

#### SOUTHEAST AIDS TRAINING AND EDUCATION CENTER

Update in Cardiovascular Health for the HIV Provider

Mehul Tejani, M.D., Schuyler Livingston, M.D. Division of General Medicine and Geriatrics Emory University School of Medicine



#### Disclosures

Dr. Livingston nor Dr. Tejani do not have any relevant conflicts of interest, financial or otherwise.



#### **Objectives**

For patients living with HIV/AIDS:

- Treat hypertension, with consideration of updated guidelines (JNC 8)
- Manage lipid-lowering therapy, with consideration of updated guidelines (ATP IV)
- Choose appropriate therapy for prevention of recurrent CVA
- Provide evidence-based treatment for systolic heart failure



#### Case 1

49 year old African American male on Atripla since 2008, CD4 count of 345 and HIV viral load <40 copies/mL presents for routine followup. His only complaint is of BPH symptoms but not interested in meds.

On intake, vital signs show a BP of 145/85. The blood pressure is manually repeated and found to be 144/88. In review of his chart, it is noticed that his blood pressure at the last visit was also 145/85.

His history is notable for only HIV, and he is on no other medications.

His lab studies aside from above are notable for a Cr of 0.9, and a urinalysis shows no protein.



# Case 1

Should you recommend treatment for hypertension?

Yes

No





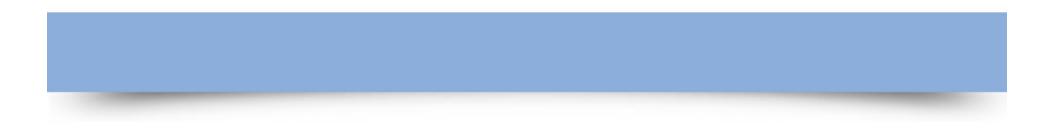
Should you recommend treatment for hypertension?

Yes

No

This 49 year old patient has had a systolic blood pressure (SBP) above 140.





Which of the following would be an appropriate first treatment?

- A. Recommend dietary changes to decrease salt intake
- B. Hydrochlorothiazide (HCTZ)
- C. Lisinopril
- D. Amlodipine
- E. Metoprolol



## HIV and Hypertension

- Unlike some of the upcoming topics, no clear link between HIV and hypertension
- Furthermore, thankfully minimal interaction between antiretroviral medications and antihypertensive medications
- Antihypertensive regimen may change with concomitant kidney disease, which may be due to HIV or ARVs



### Joint National Committee 8 (JNC 8) Guidelines

**Clinical Review & Education** 

Special Communication

#### 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Paul A. James, MD; Suzanne Oparil, MD; Barry L. Carter, PharmD; William C. Cushman, MD; Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler, MD; Daniel T. Lackland, DrPH; Michael L. LeFevre, MD, MSPH; Thomas D. MacKenzie, MD, MSPH; Olugbenga Ogedegbe, MD, MPH, MS; Sidney C. Smith Jr, MD; Laura P. Svetkey, MD, MHS; Sandra J. Taler, MD; Raymond R. Townsend, MD; Jackson T. Wright Jr, MD, PhD; Andrew S. Narva, MD; Eduardo Ortiz, MD, MPH

jama.com



February 5, 2014

Volume 311, Number 5 Pages 437-538



## Joint National Committee 8 (JNC 8) Guidelines

Summary of Recommendations:

- For population ≥ 60, start treatment at SBP ≥ 150 or a DBP ≥ 90, for a goal of SBP < 150 and DBP < 90</li>
  - If these patients are already on treatment at lower targets and tolerating treatment without side effects, there is no need to alter therapy
- For patient < 60, start treatment at SBP ≥ 140 or a DBP<</li>
   ≥ 90, for a goal of SBP < 140 and DBP < 90</li>
- These goals do not change for patients with diabetes or chronic kidney disease



## JNC 8 Guidelines continued – What to start with

Summary of Recommendations:

- For the nonblack population, initial or add-on treatment should include thiazide diuretics, calcium channel blockers (CCBs) or ACE inhibitors (ACEI) or angiotensin receptor blockers (ARB)
- For the black population, initial treatment should include thiazide diuretics or CCBs
  - This recommendation stems from a prespecified subgroup analysis of data from a single large trial (ALLHAT) that was rated good
- In patients 18 years or older with CKD and HTN, start or add on ACEI or ARB



## Differences from JNC 7

- Variation in treatment goals for patients with DM or CKD
- Recommended 5 classes of therapy, but thiazides considered first line unless there were compelling reasons to use other classes, e.g. diabetes, CKD, CHF, CAD
- Less attention to measurement methods, secondary HTN, resistant HTN, adherence, and special populations



## How JNC 8 Compares to Other Guidelines

Table 6 Guideline Comparisons of Goal BP and Initial Drug Therapy for Adults With Hypertension

Guideline	Population	Goal BP, mm Hg	Initial Drug Treatment Options				
ESH/ESC 2013 <sup>37</sup>	General nonelderly	<140/90					
	General elderly <80 y	<150/90	Diuretic, β-blocker, CCB, ACEI, or ARB				
	General ≥80 y	<150/90					
	Diabetes	<140/85	ACEI or ARB				
	CKD no proteinuria	<140/90					
	CKD + proteinuria	<130/90	ACEI or ARB				
CHEP 2013 <sup>38</sup>	General <80 y	<140/90	Thiazide, β-blocker (age <60y), ACEI				
	General ≥80 y	<150/90	(nonblack), or ARB				
	Diabetes	<130/80	ACEI or ARB with additional CVD risk ACEI, ARB, thiazide, or DHPCCB witho additional CVD risk				
	CKD	<140/90	ACEI or ARB				
ADA 2013 <sup>39</sup>	Diabetes	<140/80	ACEI or ARB				
KDIGO 2012 <sup>40</sup>	CKD no proteinuria	≤140/90					
	CKD + proteinuria	≤130/80	ACEI or ARB				
NICE 2011 <sup>41</sup>	General <80 y	<140/90	<55 y: ACEI or ARB				
	General ≥80 y	<150/90	≥55 y or black: CCB				
ISHIB 2010 <sup>42</sup>	Black, lower risk	<135/85					
	Target organ damage or CVD risk	<130/80	Diuretic or CCB				

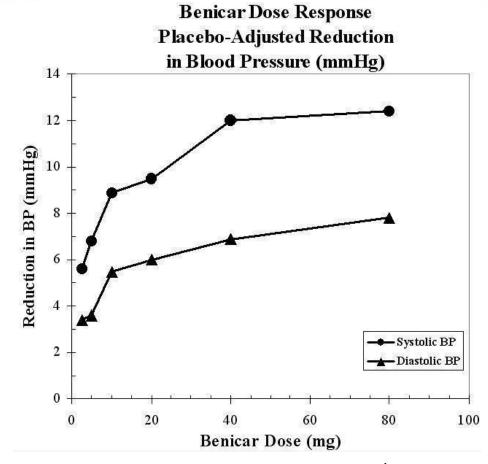


## Final JNC 8 Guideline

- If goal BP not met within 1 month, increase and maximize the dose of initial drug OR add a second drug
- If still not controlled, titrate a 3<sup>rd</sup> drug from the recommended drug classes
- If BP still not controlled or if unable to use drug from recommended classes due to contraindication, add additional meds from other classes
- Do not use ACEI and ARBs simultaneously



#### Justification for adding med before maximizing dose



www.drugs.com



#### Back to Case 1

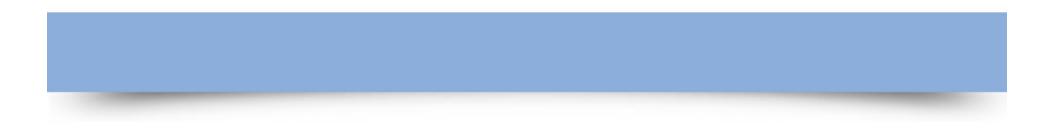
49 year old African American male on Atripla since 2008, CD4 count of 345 and HIV viral load <40 copies/mL presents for routine followup. His only complaint is of BPH symptoms but not interested in meds.

On intake, vital signs show a BP of 145/85. The blood pressure is manually repeated and found to be 144/88. In review of his chart, it is noticed that his blood pressure at the last visit was also 145/85.

His history is notable for only HIV, and he is on no other medications.

His lab studies aside from above are notable for a Cr of 0.9, and a urinalysis shows no protein.





Which of the following would be an appropriate first treatment?

- A. Recommend dietary changes to decrease salt intake
- B. Hydrochlorothiazide (HCTZ)
- C. Lisinopril
- D. Amlodipine
- E. Metoprolol





Which of the following would be the appropriate first treatment?

- A. Recommend dietary changes to decrease salt intake
- B. Hydrochlorothiazide (HCTZ)
- C. Lisinopril
- D. Amlodipine
- E. Metoprolol



#### **Evolution of Case 1**

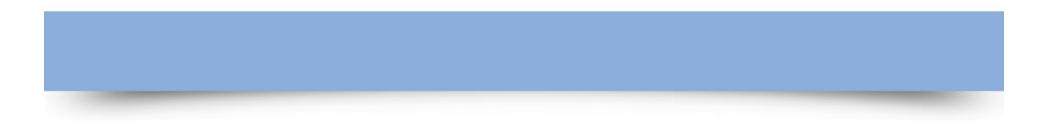
Due to the patient's complaint of BPH symptoms, you elect to avoid starting on a diuretic and place him on amlodipine 5 mg.

After 3 years of controlled BP readings, he has elevated BP measurements at a local grocery store which are consistently in the 150s/90s.

You initially try to increase the dose of his amlodipine to 10 mg, but he complains of bothersome ankle and foot edema, so he reduces his own dose back to 5 mg with resolution of symptoms.

His other medications have not changed, and his labs have been stable.

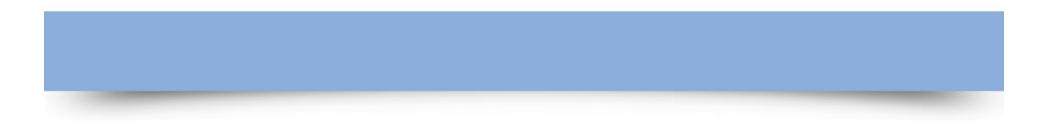




Assuming he has been adherent, which one of the following would be next best treatment?

- A. Recommend dietary changes to decrease salt intake
- B. HCTZ
- C. Lisinopril
- D. Metoprolol





Assuming he has been adherent, which one of the following would be next best treatment?

- A. Recommend dietary changes to decrease salt intake B. HCTZ
- C. Lisinopril
- D. Metoprolol



## ACCOMPLISH Trial

- Performed to analyze combination therapy for hypertension
- 111,506 patients randomized to 2 arms:
  - Benazapril + amlodipine
  - Benazapril + HCTZ
- Primary outcome of composite of death from CV disease, nonfatal MI, nonfatal stroke, hospitalization for angina, coronary revascularization, resuscitation after sudden cardiac arrest
- Average BP control was marginally better in the benazapril + amlodipine arm, 1 mm Hg systolic and diastolic better
- The amlodipine arm had an absolute risk reduction of 2.2% and a RRR of 19.6%



## **Questions?**



#### Case 2: "My best friend just had a heart attack"

- 58 yo AA male, HIV Dx 2012 with cryptosporidiosis
  - Viral load ND x 6 mos
  - CD4 210/16%
  - Baseline genotype: M184V

- PMH: HTN (140/94 today)
- Meds:
  - DRV/r, TDF/FTC
  - Amlodipine 5 mg daily
- Soc Hx: 1 ppd smoker x 30 yrs

Date	LDL	TG's	HDL	Non-HDL
8/2012	90	140	30	120
5/2013	110	250	38	150
4/2014	125	290	36	156



#### What is the best treatment option?

- A) Gemfibrozil 600 mg BID
- B) Fenofibrate 160 mg daily
- C) Simvastatin 40 mg daily
- D) Rosuvastatin 40 mg daily
- E) Pravastatin 20 mg daily
- F) Atorvastatin 10 mg daily
- G) Work on diet and lifestyle
- H) Replace boosted-darunavir with an integrase inhibitor



#### What is the best treatment option?

- A) Gemfibrozil 600 mg BID
- B) Fenofibrate 160 mg daily
  - Minimal change in CVD risk with fibrate therapy (A + B)
- C) Simvastatin 40 mg daily (interacts with RTV, amlodipine)
- D) Rosuvastatin 40 mg daily (max dose 10 mg with RTV)
- E) Pravastatin 20 mg daily (low intensity, should uptitrate)
- F) Atorvastatin 10 mg daily (moderate intensity w/ RTV interaction)
- G) Work on diet and lifestyle
- H) Replace boosted-darunavir with an integrase inhibitor
  - Complicated by partial NRTI resistance



#### **Risk Calculators for 10-year CVD risk**

#### ATP III (Framingham)

DM, CVA, PVD = coronary equivalents (>20% 10-yr risk) Inputs

- Age, gender
- Total cholesterol, HDL
- Systolic BP, on BP medication?
- Smoking status

This patient: 23% 10-year risk of CAD

#### ATP IV (2013)

Additional inputs: ethnicity, diabetes This patient: 26% 10-yr risk of CAD, 69% lifetime risk



## **ATP III Risk Calculator (Framingham)**

#### Risk Assessment Tool for Estimating Your 10-year Risk of Having a Heart Attack

The risk assessment tool below uses information from the Framingham Heart Study to predict a person's chance of having a heart attack in the next 10 years. This tool is designed for adults aged 20 and older who do not have heart disease or diabetes. To find your risk score, enter your information in the calculator below.

Age:	58 years
Gender:	Female Imale Female
Total Cholesterol:	192 mg/dL
HDL Cholesterol:	36 mg/dL
Smoker:	🔍 No 💌 Yes
Systolic Blood Pressure:	140 mm/Hg
Are you currently on any medication to treat high blood pressure.	🔍 No 🖲 Yes

Calculate Your 10-Year Risk



Link: http://cvdrisk.nhlbi.nih.gov/



#### **ATP IV Risk Calculator**

STATEMENTS &	GUIDELINES	SESSIONS	EDUCATION	RESEARCH	SCIENCE NE	WS	MEMBERSHIP	COUNCILS	LIBRARY	EARLY CAREER
Ву Торіс	By Publicatio Date	on Polic Develo	ties & opment In	Journal formation (	Professional Online Network		rention lelines			





## 2013 Prevention Guidelines Tools CV RISK CALCULATOR

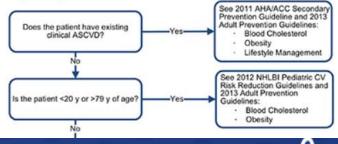
This downloadable spreadsheet is a companion tool to the 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk. The spreadsheet enables health care providers and patients to estimate 10-year and lifetime risks for atherosclerotic cardiovascular disease (ASCVD), defined as coronary death or nonfatal myocardial infarction, or fatal or nonfatal stroke, based on the Pooled Cohort Equations and the work of Lloyd-Jones, et al., respectively. The information required to estimate ASCVD risk includes age, sex, race, total cholesterol, HDL cholesterol, systolic blood pressure, blood pressure lowering medication use, diabetes status, and smoking status.

Estimates of 10-year risk for ASCVD are based on data from multiple community-based populations and are applicable to African-American and non-Hispanic white men and women 40 through 79 years of age. For other ethnic groups, we recommend use of the

The American Heart Association and the American College of Cardiology are excited to provide a series of new cardiovascular prevention guidelines for the assessment of cardiovascular risk, lifestyle modifications that reduce risk, management of elevated blood cholesterol, and management of increased body weight in adults. To support the implementation of these guidelines, the new Pooled Cohort Equations CV Risk Calculator and additional Prevention Guideline Tools are available below. Others may be developed and available in the near future.



Figure 1. Implementation of Risk Assessment Work Group Recommendations



http://my.americanheart.org/professional/StatementsGuidelines/Prevention Guidelines/Prevention-Guidelines\_UCM\_457698\_SubHomePage.jsp

#### **Increased CAD risk in HIV/AIDS**

- Veterans Aging Cohort Study (VACS), 2013 data
  - N = 83,000
  - ~50% increase in risk of myocardial infarction in veterans with HIV compared to matched controls
- <u>D:A:D cohort (2013 data)</u>
  - 32,663 patients with HIV (Europe, Australia), prospective cohort
  - 1,010 vascular events, average f/u ~ 6 years
  - Framingham risk score underestimated 5-yr risk by 30-50%
- <u>SMART study- RCT (2006, 2008 data)</u>
  - CD4-guided ART interruptions (DC) vs. continuous ART (VS)
  - 1.3% CVD rate (DC) vs 0.8% (VS) --- study ended early
  - CVD rate equalized with re-initation of ART

## ATP IV- New Guidelines

Intensity of Statin Therapy	Risk Groups	Drugs
High (~50% LDL lowering)	Known ASCVD LDL >190 DM w/10-yr risk > 7.5%	Atorvastin 40-80 mg* (20 mg with RTV or COBI) Rosuvastatin 20-40 mg* (10 mg with RTV or COBI)
Moderate (30-50% LDL lowering)	40-75 yo, 10 yr-risk > 7.5% Known ASCVD, >75 yo Age 40-75, DM with 10 yr-risk < 7.5%	Atorvastatin 10-20 mg* Rosuvastatin 5-10 mg* Pravastatin 40-80 mg Simvastatin 20-40 mg* Lovastatin 40 mg*
Low (<30% LDL lowering)		Lower doses
ASCVD= History of CAD (N History of CVA or History of PVD	*RTV/COBI interaction	

٦

#### **Additional Updates**

#### ATP IV

- No more LDL targets
- Less frequent lipid monitoring
- Minimal support for other LDL-lowering therapies (niacin, ezetemibe)

#### **Antiretroviral Therapy and Lipids**

- Favorable lipid profiles with integrase-inhibitor based regimens
- Drug interactions with cobicistat are equivalent to ritonavir

#### Final Note

- Efavirenz, etravirine decrease levels of multiple statins



#### **Statins- Safety Issues**

#### <u>Myopathy (2-11%)</u>

- Occurs at same rate as placebo.
- Gradual onset over weeks months. Gradual resolution
- Rechallenge recommended. Consider pravastatin.
- Increased risk with combination fibrate therapy
- Rhabdo (0.06%)
- Check CPK only if symptomatic

#### <u>Type 2 Diabetes Mellitus, new onset (0.2 – 0.4%)</u>

**LFT increase** to > 2-3 upper limit normal (<1.5%, same as placebo)

- No LFT monitoring required.

#### **Cognitive Deficits?**

- Possible rare cases, reversible



#### Case 2

Questions?

slivingston@emory.edu



#### Case 3

A 65 year old male with HIV, CD4 1100 and undetectable VL, on HIV regimen of atazanavir, ritonavir, tenofovir/emtricitabine presents for followup after a recent admission for a stroke.

In addition to HIV, he has poorly controlled insulin-dependent DM with last Hemoglobin A1c 12.3%. He also has HTN which is controlled on lisinopril and amlodipine.

He was admitted after waking up from sleep with inability to move his right side and inability to speak. He was found to have a left MCA stroke without hemorrhage. Due to the fact that the timing of the stroke was unknown, no tPA was given. He had a negative workup for a cause of his stroke including an MRI/MRA of his head and neck, and a transthoracic echocardiogram. He was also placed on a monitor for the duration of his admission without identified arrhythmias.

Which of the following medications should be started for this patient?

- 1. Pravastatin 10 mg
- 2. Rosuvastatin 10 mg
- 3. Aspirin 81 mg
- 4. Clopidogrel 75 mg
- 5. Clopidogrel 75 mg + aspirin 81 mg



Which of the following medications should be started for this patient?

- 1. Pravastatin 10 mg
  - Not recommended as too low potency
- 2. Rosuvastatin 10 mg
  - Recommended, would be higher if not for ritonavir use
- 3. Aspirin 81 mg
  - Would be acceptable
- 4. Clopidogrel 75 mg
  - Would also be acceptable
- 5. Clopidogrel 75 mg + aspirin 81 mg
  - Controversial, would be reasonable for the first 90 days after the event, but not likely after that



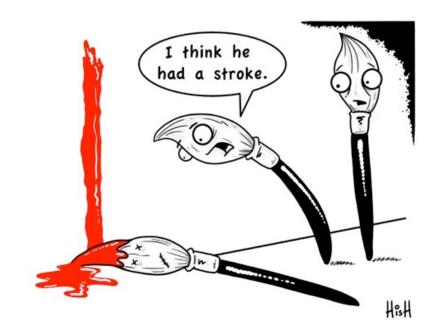
## HIV and CVA

- Similar to cardiovascular disease, HIV patients may have increased risk of stroke
- Risk modification should be done as for any patient, with particular attention to dyslipidemia as previously discussed
- No specific recommendations for secondary prevention of stroke/TIA in persons with HIV





## Secondary stroke prevention guidelines



- Published July 2014 in Stroke
- Consensus statement published by the American Heart Association and the American Stroke Association (AHA/ASA)
- Several guidelines regarding medical therapy and surgical intervention
- Also specific recommendations depending on cardiac risk factors



## Selected key stroke guidelines

### What we will discuss

- Antiplatelet therapy
- Atrial fibrillation
- Modifiable comorbidities
- Lifestyle modifications
- Carotid disease

### What we will not discuss

- Structural heart disease, including thrombus, valvular disease, cardiomyopathy, and septal defects
- Hypercoagulability
- Sickle cell disease
- Pregnancy/breastfeeding



## Antiplatelet therapy

- For noncardioembolic ischemic strokes, antiplatelet therapy is recommended over anticoagulation
- Aspirin 50-325 mg or aspirin 25 + dipyridamole 200 bid has best evidence for recommendation
- Clopidogrel 75 also reasonable
- Combination ASA and clopidogrel may be started within 24 hours and continued for 90 days, but not recommended long term due to increased risk of bleeding
  - Large older RCTs MATCH and CHARISMA looking at this showed increased risk without benefit of combination therapy
  - But more recent RCTs FASTER and CHANCE which used combination treatment for limited time showed benefit without significant increase in adverse events



## **Atrial fibrillation**

- Present in 20-30% of stroke patients, but usually only found 10% of the time during admission
- For that reason, prolonged rhythm monitoring up to 30 days may be reasonable within 6 months of index event
- Coumadin, dabigatran, apixaban, or rivaroxaban are all indicated for stroke prevention in non-valvular afib
  - However, novel oral anticoagulants have several interactions with ARVs (e.g. rivaroxaban with PIs, apixaban with NNRTI) without ability to be monitored
- Combination oral anticoagulation with antiplatelet therapy is not recommended for all patients, but reasonable for patients who also have known CAD



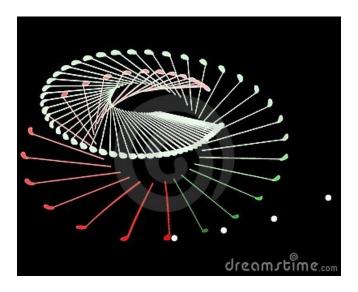
## Modifiable comorbidities

- HTN treat to goals as previously discussed under JNC 8 guidelines, possibly targeting SBP of 140 even in elderly patients
  - No specific recommendation on choice of drug, though trials favor thiazide + ACEI or ARB
  - Data is weak for stroke, so other comorbidities such as CKD or CAD should guide choice of treatment
- Dyslipidemia statin therapy with intensive lipid-lowering effects is recommended if thought to be atherosclerotic, regardless of LDL
  - Largest known trial is the SPARCL which showed benefit with atorvastatin with a 3.5% ARR over 5 years for major CV events, even with average LDL of 133



## Modifiable comorbidities

- DM if the patient has never been diagnosed with diabetes, screening is appropriate
  - If known to have DM, treat according to ADA recommendations
- Obesity weight loss can improve cardiovascular risk factors, but benefit in secondary prevention of stroke/TIA uncertain





## Lifestyle modifications

- Physical inactivity for patients who are capable, at least 3-4 weekly sessions of moderate to vigorous aerobic physical exercise lasting an average of at least 40 minutes is recommended
- Diet reduce intake of sodium, reasonable to recommend a Mediterranean diet
  - No vitamin supplementation indicated unless known deficiency





## Lifestyle modifications



Well, maybe a little drinking. Up to 2 for a man and 1 for a woman.



## Symptomatic carotid artery stenosis

- If the stenosis is 70-99%, carotid endarterectomy (CEA) is recommended if the perioperative risk of MI is < 6%</li>
- For 50-69%, CEA may still be appropriate depending on patient characteristics
- When indicated for a TIA or non-disabling stroke, revascularization within 2 weeks rather than delaying is reasonable
- Carotid artery stenting (CAS) is an appropriate option
   instead of CEA in certain populations with stenosis of
   70% or more, primarily in younger patients (<70) or when</li>
   anatomic or medical conditions create high risk for CEA
- External or internal carotid artery bypass is not indicated
- Routine imaging for followup of carotid artery stenosis with ultrasonography is not recommended





## **Questions?**



## Case 4: "I swelled up and I could hardly breathe"

- 50 year-old African-American female, new to clinic
- 5-day hospitalization last month for heart failure
- New Dx of HIV while hospitalized (CD4 330)
- PMH
  - Long-standing HTN with intermittent treatment
- Soc Hx
  - Remote ETOH, cocaine abuse

### TTE

- EF 30%
- No wall motion abnormalities
- No valvular dysfunction

Normal renal function

#### Meds (since discharge)

- Metoprolol 12.5 mg BID
- Lisinopril 10 mg daily
- Furosemide 40 mg daily



### Case 4- February 2013

- Vitals
  - HR 92, BP 166/100
  - O2 sat 95% on RA
- Exam
  - RRR, no m/r/g, no JVD
  - CTAB, no r/r/w
  - Trace pedal edema
- Labs
  - Cr 1.1, BUN 15
  - Na 136, K 3.2

#### <u>GOALS</u>

- Gradually increase beta blocker dose to achieve HR 60-70
- 2) Control BP by maximizing preferred agents
- 3) Educate on salt balance and diuretic therapy



## May 2013- "That green pill is making my lips swell"

- HR 66, BP 130/90
- Meds
  - Carvedilol 25 mg BID
  - Lisinopril 20 mg daily
  - Furosemide 40 mg daily
  - FTC/TDF/COBI/EVG daily (started 3/2013)

#### Exam

- Lungs CTAB
- No pedal edema, no JVD
- Mild diffuse lip swelling
- No tongue swelling or dysphonia
- Cr 1.3, BUN 18



## **ACE-Inhibitors: Adverse effects**

### Cough (5-10%)

- Onset may be early (days) or delayed (up to 6-10 months)
- Resolves over the course of days to weeks

#### Angioedema (0.1-0.5%)

- Onset may be immediate, or delayed (>1 year)
- Alternative: ARB if strong indication (systolic HF, DM nephropathy)

#### Hyperkalemia, Acute Kidney Injury (1-2%)

- ARB contraindicated
- In heart failure, consider replacing with hydralazine, isosorbide mononitrate (Imdur) or dinitrate (Isordil)



### November 2013- "I had a little too much turkey"

- HR 66, BP 148/92
- O2 sat 96%
- Weight: 170 lbs (from 163)
- + orthopnea, +DOE
- No chest pain, no palpitations.
- No NSAID use.
- Losartan 50 mg
- Carvedilol 25 mg BID
- Furosemide 40 mg daily

#### Exam

- 1+ BLE pitting edema to knees
- CTAB, faint basilar rales, no respiratory distress
- RRR, no m/r/g
- JVD noted half-way up the neck at 45 degrees
- Cr 1.4, BUN 22
- Na 136, K 3.8
- EKG unchanged



### **Treatment Options**

- A) Hospital admission for further evaluation and intravenous diuretic therapy
- B) Increase furosemide to 40 mg BID
- C) Increase furosemide to 80 mg daily
- D) Increase furosemide to 80 mg BID until follow-up in 1 month
- E) Have the patient take furosemide 80 mg BID for the next 3 days
- F) Use an alternative diuretic



### **Treatment Options**

- A) Hospital admission for further evaluation and intravenous diuretic therapy
- B) Increase furosemide to 40 mg BID
- C) Increase furosemide to 80 mg daily
- D) Increase furosemide to 80 mg BID until follow-up in 1 month, with weekly lab monitoring
- E) Have the patient take furosemide 80 mg BID for the next 3 days, then resume previous dose
- F) Use an alternative diuretic



### **Loop Diuretics**

#### **Furosemide**

- Dosage must meet an adequate threshold for response
- Higher doses required with:
  - Volume overload (decreased absorption with gut edema)
  - CKD
  - Exposure to loop diuretics
- Each dose lasts about 6 hours
- Twice daily dosing often required to achieve negative fluid balance

#### <u>Alternatives</u>

- Torsemide
- Bumetanide



## **Medical Management of HFrEF (EF <40%)**

### **Beta Blockers**

- Metoprolol succinate/tartrate
- Carvedilol (better BP lowering)
- Decreased mortality
- Titrate to HR 60-70

### **ACE-Inhibitors/Angiotensin Receptor Blockers**

- Decreased mortality
- Risk of hyperkalemia, acute kidney injury



## **Medical Management of HFrEF (EF <40%)**

#### **Aldosterone Receptor Blockers**

- Eplerenone, Spironolactone
- Reduce mortality in symptomatic HFrEF (EF <35% or <40% post-MI)
- Watch for hyperkalemia (2-5% in RCT's, likely higher in practice)
- Avoid if GFR <30, or baseline K near 5.0

#### Hydralazine + Isosorbide mononitrite

- Decreased mortality in African-American patients with reduced EF, when added to B-blocker + ACE-I or ARB + spironolactone
- Second-line therapy (afterload reduction) for ACE-I/ARB intolerance



## Case 4

Questions?

slivingston@emory.edu



# Thank You!



## References – Case 1

- Lewington S, Clarke R, Qizilbash N, Peto R, Collins R; Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002 Dec 14;360(9349):1903-13.
- James PA, Oparil S, Carter BL, et al. 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311(5):507-520.
- 3. Jammerson K, Weber MA, Bakris GL, et al. for the ACCOMPLISH Trial Investigators. Benazapril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. N Engl J Med 2008; 359:2417-2428.
- Kernan WN, Ovbiagele B, et al. Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2014;45:2160–2236.



### References – Case 3

- Amarenco P, Bogousslavsky J, Callahan A 3rd, Goldstein LB, Hennerici M, Rudolph AE, Sillesen H, Simunovic L, Szarek M, Welch KM, Zivin JA; Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators. High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med. 2006;355:549–559.
- Arima H, Chalmers J, Woodward M, Anderson C, Rodgers A, Davis S, Macmahon S, Neal B; PROGRESS Collaborative Group. Lower target blood pressures are safe and effective for the prevention of recurrent stroke: the PROGRESS trial. J Hypertens. 2006;24:1201–1208.
- Schrader J, Lüders S, Kulschewski A, Hammersen F, Plate K, Berger J, Zidek W, Dominiak P, Diener HC; the MOSES Study Group. Morbidity and Mortality After Stroke, Eprosartan Compared With Nitrendipine for Secondary Prevention: principal results of a prospective randomized controlled study (MOSES). Stroke. 2005;36:1218–1226.
- Diener H-C, Bogousslavsky J, Brass LM, Cimminiello C, Csiba L, Kaste M, Leys D, Matias-Guiu J, Rupprecht H-J; MATCH Investigators. Aspirin and clopidogrel compared with clopidogrel alone after ischemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomized, double-blind, placebo-controlled trial. Lancet. 2004;364:331–337.



## References – Case 3

- Bhatt DL, Fox KA, Hacke W, Berger PB, et al. CHARISMA Investigators. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. N Engl J Med. 2006; 354:1706-1717.
- Wang Y, Zhao X, Liu L, Wang D, Wang C, Li H, Meng X, Cui L, Jia J, Dong Q, Xu A, Zeng J, Li Y, Wang Z, Xia H, Johnston SC; CHANCE Investigators. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. N Engl J Med. 2013;369:11–19.
- Kennedy J, Hill MD, Ryckborst KJ, Eliasziw M, Demchuk AM, Buchan AM; FASTER Investigators. Fast assessment of stroke and transient ischaemic attack to prevent early recurrence (FASTER): a randomised controlled pilot trial. Lancet Neurol. 2007;6:961–969.



### References – Cases 2 and 4

- 1. Stone, NJ et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology. 2013, Nov 12.
- 2. The AIM-HIGH investigators. Niacin in Patients with Low HDL Cholesterol Levels Receiving Intensive Stain Therapy. The New England Journal of Medicine 2011; 365:2255-2267
- 3. Freiberg MS et al. HIV infection and the risk of acute myocardial infarction. JAMA Intern Med. 2013 Apr 22;173(8):614-22. doi: 10.1001/jamainternmed.2013.3728.
- 4. Friis Moller et al. D:A:D Study Group. Prediction of Global CVD Risk in HIV-Positive Persons. European AIDS Clinical Society 14th European AIDS Conference. Abstract PS1/3, presented October 17, 2013.
- 5. El-Sadr et al. The SMART study group. Risk for opportunistic disease and death after reinitiating continuous antiretroviral therapy in patients with HIV previously receiving episodic therapy. A randomized trial. Ann Intern Med. 2008;149:289-299



## References (cont) – Cases 2 and 4

6. Yancy CW, Jessup M, Bozkurt B, et al. (October 2013). "2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines". *J. Am. Coll. Cardiol.* **62** (16): e147–239.

7. DrugDex Database. Micromedex. Current Topics on "ACE-Inhibitor Induced Cough," "ACE-Inhibitor Induced Angioedema," "ACE-Inhibitor Induced Acute Kidney Injury."

