DIAGNOSTIC ISSUES

CLINICAL DIAGNOSIS OF HYPERTENSION

1. **Hypertensive urgency or emergency during first visit**?
   - Yes → hypertension diagnosed
   - No → proceed to step 2
2. **What is the blood pressure during initial visit**?
   - SBP ≥180 mmHg and/or DBP ≥110 mmHg → repeat BP at least 2 more times at the same visit (discard first reading and average latter 2 readings). If mean BP 180/110 or greater, diagnosis of hypertension is confirmed
   - SBP 140–179 mmHg and/or DBP 90–109 mmHg (or mean automated office BP taken using an automated device that performs multiple readings with the patient alone in the room is SBP 135–179 and/or DBP 85–109 mmHg), then obtain out-of-office readings before second visit
   - SBP 130–139 and/or DBP 85–89 mmHg → annual follow-up
3. **Out-of-office readings can be measured using 24-hour ambulatory monitoring (ABPM) or a home BP series (HBPM).** ABPM is preferred. Further information on how to perform these can be found at www.hypertension.ca
4. **What is the average blood pressure from the ambulatory BP monitor**?
   - Mean awake SBP ≥135 mmHg or DBP ≥85 mmHg → hypertension diagnosed

DIAGNOSTIC ISSUES (CONT'D)

- Mean awake SBP <135 mmHg and DBP <85 mmHg → long-term follow-up
- Mean 24-h SBP ≥130 mmHg or DBP ≥80 mmHg → hypertension diagnosed
- Mean 24-h SBP <130 mmHg or DBP <80 mmHg → long-term follow-up

5. **What is the average blood pressure from home BP monitoring**?
   - Average SBP ≥135 or DBP ≥85 mmHg → hypertension diagnosed
   - Average SBP <135 or DBP <85 mmHg → repeat home BP monitoring (to confirm average BP <135/85 mmHg), or consider ambulatory BP monitoring (step 8), then long-term follow-up

CHEP Hypertension 2015 Guidelines
http://www.hypertension.ca

ACUTE MANAGEMENT

ACUTE—ABC, O_2, IV

HYPERTENSIVE EMERGENCY—*labetalol* 20 mg IV bolus initially, then 20–80 mg q10min, or 2 mg/min IV infusion (loading) then 2–8 mg/min, maximum total dose of 300 mg. *Nitroprusside* 0.25–0.5 μg/kg/min IV initially, increase by 0.5 μg/kg/min increments, to usually target 3 μg/kg/min (rarely >4 μg/kg/min, maximum 10 μg/kg/min). *Nicardipine* 5 mg/h IV initially, titrate to a maximum of 15 mg/h. *Fenoldopam* 0.1 μg/kg/min IV initially, titrate dose q15min. Consider ICU admission. Workup and treatment of underlying causes once stabilized

HYPERTENSIVE URGENCY—*furosemide* 20–40 mg PO/IV × 1 dose. *Clonidine* 0.1–0.3 mg PO BID. *Captopril* 25–50 mg PO TID. *Labetalol* 5–20 mg IV q15min or *hydralazine* 5–20 mg IV q15min to keep SBP <170 mmHg. Lower BP over hours to days, 25–30% lower than baseline; avoid lowering BP too rapidly (risk of stroke and MI if BP dropped to below minimum level required to maintain tissue perfusion). Workup and treatment of underlying cause once stabilized

LONG-TERM MANAGEMENT

LIFESTYLE CHANGES—**healthy diet** (high in fresh fruits, vegetables, and low fat dairy products; low in saturated fat and salt <100 mmol/day). **Physical activity** (optimum 30–60 min of moderate cardiopulmonary activity 4–7×/week). **Reduction in alcohol** (<2 drinks/day in men and <1 drink/day in women). **Weight loss** (in those with BMI >25 kg/m^2, lose >5 kg). **Smoke free environment**

ANTIHYPERTENSIVES ★ABCD★

- **ACE INHIBITOR**—*ramipril* 2.5–10 mg PO daily-BID, *captopril* 12.5–50 mg PO TID, *perindopril* 2–8 mg PO daily, *lisinopril* 2.5–10 mg PO daily, *trandolapril* 1–8 mg PO daily
- **ARB**—*candesartan* 8–32 mg PO daily, *losartan* 50–100 mg PO daily, *irbesartan* 150–300 mg PO daily, *valsartan* 80–320 mg PO daily
- **β-BLOCKERS**—not recommended as first-line agent for uncomplicated hypertension in those ≥60-years old. *Metoprolol tartrate* 50–100 mg PO BID, *atenolol* 50–100 mg PO daily, *labetalol* 100–400 mg PO TID, *bisoprolol* 5–10 mg PO daily
- **CALCIUM CHANNEL BLOCKERS**—*amlodipine* 2.5–10 mg PO daily, *diltiazem CD* 180–360 mg PO daily
- **DIURETICS**—*chlorthalidone* 12.5–25 mg PO daily, *indapamide* 1.25–2.5 mg PO daily, *hydrochlorothiazide* 12.5–25 mg PO daily, *spironolactone* 12.5–50 mg PO daily
- **α1 BLOCKERS**—*terazosin* 1–20 mg PO daily, *doxazosin* 1–16 mg PO daily
- **α1 AGONIST**—*clonidine* 0.1–0.5 mg PO BID
- **OTHERS**—minoxidil, phentolamine, hydralazine

TREAT UNDERLYING CAUSE

TREATMENT ISSUES

ACE INHIBITORS/ANGIOTENSIN RECEPTOR BLOCKERS

- **INDICATIONS**—HF, post-MI, diabetes, proteinuria, renal failure (with caution), LVH
- **CONTRAINDICATIONS**—pregnancy, ESRD, bilateral RAS
- **ADVERSE EFFECTS**—cough (with ACE inhibitor), angioedema, hyperkalemia

β-BLOCKERS

- **INDICATIONS**—resting tachycardia, HF, migraine, glaucoma, CAD/post-MI
- **CONTRAINDICATIONS**—asthma, severe PVD, Raynaud's phenomenon, depression, bradycardia, second or third degree heart block and hypoglycemia-prone diabetics
- **ADVERSE EFFECTS**—depression, ↓ exercise tolerance, bradycardia, hypotension

TREATMENT ISSUES (CONT'D)

CALCIUM CHANNEL BLOCKERS

- **DIHYDROPYRIDINE** (potent vasodilators)—nifedipine, amlodipine, felodipine, nicardipine
- **NON-DIHYDROPYRIDINE** (heart rate control)—verapamil (cardiac depressant activity), diltiazem (some cardiac depressant, some vasodilator)
- **INDICATIONS**—angina pectoris, recurrent SVT (verapamil), Raynaud's phenomenon (dihydropyridine), migraine, heart failure due to diastolic dysfunction, esophageal spasm
- **CONTRAINDICATIONS**—second or third degree heart block (non-dihydropyridine), HF with moderate to marked systolic dysfunction
- **ADVERSE EFFECTS**—nifedipine (dizziness, headache, flushing, and peripheral edema), verapamil (↓ cardiac contractility, conduction, and constipation), diltiazem (both side effects but a lot less severe)

DIURETICS

- **INDICATIONS**—most patients (particularly those of African descent)
- **CONTRAINDICATIONS**—allergy
- **ADVERSE EFFECTS**—↓ K, ↑ Ca (thiazides), hyperuricemia, ↑ cholesterol, ↑ glucose, ↑ insulin resistance, impotence

TREATMENT ISSUES (CONT'D)

BLOOD PRESSURE TREATMENT TRIGGERS AND TARGETS

	Blood pressure (mmHg)
When to start therapy?	
No macrovascular target organ damage or other independent cardiovascular risk factors	≥160/100
Macrovascular target organ damage or other independent cardiovascular risk factors	≥140/90
Very elderly	≥160
What should the targets be?	
Diabetes	<130/80
All others (including non-diabetic chronic kidney disease)	<140/90
Very elderly (≥80-years old)	<150 (systolic)

CHEP Hypertension 2014 Guidelines
http://www.hypertension.ca

OVERALL APPROACH TO CHOICE OF THERAPY

Condition	**Drug of Choice**
HTN without other indications	A/B/C/D → AC/AD/BC/BD → ABC/ACD/BCD/ABD → ABCD Avoid B as first line if age ≥60 ACEi may be less effective in those of African descent
Isolated systolic hypertension	ARB/C1/D → ARB plus either C1 or D → ARB plus C1 plus D Avoid B
Angina	ACEi/B → ACEi plus B → add C1
Prior myocardial infarction	AB → ABC
Heart failure	AB → ABD (including spironolactone) → ACEi/ARB/B/D. Avoid hydralazine and minoxidil if LVH
Prior cerebrovascular disease	AD → add other agents
Peripheral vascular disease	A/B/C/D plus ASA. Avoid B if severe PVD
Diabetes without nephropathy	A/C1/D → AC1/AD → add B or C2
Diabetes with nephropathy	A → AC/AB/AD
CKD ± proteinuria	A → AD → add other agents
Asthma	A/C/D. Avoid B
BPH	α-blockers
Migraine	B
Thyrotoxicosis	B
Essential tremor	B
Postural hypotension	Avoid vasodilators and diuretics
Raynaud's	C (dihydropyridine)

TREATMENT ISSUES (CONT'D)

Condition	Drug of Choice
Gout	Avoid D
Hyperkalemia	C/D. Avoid aldosterone antagonists
Hyponatremia	A/B/C. Avoid D
Pregnancy	Labetalol/methyldopa/nifedipine. Avoid ACE inhibitors and ARB (teratogenic)

where *A* ACE inhibitors/ARBs, *B* β-blockers, *C* calcium channel blockers, *C1* long-acting dihydropyridine CCB, *C2* non-dihydropyridine CCB, *D* diuretics

SPECIFIC ENTITIES

RENAL ARTERY STENOSIS (RAS)

- **PATHOPHYSIOLOGY**—causes include atherosclerosis and fibromuscular dysplasia
- **CLINICAL FEATURES**—systemic atherosclerosis, uncontrolled hypertension, flash pulmonary edema, asymmetrical kidneys, renal failure with ACE inhibitor, and renal bruits
- **DIAGNOSIS**—MR angiogram (preferred as noninvasive and high sensitivity/specificity), CT angiogram (anatomical information), duplex US (anatomic and functional information), captopril-enhanced radioisotope renogram (functional information), contrast angiogram (gold standard)
- **TREATMENTS**—**medical** (cornerstone of management of atherosclerotic disease; risk factor reduction with blood pressure control [avoidance of ACE inhibitors/ARBs in *severe bilateral* renal artery stenosis], statin therapy, and antiplatelet agent), **angioplasty** (*not routinely recommended* for atherosclerotic disease because outcomes similar to medical therapy alone; consider if fibromuscular dysplasia, severe or refractory hypertension, recurrent flash pulmonary edema, or acute decline in renal function due to renal artery stenosis. Unlikely to restore renal function if small kidneys or high creatinine >300 μmol/L [3.4 mg/dL]), **surgery**

NEJM 2001 344:6
NEJM 2009 361:20
NEJM 2014 370:1

DIFFERENTIAL DIAGNOSIS OF ABDOMINAL BRUITS

- **CARDIOVASCULAR**—abdominal aortic aneurysm, aortocaval fistula
- **RENAL VASCULAR**—renal artery stenosis
- **GI VASCULAR**—celiac artery compression syndrome, mesenteric ischemia
- **HEPATIC VASCULAR**—cirrhosis, hepatoma, AV malformation, arterioportal fistula, Cruveilhier–Baumgarten sign (cirrhosis, portal hypertension, and caput medusa)

SPECIFIC ENTITIES (CONT'D)

- **SPLENIC VASCULAR**—splenic AV fistula, splenic artery dissection, splenic enlargement
- **PANCREATIC VASCULAR**—pancreatic carcinoma

RATIONAL CLINICAL EXAMINATION SERIES: IS LISTENING FOR ABDOMINAL BRUITS USEFUL IN THE EVALUATION OF RENOVASCULAR HYPERTENSION?

	LR+	LR–
Systolic and diastolic abdominal bruit	39	0.6
Any epigastric or flank bruit, including isolated systolic bruit	6.4	0.4
Systolic bruit	*4.3*	*0.5*
History of atherosclerotic disease	*2.2*	*0.5*

APPROACH—"given the high prevalence (7–31%) of innocent abdominal bruits in the younger age groups, it is recommended that if a systolic abdominal bruit is detected in a young, normotensive, asymptomatic individual, no further investigations are warranted. In view of the low sensitivity, the absence of a systolic bruit is not sufficient to exclude the diagnosis of renovascular hypertension. In view of the high specificity, the presence of a systolic bruit (in particular a systolic–diastolic bruit) in a hypertensive patient is suggestive of renovascular hypertension. In view of the lack of evidence to support characterizing bruits as to pitch, intensity and location, bruits should be reported only as systolic or systolic/diastolic"

JAMA 1995 274:16
The Rational Clinical Examination. McGraw-Hill, 2009

Related Topics
Aortic Dissection (p. 27)
Hyperaldosteronism (p. 398)
Pheochromocytoma (p. 398)

Hyperlipidemia

ACC/AHA 2013 Cholesterol Guidelines
Canadian Cardiovascular Society 2012 Dyslipidemia Guidelines

DIFFERENTIAL DIAGNOSIS OF HYPERCHOLESTEROLEMIA

PRIMARY—polygenic, familial hypercholesterolemia (IIa; suspect when total cholesterol >6 mmol/L [>232 mg/dL], LDL >5 mmol/L [>193 mg/dL]), sitosterolemia
SECONDARY—obesity, diabetes, hypothyroidism, nephrotic syndrome, medications (thiazides), cholestatic liver disease (primary biliary cirrhosis)

DIFFERENTIAL DIAGNOSIS OF HYPERTRIGLYCERIDEMIA

PRIMARY—dietary, familial hypertriglyceridemia (IV; suspect when TGL >5 mmol/L [>440 mg/dL]), LPL deficiency (I), dysbetalipoproteinemia (III), ApoCII deficiency
SECONDARY—obesity, diabetes, nephrotic syndrome, hypothyroidism, alcoholism, drugs (estrogen, tamoxifen, β-blockers, glucocorticoids, cyclosporine, glucocorticoids, novel antipsychotics, protease inhibitors, isotretinoin)

DIFFERENTIAL DIAGNOSIS OF COMBINED HYPERCHOLESTEROLEMIA AND HYPERTRIGLYCERIDEMIA

PRIMARY—familial combined hyperlipidemia (IIb), mixed hypertriglyceridemia (V), dysbetalipoproteinemia (III)
SECONDARY—diabetes, nephrotic syndrome, hypothyroidism, drugs (glucocorticoids, immunosuppressives, protease inhibitors), lipodystrophies

DIFFERENTIAL DIAGNOSIS OF LOW HDL

PRIMARY—familial hypoalphalipoproteinemia, Tangiers disease, ApoAI mutation, LCAT deficiency
SECONDARY—drugs (anabolic steroids, isotretinoin)

CLINICAL FEATURES

HISTORY—past medical history (diabetes, CAD, HF, stroke, TIA, renal disease, hypertension, liver disease, gallstones, hypothyroidism, HIV), medications

- **HYPERTRIGLYCERIDEMIA**—pancreatitis, chylomicronemia syndrome (dyspnea, confusion), hyponatremia, transaminitis, milky plasma (with blood work)
- **HYPERCHOLESTEROLEMIA**—premature atherosclerosis, aortic sclerosis/stenosis

PHYSICAL

- **HYPERTRIGLYCERIDEMIA**—lipemia retinalis (when TGL ≥22.6 mmol/L), eruptive xanthomas (commonly on buttocks, extensor surfaces of arms, back; when TG 11.3-22.6 mmol/L), hepatosplenomegaly
- **HYPERCHOLESTEROLEMIA**—tendon xanthomas (most commonly in Achilles tendon and extensor surfaces of hands), xanthelasmas, tuberous xanthomas (over areas susceptible to trauma), corneal arcus (premature when <40-years of age)

INVESTIGATIONS

BASIC

- **LABS**—total chol, TGL, LDL, HDL, apoB, Lp(a), fasting glucose, HbA1C, Cr, TSH, hsCRP, CK, AST, ALT, ALP, bilirubin, LDH

MANAGEMENT

LIFESTYLE CHANGES—**diet** (↑ fruit and vegetable intake, ↑ mono- and polyunsaturated fats, ↓ saturated fats and trans-fatty acid to <7% of calories, ↑ omega-3 fatty acid from fish and plant sources, *salmon oil* 3–9 g can ↓TGL). **Exercise**, **smoking avoidance**

MEDICATIONS

- **HMG-CoA REDUCTASE INHIBITORS** (↓↓ LDL ↑ HDL, ↓ TGL)—*atorvastatin* 10–80 mg PO daily, *rosuvastatin* 5–40 mg PO daily, *simvastatin* 10–80 mg PO daily, *pravastatin* 10–40 mg PO daily. Main side effects include myalgias, myopathy, and transaminitis
- **NPC1L1 TRANSPORTER INHIBITOR** (↓ LDL)—*ezetimibe* 10 mg PO daily
- **FIBRATES** (↓ LDL ↑ HDL, ↓↓ TGL)—*fenofibrate nanocrystallized tablet* [Lipidil EZ] 145 mg PO daily without regard to meals (best oral absorption), *fenofibrate micronized tablet* [Lipidil Supra] 160–200 mg PO with dinner (moderate oral absorption and modestly improved with food), *fenofibrate micronized capsule* [Lipidil Micro] 200 mg PO with dinner (poor oral absorption but improved with food), *gemfibrozil* 600 mg PO daily (safe in pregnancy beginning in second trimester). Main side effects include rash, pruritis, GI upset, gallstones, and myalgia

MANAGEMENT (CONT'D)

- **BILE-ACID SEQUESTRANTS** (↓ LDL, ↑ cholesterol synthesis)—*cholestyramine* 2–24 g PO daily, *colestipol* 5–30 g PO daily in divided doses. Main side effects include constipation, vitamin K deficiency, and drug interactions (bind to other drugs and prevent absorption)
- **NIACIN** (↓ TGL, ↓ LDL, ↑↑ HDL)—*nicotinic acid* 1–3 g PO daily. Main side effects include ↑ blood sugar, flushing (treat with ASA), hepatotoxicity, and gastric irritation
- **OMEGA-3 FATTY ACIDS** (↓ TGL, ↑ LDL)—*eicosapentaenoic acid/docosahexaenoic acid (EPA/DHA)* 3–4 g PO daily. Main side effects include ↑ blood sugar; flushing, hepatotoxicity, and gastric irritation
- **PCSK9 INHIBITOR** (↓↓↓ LDL)—*evolocumab*. Inhibits PCSK9 from binding to LDL receptor on hepatocytes, thus facilitating removal of LDL from circulation. Approved and possibly on market by 2016
- **ASPIRIN**—*ASA* 81 mg PO daily for secondary prevention

TREAT SECONDARY CAUSES/METABOLIC SYNDROME IF PRESENT

TREATMENT ISSUES

RISK CATEGORIES

- **HIGH**—10-year risk of cardiovascular event ≥20%, as estimated using validated risk calculator (Framingham Risk Score, Reynolds Risk Score); clinical vascular disease (e.g., CAD, CVA, TIA, PVD); abdominal aortic aneurysm; diabetes and age ≥40 years or >15 years duration and age ≥30 years or presence of microvascular disease; chronic kidney disease; high-risk hypertension. All high risk patients require treatment
- **MODERATE**—10-year risk of cardiovascular event 10–19%. Consider initiating treatment if LDL ≥3.5 mmol/L [135 mg/dL]; or LDL <3.5 mmol/L [135 mg/dL] *and* ApoB ≥1.2 g/L [120 mg/dL]; or LDL <3.5 mmol/L [135 mg/dL] *and* non-HDL-C ≥ 4.3 mmol/L [166 mg/dL]; LDL <3.5 mmol/L [135 mg/dL] *and* hsCRP >2 mg/L in men age >50 or women age >60
- **LOW**—10-year risk of cardiovascular event <10%. Consider initiating treatment if LDL ≥5.0 mmol/L [≥193 mg/dL]

TREATMENT ISSUES (CONT'D)

HYPERCHOLESTEROLEMIA

- **AMERICAN TREATMENT GUIDELINES**—treat according to severity of cardiovascular risk with appropriate intensity of statin irrespective of actual lipid levels achieved

INTENSITY OF STATIN THERAPY (ACC/AHA 2013 Guidelines)

High-intensity	Moderate-intensity	Low-intensity
↓ LDL-C by approximately ≥50%	↓ LDL-C by approximately 30 to <50%	↓ LDL-C by approximately <30%
Atorvastatin 40–80 mg PO daily	Atorvastatin 10–20 mg PO daily	Simvastatin 10 mg PO daily
Rosuvastatin 20–40 mg PO daily	Rosuvastatin 5–10 mg PO daily	Pravastatin 10–20 mg PO daily
	Simvastatin 20–40 mg PO daily	Lovastatin 20 mg PO daily
	Pravastatin 40–80 mg PO daily	Fluvastatin 20–40 mg PO daily
	Lovastatin 40 mg PO daily	
	Fluvastatin XL 80 mg PO daily	
	Fluvastatin 40 mg PO BID	

- **CANADIAN TREATMENT GUIDELINES**—"treat to target" with specific lipid levels as goal of therapy

TREATMENT TARGETS BASED ON RISK CATEGORY (CCS 2012 Guidelines)

	High risk	Moderate risk	Low risk
LDL	≤2 mmol/L [≤77 mg/dL] or ≥50% ↓ LDL	≤2 mmol/L [≤77 mg/dL] or ≥50% ↓ LDL	≥50% ↓ LDL
ApoB	≤0.80 g/L [<80 mg/dL]	≤0.80 g/L [≤80 mg/dL]	
non-HDL-C	≤2.6 mmol/L [≤100 mg/dL]	≤2.6 mmol/L [≤100 mg/dL]	

TREATMENT ISSUES (CONT'D)

HYPERTRIGLYCERIDEMIA

- **TREATMENT**—dietary modification (with reduced fat, simple sugars, and calories) and alcohol abstinence. Severe cases (TG >11.3 mmol/L [1,000 mg/dL]) should be treated pharmacologically because of associated risk of pancreatitis. Target <4.5 mmol/L [<400 mg/dL]

SPECIAL CASES

- **FAMILIAL HYPERCHOLESTEROLEMIA**—lifestyle modification and pharmacologic therapy with potent statin (atorvastatin, rosuvastatin) plus add-on therapy with bile-acid sequestrant or ezetimibe, or both. Consider PCSK9 inhibitor when available. Homozygotes may require LDL apheresis or possible liver transplantation (to provide functional LDL receptors). Consider genetic counseling for affected family members
- **FAMILIAL COMBINED HYPERLIPIDEMIA**—lifestyle modification (weight reduction and dietary changes) and pharmacologic therapy with statin plus add-on therapy with ezetimibe or fibrate
- **DYSBETALIPOPROTEINEMIA**—identify and treat comorbidities (diabetes, obesity, hypothyroidism). Pharmacologic therapy often unnecessary, but when needed, consider statin or fibrates. Consider genetic counseling (for apoE2 gene) for affected family members

TREATMENT ISSUES (CONT'D)

- **CHYLOMICRONEMIA SYNDROME**—dietary modification (total fat restriction initially until TG <11.3 mmol/L [1,000 mg/dL] then fat-limited diet), alcohol abstinence, optimize glycemic control, and discontinue offending medications. Pharmacologic therapy with fibrate plus add-on therapy with statin or orlistat

SPECIFIC ENTITIES

METABOLIC SYNDROME (syndrome X or insulin resistance syndrome)—National Cholesterol Education Program's Adult Treatment Panel (ATP) III report criteria ≥3 of the following five features:

- ↑ **TGL**— ≥ 1.7 mmol/L [≥150 mg/dL]
- ↓ **HDL**—♀ <1.30 mmol/L [<50 mg/dL], ♂ <1.04 mmol/L [<40 mg/dL]
- **INSULIN RESISTANCE**—fasting glucose ≥5.6 mmol/L [≥100 mg/dL] (modified; originally defined as fasting glucose ≥6.1 mmol/L [≥110 mg/dL])
- **WAIST CIRCUMFERENCE**—♂ >102 cm [>40 in.], ♀ >88 cm [>35 in.]. May consider ethnic-specific cut-offs where appropriate (Europid ♂ ≥94 cm [≥37 in.], ♀ ≥ 80 cm [≥31.5 in.]; South Asian/Chinese: ♂ ≥90 cm [≥35.5 in], ♀ ≥80 cm [31.5 in.]; Japanese: ♂ ≥85 cm [33.5 in.], ♀ ≥90 cm [35.5 in.])
- **HYPERTENSION**— ≥ 130/85 mmHg or on treatment

FAMILIAL DYSLIPIDEMIAS (FREDRICKSON CLASSIFICATION)

Type	Mechanism	Lipid profile	Tendon xanthoma	Palmar xanthoma	Eruptive xanthoma	Xanthelasma	Tuberous xanthoma	Cardiac risk
Type I. Hyperchylomicronemia (LPL deficiency)	LPL deficiency resulting in chylomicron accumulation	↑↑ TGL			✓	✓		-
Type IIa. Familial hypercholesterolemia	LDL receptor defect	↑ TC (LDL) +/− ↑ TG +/− ↑ apoB	✓			✓	✓	++
Type IIb. Familial combined hyperlipidemia	↑ hepatic production of VLDL	↑ apoB +/− ↑ TG +/− ↑ TC (LDL)				✓	(sometimes)	+
Type III. Dysbetalipoproteinemia	ApoE Δ (apoE2/E2); ↓ clearance of chylomicron and VLDL remnants	↑ TGL ↑ TC (VLDL, IDL)	(sometimes)	✓		✓	✓	+ (and PVD)
Type IV. Hypertriglyceridemia	↑ hepatic production of VLDL	↑ TC (VLDL) ↑ TGL ↓ HDL			✓	✓		+
Type V. Mixed hypertriglyceridemia	↑ production and ↓ clearance of VLDL and chylomicrons	↑↑ TGL ↑ TC (VLDL)			✓	✓		-

Smoking Issues

See SMOKING ISSUES (p. 480)

Approach to ECG

AHA/ACCF/HRS 2009 Recommendations
Circulation 2007 115:10
Circulation 2009 119:10

TEN STEPS TO ECG

1. **ID**—name and age, date, technique (12 lead, calibration, paper speed)
2. **RATE**—normal 60–100 beats/min. 300/150/100/75/60/50 rule
3. **RHYTHM**—regular/irregular, wide/narrow complex, sinus, atrial, atrioventricular, ventricular
4. **AXIS**—deviation, rotation
5. **PR INTERVAL**—normal 120–200 ms; first, second, third degree AV block
6. **QRS INTERVAL**—normal 80–110 ms, intraventricular conduction delay 110–120 ms, RBBB, LBBB, LAFB, LPFB
7. **QT INTERVAL**—QT <50% of RR interval; normal QTc 390–460 ms (women), 390–450 ms (men)
8. **HYPERTROPHY/ENLARGEMENT**—RAE, LAE, RVH, LVH
9. **ISCHEMIA**—ST elevation/depression, T wave inversion
10. **INFARCTION**—Q waves
11. **SPECIAL CONDITIONS**

CHEST LEADS PLACEMENT

V1—4th intercostal space, right sternal border
V2—4th intercostal space, left sternal border
V3—halfway between V2 and V4
V4—5th intercostal space, left mid-clavicular line
V5—5th intercostal space, left anterior axillary line
V6—5th intercostal space, left mid-axillary line

RATE AND RHYTHM

SINUS—P before QRS, QRS after P, P upright I + II, P down aVR. Normal (rate 60–100), tachycardia (rate >100), bradycardia (rate <60), arrhythmia (variable)
ATRIAL—rate 60–80 normally, variable P wave, short PR interval
JUNCTIONAL (mid and distal region of AV node)—rate 40–60, no P wave or inverted P wave
VENTRICULAR (His bundle, bundle branches, ventricle)—rate 20–40, no P wave

TACHYCARDIA

REGULAR NARROW COMPLEX TACHYCARDIA—sinus tachycardia, atrial flutter with fixed block (rate 300, 150, 100), supraventricular tachycardia (atrial tachycardia, AV nodal reentry, orthodromic AVRT (WPW), accelerated junctional tachycardia
IRREGULAR NARROW COMPLEX TACHYCARDIA—sinus tachycardia/arrhythmia, premature atrial contractions, multifocal atrial tachycardia, ectopic atrial tachyarrhythmia with variable block, atrial flutter with variable block, atrial fibrillation
REGULAR WIDE COMPLEX TACHYCARDIA—ventricular tachycardia, supraventricular tachycardia with aberrant conduction, pacemaker-mediated tachyarrhythmia, antidromic AVRT (WPW), metabolic abnormality (e.g., TCA overdose, hyperkalemia), artifact
IRREGULAR WIDE COMPLEX TACHYCARDIA—monomorphic ventricular tachycardia (during "warm-up phenomenon"), polymorphic ventricular tachycardia, atrial fibrillation with pre-excitation (WPW), irregular supraventricular tachycardia with aberrant conduction, coarse ventricular fibrillation, artifact
DISTINGUISHING FEATURES SUGGESTIVE OF VT RATHER THAN SVT WITH ABERRANT CONDUCTION—older age, history of coronary artery disease (>90% pre-test probability), history of structural heart disease (>90% pre-test probability), AV dissociation (dissociated P waves, fusion beats, capture beats), atypical bundle branch block morphology, concordance of precordial leads, QRS width >160 ms in LBBB or >140 ms in RBBB, extreme LAD (−90° to −180°). Hemodynamic stability (or instability) is not a useful distinguishing feature

BRADYCARDIA AND PROLONGED PR

SINUS—sinus bradycardia, sick sinus syndrome / sinus node dysfunction, sinus exit block, tachycardia-bradycardia syndrome (SSS + AF usually)
AV BLOCK—prolonged PR interval

- **FIRST DEGREE**—PR >200 ms constantly
- **SECOND DEGREE**

BRADYCARDIA AND PROLONGED PR (CONT'D)

- **MOBITZ TYPE I** (Wenckebach)—PR progressively longer and then dropped QRS
- **MOBITZ TYPE II**—PR constant and then sudden dropped QRS. When any but not all ventricular beats are dropped, second degree block exists

• **THIRD DEGREE**—complete blockage with independent atrial and escape rhythms (junctional or ventricular escape)

PROLONGED QRS—BUNDLE BRANCH BLOCK AND HEMIBLOCK

ANATOMY—SA node (RCA 59%, LAD 38%, both 3%) → AV node (RCA 90%, LCX 10%) → bundle of His (RCA) → right bundle (LAD), left anterior fascicle (LAD, RCA), and left posterior fascicle (RCA, LAD)

RBBB—QRS ≥120 ms, slurred S wave in I and V6 and rSR′ in V1–3 with R′ taller than r. May also see QR′ complex in V1 (suggestive of old or new infarct). QRS polarity positive in V1–2. Causes include LAD involvement/anterior infarction, may be benign in young people

LBBB—QRS ≥120 ms, broad notched or slurred R in I, aVL, V5, and V6, with no Q waves; broad monomorphic S in V1, may have small r wave. QRS polarity negative in V1–2. Causes include hypertension, CAD, dilated cardiomyopathy, rheumatic heart disease, infiltrative diseases, benign or idiopathic

LEFT ANTERIOR FASCICULAR BLOCK—QRS <120 ms, left axis deviation −45° to −90°, qR in aVL, R-peak time in aVL of 45 ms or more. May be benign, LAD involvement/anterior infarction. Shortcut to diagnosis—I up, II down, aVF down

LEFT POSTERIOR FASCICULAR BLOCK—right axis deviation 90–180°, QRS <120 ms, rS in I and aVL, and qR in III and aVF

PROLONGED QT

NORMAL—QTc = square root (QT in seconds/RR interval in seconds); QT <50% of RR interval; normal QTc 390–460 ms (women), 390–450 ms (men)

CAUSES—**genetic**, **metabolic** (hypokalemia, hypomagnesemia, hypocalcemia), **antiarrhythmics** (quinidine, procainamide, amiodarone, sotalol), **antibiotics** (macrolide, trimethoprim–sulfamethoxazole, fluoroquinolone), **psychotropics** (TCA, SSRI, haloperidol, risperidone), **analgesics** (methadone), **structural heart disease** (HF, LVH, acute ischemia), **others** (HIV, anorexia nervosa, stroke, brain injury)

PROLONGED QT (CONT'D)

PROGRESSION—may result in torsades de pointes, VT, and sudden death (amiodarone less likely)

TREATMENTS—remove offending agent(s), overdrive pacing, isoproterenol infusion, magnesium

HYPERTROPHY CRITERIA

RAE—tall peaked P in II and aVF (>2.5 mm high); large initial component of biphasic P in V1 (p pulmonale)

LAE—wide notched P in II (>2.5 mm long); biphasic P in V1 with broad negative phase; P wave duration >120 ms (p mitrale)

LVH—tall R in aVL (>11 mm); R in V5 or V6 (whichever is taller) plus S in V1 >35 mm; R in V5 or R in V6 > 27 mm; poor R wave progression in precordial leads; ST depression and T wave inversion in lateral leads (I, aVL, V5–6) suggestive of ventricular strain; R in aVL plus S in V3 >28 mm in male or >20 mm in female (Cornell criteria). Diagnosis difficult with LBBB, consider LVH if S in V1 + R in V5 >45 mm (Klein criteria)

RVH—right axis deviation (>110°); R > S wave in V1 and R >7 mm; persistent S waves V5–6; ST depression and T wave inversion V1–3

DIFFERENTIAL DIAGNOSIS FOR DOMINANT R WAVE IN V1—RV hypertrophy, right bundle branch block, posterior myocardial infarction, pre-excitation (Wolff–Parkinson–White), dextrocardia, Duchenne muscular dystrophy, hypertrophic cardiomyopathy, normal variant, incorrect lead placement, juvenile pattern

ISCHEMIA/INFARCT MORPHOLOGY

HYPERACUTE T WAVES—starts in seconds

ST ELEVATION—transmural injury, starts in minutes

ST DEPRESSION—subendocardial infarction. Consider posterior infarct if in V1/V2

T WAVE INVERSION—starts in hours, stays for weeks, and flips back in months

Q WAVES—starts in 8 h. If no reperfusion, stays forever. Considered significant if >1 block wide and height >1/3 of QRS

ACCELERATED IDIOVENTRICULAR RHYTHM—suggests reperfusion post-infarction (HR <100, intermittent)

VOLTAGE CRITERIA

NORMAL—QRS >5 mm high in limb leads, QRS >10 mm high in precordial leads

LOW—thick chest wall, COPD, pericarditis, pleural effusion, amyloidosis, myxedema, hemochromatosis

DIFFERENTIAL DIAGNOSIS OF ST ELEVATION

NORMAL MALE PATTERN—1–3 mm elevation, concave, most marked in V2

ST ELEVATION OF NORMAL VARIANT—seen in V4–5, short QT, high QRS voltage

BENIGN EARLY REPOLARIZATION—most marked in V4 with notching at J point, upright T waves. Reciprocal ST depression in aVR, not in aVL, when limb leads are involved

ACUTE MI—ST segment with a plateau of shoulder or upsloping, reciprocal behavior between aVL + III

PRINZMETAL'S ANGINA—same as MI but transient

ACUTE PERICARDITIS—diffuse ST elevation, ST depression in aVR. Elevation seldom >5 mm, PR segment depression (best seen in II)

ACUTE MYOCARDITIS—diffuse ST elevation, may simulate acute MI/pericarditis

AORTIC DISSECTION—obstruction of right coronary artery by dissection flap

LV ANEURYSM—persistent ST elevation after MI

DIFFERENTIAL DIAGNOSIS OF ST ELEVATION (CONT'D)

PULMONARY EMBOLISM—changes simulating MI seen often in both inferior and anteroseptal leads

STRESS (TAKOTSUBO) CARDIOMYOPATHY—transient apical and/or mid LV systolic dysfunction that mimics myocardial infarction, in the absence of obstructive CAD

LBBB—concave, ST segment deviation discordant from QRS. In the presence of LBBB, features suggestive of infarction include concordant ST segment changes (ST elevation ≥1 mm in leads with positive QRS complex and ST depression ≥1 mm in V1–3), disconcordant ST-segment changes (ST elevation ≥5 mm in leads with negative QRS complex) (Sgarbossa criteria)

LVH—concave, other features of LVH

HYPERKALEMIA—see below

HYPOTHERMIA—Osborne waves may be seen

NEJM 2003 349: 22

INFARCTION ZONES

Territory	Leads	Artery	Comment
Inferior	II, III, aVF[a]	RCA, LCX[b]	RV, SA, AV nodes
Lateral	I, aVL, V5, V6	LCX, RCA	
Posterior	V1i, V2i, V8, V9[c]	RCA	
Anterior	V1–V4[d]	LAD	May be massive LV
RV	R leads (V1), V4R	RCA	Preload

[a]Evidence of inferior MI should trigger one to automatically check V4R to assess for RV infarction, which occurs in up to 40% of patients with inferior MI. May see increased JVP and clear lung fields clinically. ST elevation in V4R is diagnostic and prognostic

[b]Inferior infarcts may be related to either RCA (ST elevation in III > II and ST depression in I, aVL, or both >1 mm) or LCX (ST elevation in I, aVL, V5–6 and ST depression in V1–3)

[c]i = inverted. ST depression in V1–V2 in a regular ECG should trigger one to automatically request for posterior leads to check for posterior MI. Posterior infarct may be associated with inferior and lateral infarct as these territories are all supplied by RCA

[d]V1–V2 = septal, V3–V4 = anterior

SPECIAL CONDITIONS

HYPERTHYROIDISM—tachycardia, non-specific ST-T changes, biphasic T in V2–V6

DIGITALIS EFFECT—slowing SA, AV. Gradual downward sloping/scooping of ST. ST depression in I, II, aVF, V2–V6

DIGITALIS TOXICITY—unifocal or multifocal PVCs, first degree heart block, ventricular bigeminy, paroxysmal atrial tachycardia (often with 2:1 AV conduction), bidirectional VT, atrial fibrillation with complete heart block (regular escape rhythm)

SPECIAL CONDITIONS (CONT'D)

HYPERKALEMIA—tall, peaked T wave (especially precordial leads. Definitions of "tall T wave" include a height >5 mm in limb lead or 10 mm in precordial lead or a T wave height >50% of the entire QRS excursion in same lead), widened QRS, wide and flat P wave

HYPOKALEMIA—flattened T wave/inversion, U wave

COPD—RAD, ↓ amplitude, multifocal atrial tachycardia

SPECIAL CONDITIONS (CONT'D)

HYPERCALCEMIA—short QT
HYPOCALCEMIA—prolonged QT
WOLFF–PARKINSON–WHITE SYNDROME—short PR (<120 ms), delta wave, prolonged QRS (>120 ms), symptomatic tachycardia. Pharmacological treatments include amiodarone and procainamide. **AV nodal blocking drugs** (**adenosine**, **β-blockers**, **verapamil**/**diltiazem**, **digoxin**) **are contraindicated in patients with WPW and AF as they may precipitate VF**. Consider catheter ablation if symptomatic arrhythmias, AF, or atrial flutter. If failed, consider surgical ablation
BRUGADA SYNDROME—type 1: high take-off and cove-shaped ST-segment elevation (≥2 mm) in V1–V2. Type 2: saddle-back ST-T pattern in V1–V2