

Controlling Blood Pressure

*SPRINTing Toward the ACC/AHA
Guidelines*

Michael E Grant, MD, FACP, FASN

“The Greater the Ignorance, the Greater the Dogmatism”

William Osler, 1914

Introduction

- How did we get here? Rise and fall of the **JNC's**
- The Game Changer - **SPRINT** Trial
- **ACC/AHA** Guidelines
- How do we get our patients to goal BP?

Rise and Fall of the JNCs

Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC) - sponsor - NHBLI - 7 official publications 1977-2003

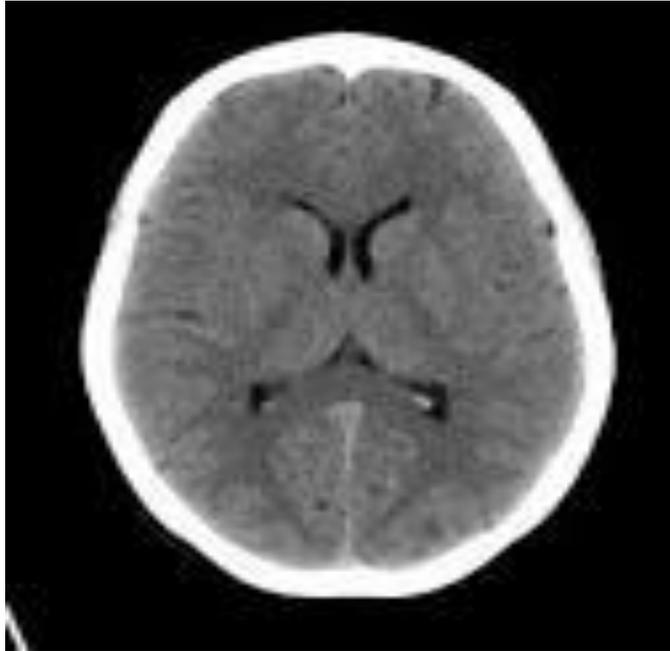
- JNC 1-3: treatment recommendations based on DBP - no treatment unless DBP > 105mmHg
- Few Randomized controlled trials - Veteran's trial 1967 used reserpine, hydralazine and a diuretic and showed treating to a DBP of 105 resulted in a significant reduction in CVA, CHF and Renal Damage
- JNC 3 (1984) defined HTN as Mild (DBP 90-104mmHg); Moderate (DBP 105-114mmHg) and Severe (DBP > 115mmHg)
- SBP < 140 mmHg (normal); 140-159mmHg (borderline); > 160mmHg (isolated systolic HTN)

SBP vs DBP as Treatment Target

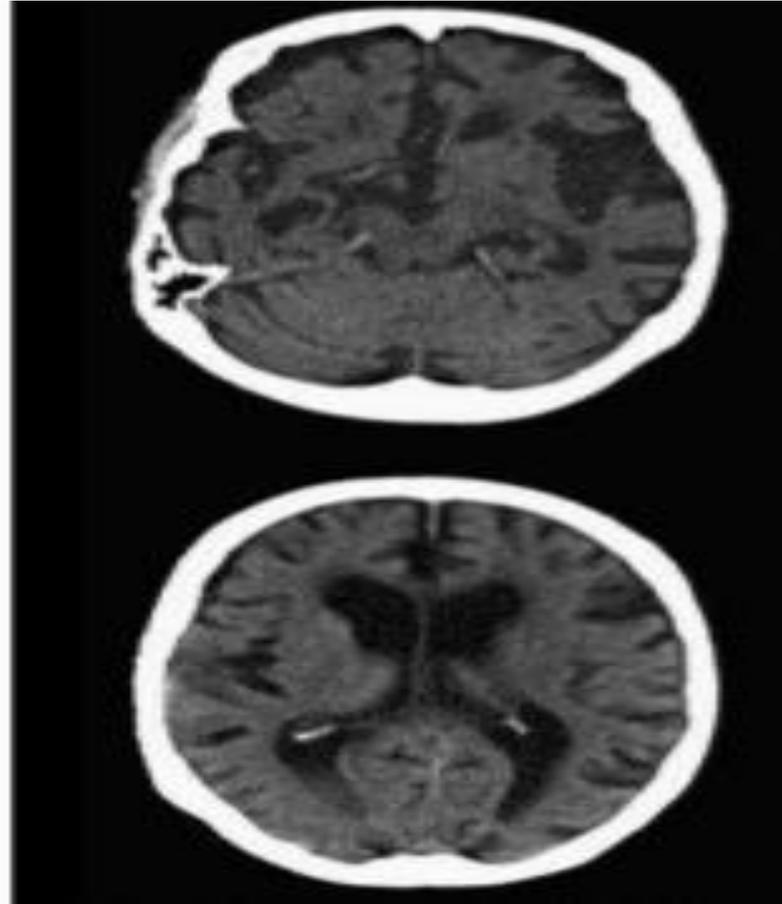
SBP is more important in adults over 50

- CV risk increases as SBP increases over 115mmHg
- DBP decreases as we age - pulse pressure widens; aorta and resistance vessels lose elasticity
- “Isolated” Systolic HTN not treated because DBP was in the “target” range (normal <85mmHg)
- SBP was not treated - “essential” for brain and organ perfusion
- Target BP - “100 plus your age” - 70 -> 170mmHg; 80 -> 180mmHg etc
- Under treatment lead to “Binzwangers” or “Multi-infarct” now “Vascular” Dementia

Which Brain do you Want at age 80?



Normal



Vascular - "Multi-infarct" Dementia

JNC 7 - The Last was Best?

- 47-page report in 2003 in JAMA
- HTN Stage 1 (140-159/90-99) or Stage 2 (>160/100)
- “Prehypertension” -120 -139/80-89 - pursue health-promoting lifestyle changes
- Allowed combination therapy as first step in pts with Stage 2 HTN
- Set lower targets for Compelling Indications such as ischemic heart disease; CHF; CKD and Diabetes: 130/80 or less and rec specific drug classes (B-Blockers; CCBs; ACE; ARBs; aldo blockers; diuretics) for specific indications
- “Crown Jewel” of BP recommendations and was considered the Standard until the **ACC/AHA** Guidelines published in 2017

The Fall of the JNCs - JNC “8”

- “JNC Late”; JNC “Ain’t”
- Originally impaneled 48 members in 2008 - most eventually left - 17 published the eventual report in JAMA in Dec 2013
- Lofty Goals: “Evidence based Medicine” - only RCTs >100 pts; followed for > one year; adults > 18 with “Hard” endpoints - death; stroke; MI; ACS; ESRD; requirement for revascularization - >6,000 papers reviewed (0.65% were considered to offer “good” evidence)

The Fall of the JNCs - JNC 8

- Didn't seem to have good evidence to support the lower BP goals of JNC 7 - led to significant conflict within the panel
- June of 2013 - NHBLI announced disbanding of the Guidelines Effort and ultimately left further Guideline development up to Scientific societies
- Ultimately the Vote for higher BP goals in pts over 60 was 12 to 5 in favor - required 2/3 majority to pass and only 17 remaining panel members voted

JNC “8”

- Evidence supported:
 - Pt's > 60: Initiate meds to lower BP if SBP > 150 or DBP > 90; if on meds and tolerating with lower BPs OK to continue
 - PT's < 60: Target BP is 140/90 or less
 - Pt's with diabetes or CKD: Target 140/90 or less
 - Non-black with no diabetes: ACE; ARB; Thiazide; CCB
 - Blacks with or without diabetes: Thiazide or CCB
 - CKD: initial agent or add on should include an ACE or an ARB but not both

Game Changer - *SPRINT* Trial - 2015

- ▶ 9361 pt's SBP 130mmHg or higher; over 50; no diabetes; increased CV Risk
- ▶ Increased CV Risk Criteria - one or more:
 - History of CV disease other than stroke
 - CKD (eGFR 20-60)
 - 10 year risk of CV disease 15% or greater by the Framingham Risk Score
 - Average age 75 or older

SPRINT Trial

- “Hard” outcomes: MI; other ACS; stroke; CHF; or death from CV cause
- Does targeting SBP of 120mmHg vs 140mmHg reduce CV morbidity and mortality?
- Achieved Targets - 121.4 mmHg for Intensive arm vs 136.2 mmHg for Standard arm
- Stopped early at 3.26 years due to significant lowering of CV composite outcomes
- Relative risk of death from CV causes was 43% lower in Intensive BP lowering group
 - ✓ 38% lower risk of heart failure
 - ✓ 27% lower risk of death from any cause

SPRINT Trial - Caveats

- Automated BP measurements (AOBP)- unobserved sitting in a quiet room for 5 min average of 3 readings
- AOBP readings 5-10mmHg lower than Std office BPs (some studies up to 16-20mmHg lower)
- Apply SPRINT results to your office
Lower target 125-130mmHg



Omron 907XL

Sprint TRIAL - Final Report

- Postintervention period results (August 2015 - July 2016)
- Heart Failure reduction benefit disappeared - with more pts in the intensive group with heart failure than in std treatment group - with disappearance of difference in BP reduction - meds had to be discontinued
- However, overall, there was a continued robust reduction in fatal and nonfatal CV events in pts with pre-existing elevated CV risk and death from any cause with intensive versus standard blood pressure lowering

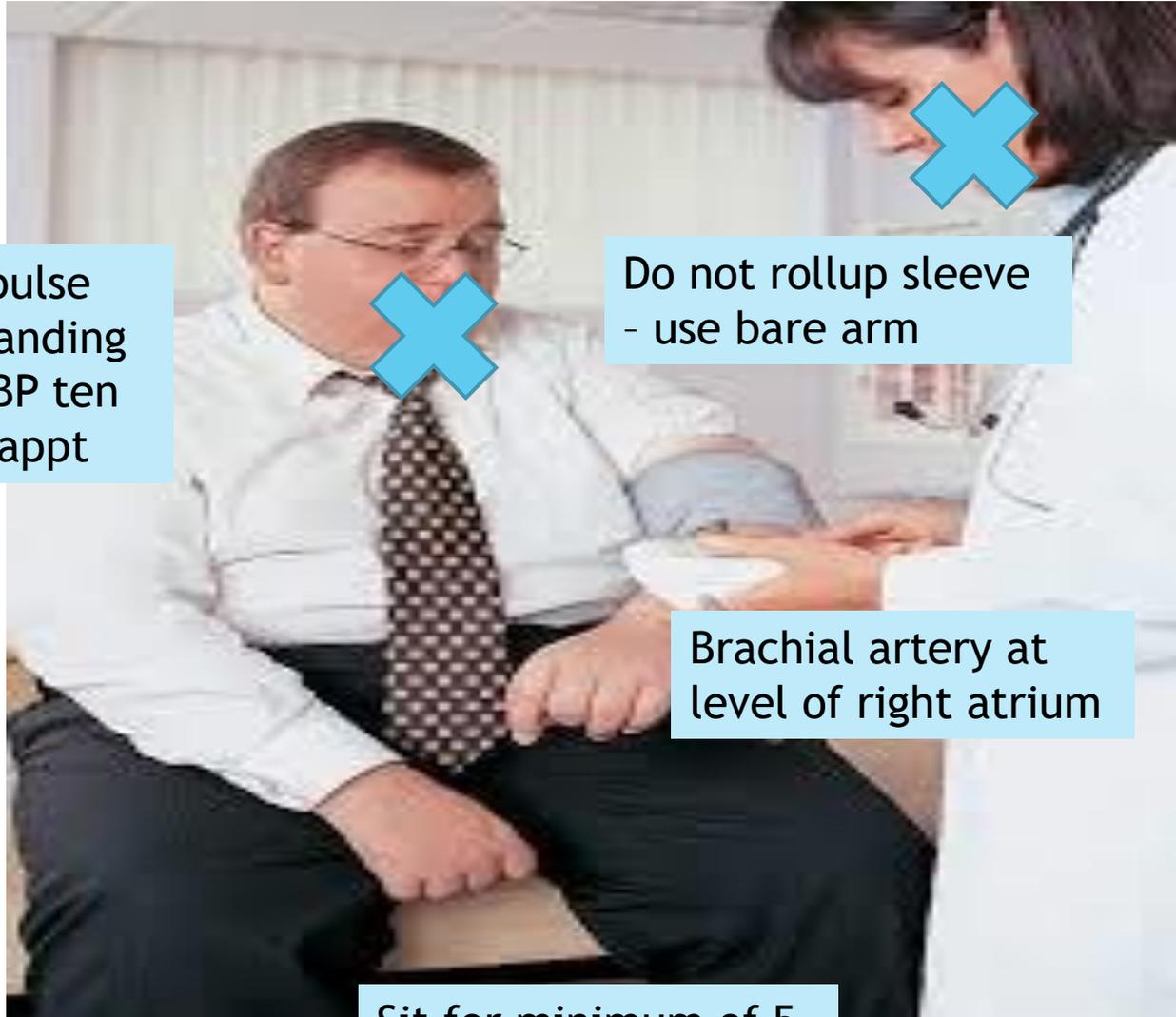
ACC/AHA Guidelines

- Normal BP: < 120/80 mmHg
- Elevated BP: SBP 120-129 - DBP < 80 mmHg
- Stage 1 Hypertension: SBP 130-139 or DBP 80-90 mmHg
- Stage 2 Hypertension: SBP \geq 140 or DBP \geq 80 mmHg
- Diagnosis based upon two or more readings at two or more visits
- First line antihypertensives: Thiazide Diuretic, CCB, ACE-I or ARB
- Initiate two first line antihypertensives with different mech of action in Stage 2 Hypertension
- Initiate pharmacologic therapy for BP > 130/80 mmHg in DM, CKD, Secondary prevention of CVD and primary prevention with ASCVD risk > 10% (<http://tools.ACC.org/ASCVD-Risk-Estimator>)
- Initiate pharmacologic therapy in adults with CVD risk < 10% at BP \geq 140/90

Impact of ACC/AHA Guidelines

- 2018 study used NHANES data comparing JNC VII with ACC/AHA guidelines in over 9,000 pts to estimate impact on pts in the US > 20 y/o
- Hypertension prevalence increased from 31.9 -> 45.6%; 72 to 103 million US adults
- Hypertension prevalence increased in all age groups:
 - ✓ 20 - 44 y/o: 10.5 -> 24.4%
 - ✓ 65 - 74 y/o: 63.6 -> 75.6%
 - ✓ Adults over 75: 75.1 -> 82%
- Biggest rise was in younger adults (also at low CV risk - have HTN but do not require treatment) - increase in medication advised goes from 34.4% - 36.2%

Guidelines Require Good Data

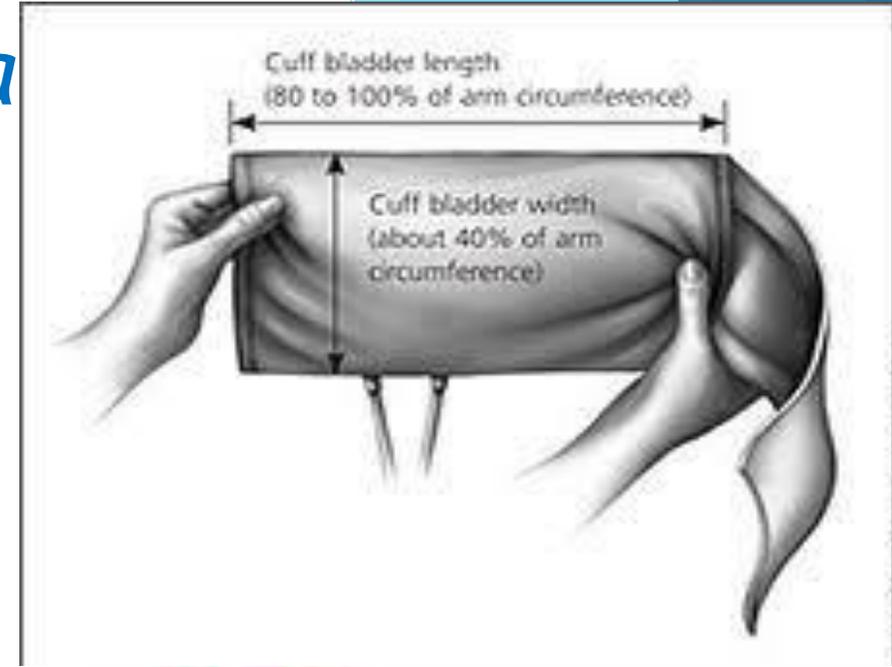


Take BP and pulse sitting and standing and recheck BP ten minutes into appt

Do not rollup sleeve - use bare arm

Brachial artery at level of right atrium

Sit for minimum of 5 - ideally 10 minutes feet flat on the floor



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The man in the previous slide is 56 y/o with a BMI of 48. His Renal function, chemistries and UA are normal. He asks which of the following non-pharmacologic interventions would improve his BP the most

- Weight loss
- Quit drinking 6 beers a night
- Stop taking OTC Naproxyn 220mg po bid
- Wear his CPAP regularly and effectively treat his OSA
- Stop the Pseudoephedrine-D pills he takes daily for his allergies

This patient's BP is 158/94 despite using a thigh cuff; waiting ten minutes; with equal measurements in both arms and no orthostatic drops

▶ You decide to begin pharmacologic therapy on this patient. The best choice of initial therapy is:

- Hydrochlorothiazide 25 mg po daily
- Benazepril 20 mg po daily
- Benazepril/HCTZ 20/25 mg one daily
- Amlodipine 5 mg po daily
- Amlodipine/Benazepril 5/20 mg one daily

Successful Pharmacologic Strategies

- ACCOMPLISH trial established superiority of combination of Amlodipine/benazepril over Benazepril/hydrochlorothiazide
- Better; stronger thiazide - chlorthalidone may be better choice - however more glucose intolerance and hypokalemia
- Once daily drug dosing - generics - Amlodipine, Lisinopril or losartan; HCTZ or chlorthalidone will control BP in most compliant patients
- Don't rely on Drug Samples

Our Pt is now on amlodipine/benazepril 10/40; chlorthalidone 25mg daily; has lost 25 lbs but BP still 144/94; you decide that he has Resistant Hypertension and want to work this up. The best approach at this point is to:

- Order a Renal Doppler Study to screen for renal artery stenosis
- 24-hour urine studies for VMA's and metanephrines
- Order Aldo/PRA levels
- Echocardiogram for coarctation of the aorta
- Add hydralazine and nighttime clonidine to the regimen

Using PRA to Guide Therapy

- John Laragh published his approach to Hypertension Mgmt in AJH Jan-Oct 2001
- Previous renin measurements unreliable (IF levels) - new assay measured angiotensin generation - very precise - ng/ml/hr

$$\text{MAP} = \text{CO} \times \text{SVR}$$

$$\text{HR} \times \text{SV}$$

$$\text{BP} = \text{Volume} \times \text{Resistance}$$

$$(30\%) \quad (70\%)$$

- Obtain PRA before treatment
 - ✓ if $< 0.65\text{ng/ml/hr}$ BP is “Volume Dependent”
 - ✓ if $> 0.65\text{ng/ml/hr}$ BP is “Renin-Dependent”

Using PRA to Guide Therapy

- Low PRA ($<0.65\text{ng/ml/hr}$) pts respond to sodium restriction and “V” drugs - diuretics; CCBs; alpha-blockers; spironolactone
- Higher PRA ($>0.65\text{ng/ml/hr}$) pts respond to “R” drugs - which block renin secretion and or the RAAS - B-Blockers; ACEI’s, ARBs; Renin Blockers
- Pts whose BP was sub-optimally controlled initially would have increased dosing and if not controlled a drug from the other class was added and increased - if control still not obtained - recheck PRA and add the appropriate V or R drug - claimed control rates much higher than with the “Set Approach” of JNC fame
- RCT 2009 showed superiority of this approach in pts with Resistant HTN treated with renin-guided therapy vs HTN Specialist “guessing” and adding next drug

Our patient is on amlodipine/benazepril 10/40mg one daily and chlorthalidone 25 mg daily - his K is now 3.3 meq/L and tCO₂ is 30; Aldo level 7.2mg/dl (sitting < 15mg/dl); PRA 0.42ng/ml/hr - ratio is 17.
The best course of action is to:

- Add losartan 100mg daily to regimen
- Add diltiazem ER 180mg daily to regimen
- Increase chlorthalidone to 50 mg daily
- Add amiloride 5mg bid to regimen
- Replace chlorthalidone with furosemide 40mg po daily

Treatment of Resistant HTN

- Plasma Renin Guided therapy - using amiloride or aldosterone antagonist if PRA < 0.65ng/ml/hr
- Check for medication adherence
- Consider 24 hour ABP study for White Coat HTN or masked HTN
- Rule out secondary causes
- Remove interfering drugs
- **ACC/AHA** guidelines 2017 suggest adding B-Blocker; followed by hydralazine and nitrate and ultimately minoxidil as add ons
- Refer to a Hypertension Specialist

64 y/o AA male with CKD Cr 2.7; eGFR 24 (CKD 4);
UPro/Cr 800mg/G on losartan 100mg; amlodipine
10mg and HCTZ 25 mg/D with suboptimal BPs 148-
160 systolic range with pitting edema

You recommend:

- Increase HCTZ to 50 mg daily
- Add minoxidil 2.5 mg daily
- Add furosemide 40 mg daily
- Add bumetanide 1mg daily
- Add torsemide 20 mg daily



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Hypertension in CKD

- As renal function declines, BP becomes more volume-dependent
- Thiazides ineffective as GFR drops below 30
- Volume control requires loop diuretics dosed properly - short acting - furosemide and bumetanide must be dosed two to three times daily - torsemide with longer half life can be dosed once daily
- Can add metolazone (2.5 -5mg qod) if therapeutic doses of loops diuretics ie bumetanide 2mg tid or torsemide 100mg daily not controlling volume - will worsen azotemia, alkalemia and E-lyte balance

I'm Nervous



70-year-old anxious man

Calls you with a list of ten BPs

from this am - 148/70 - 180/104

Having headaches - can feel his BP

Going up - thinks he will have a stroke; has multiple

BP drug intolerances - mainly dizziness; fatigue

Best advice for this pt to achieve BP target:

- Go to the ER when you feel like this
- Take clonidine 0.1mg if systolic is greater than 160mmHg
- Take an extra BP med now
- Arrange for a 24 hr ambulatory BP study

BP Targets - Real World

82 y/o pt - Assisted living; long Hx
HTN; can walk 15 feet in 20 seconds;
BP 148/72 on amlodipine 5 mg/D; no
orthostasis; asymptomatic; feels well
As his Doctor you decide to:



- Add HCTZ for SBP target of 140 or less
- Increase amlodipine dosage by 50%
- Continue current Rx
- Add hydralazine for SBP of 140mmHg or less
- Refer to Hypertension Specialist

Initiating BP Treatment in the Elderly

- ACP/AAFP Guidelines from 2017 - initiate therapy in elderly pts > 60 when systolic > 150 mmHg - special consideration for more aggressive lowering with history of stroke and CV events
- ACC/AHA Guidelines - pts > 65 with high burden comorbidity and limited life expectancy - use clinical judgement; pt preference, team-based approach to assess risk/benefit of intensive BP lowering and which drugs to use

Tips To Attain Targets

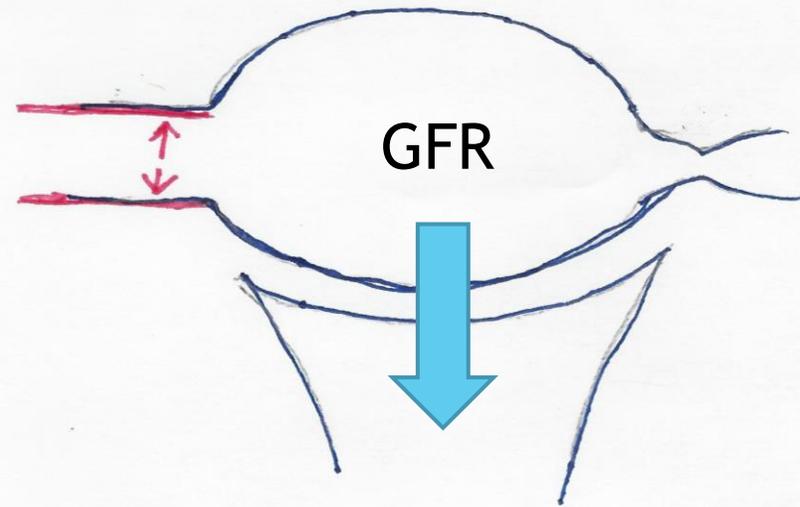
- Hypertensive patients who cannot stop NSAIDs for quality-of-life issues respond well to calcium channel blockers (NSAIDs interfere with diuretics, ACE/ARBs, B-Blockers)
- Just say no to “Drive-Bys” Cardiologists who squirt the renal arteries on the way to the heart - single view (vs three in std DSA) - unnecessary increase in contrast load and unneeded - potentially injurious renal stents
- CKD 4 pts (Cr > 2 or GFR < 30) naïve to ACE-I or ARBs - be very cautious in initiation - always recheck lab within a week to guard against hyperkalemia or rise in Cr > 30%

Tips for Achieving ACC/AHA BP Targets

- The Edema caused by stronger calcium channel blockers - ie Dihydropyridine class - amlodipine, nifedipine, felodipine etc is not due to fluid overload
- Calcium Channel Blockers are naturetic - cause net fluid negative balance

Calcium Channel Blockers and Edema

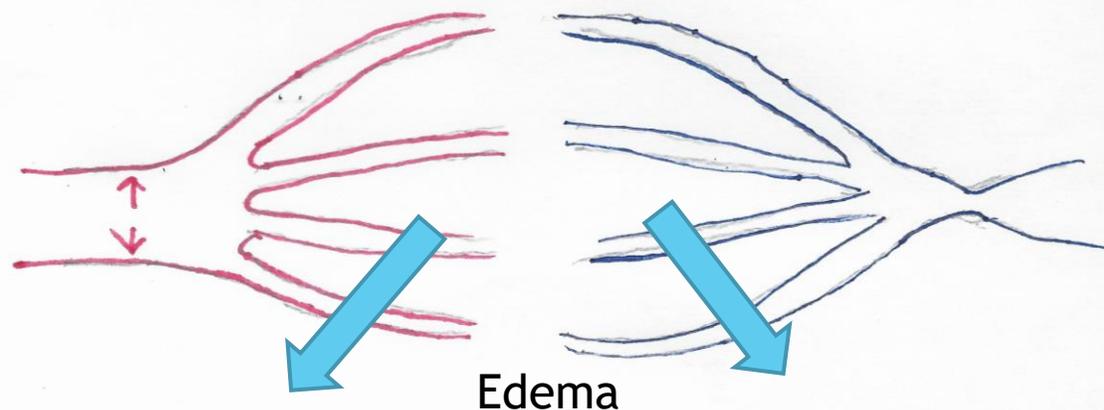
Dihydropyridine class causes afferent arteriolar vasodilation



Efferent arteriolar tone modulated by Angiotensin 2 from local renin generation - blocked by ARB or ACE-I

Pressure Naturesis

Capillary beds of lower extremities in obesity and especially in summer



ARB or ACE-I opens up venule - decreasing force for edema creation

Tips To Attain Targets

- Use once per day dosing; combination meds as possible; limit pill burden; improve compliance (inversely proportional to number of doses per day)
- Avoid drugs with short half lives
 - ✓ Prn short acting anything - ie nifedipine, clonidine, hydralazine IV
 - ✓ Clonidine - $\frac{1}{2}$ life 6 hours - rebound hypertension when wears off - “Roller Coaster” peaks and valley - drug causes CNS depression, shouldn't be used with Beta Blockers and is terrible choice for noncompliant pts - use the patch to wean this drug off (for good)
 - ✓ Hydralazine - first side-effects reported in 1953! Causes Lupus and other autoimmune drug reactions at high doses needed for efficacy - reflex tachycardia, fluid retention always - efficacy rare - possible use with a nitrate in HFrEF patients who can't take an ACE or an ARB

Tips to Attain Targets

- Dose all antihypertensives at night
- Spanish study - Hygia Chronotherapy Trial (Euro Ht J 2020) 41, 4565-4576 - Followed 19,084 Pts with HTN over 6.3 yrs with 48hr ABPM. Half of pts took all BP meds at night - the other half in the am
- Restoration of normal BP dipping in those taking pills at night with equal control of daytime BP readings in both groups
- Significant reduction in CV outcomes (45%) - MI, Stroke, CHF, need for revascularization
- Lower creatinine values; A/C ratio and improved lipid control

In Conclusion...

- History teaches us that Hypertension Guidelines will come and go - the **ACC/AHA** Guidelines provide the best current knowledge that we can utilize for our patients; however, ultimately these will be modified and replaced down the road
- The Internal Medicine physician is the one best-trained to apply the Hypertension Guidelines of the day to his or her unique patient. We know our patients well - our blood pressure treatment is individualized for maximum benefit and minimal harm. This is indeed the art of medicine

“The good physician treats the disease; the great physician treats the patient with the disease”

William Osler