


9:45 – 10:30am

**Hypertension Management:
A Moving Target**

SPEAKER
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Presenter Disclosure Information

The following relationships exist related to this presentation:

- Karol E. Watson, MD, PhD, FACC: Consultant for Merck & Co., Inc.; Daiichi Sankyo; and Quest Diagnostics.

Off-Label/Investigational Discussion

- In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

**Hypertension Management:
A Moving Target**

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**Hypertension Management:
A Moving Target**

Learning Objectives

- Review the JNC8 guidelines for hypertension in adults, with special attention to new blood pressure goals
- Consider patient factors such as age, co-morbidities, and race when prescribing anti-hypertensive therapy

**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. Published online December 18, 2013. doi:10.1001/jama.2013.284427

Important to Note...

- RCTs
- conducted 1966 to present
- Minimum 1-year follow-up period
- Sample size > 100

- JNC 7 was “The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure”
- JNC 8 is the “2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults”
- In JNC 8 they give 9 Evidence based Recommendations
- “... these recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient.”

Strength of Recommendation		
Grade		
A	Strong recommendation: There is high certainty based on evidence that the net benefit is substantial.	2
B	Moderate recommendation: There is moderate to high certainty based on evidence that the net benefit is moderate to substantial	3
C	Weak recommendation: There is at least moderate certainty based on evidence that there is a small net benefit.	1
D	Recommendation against: There is at least moderate certainty based on evidence that it has no net benefit or that risks/harms outweigh benefits.	0
E	Expert opinion ("There is insufficient evidence or evidence is unclear or conflicting, but this is what the Panel recommends.") Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, but the Panel thought it was important to provide clinical guidance and make a recommendation. Further research is recommended in this area.	5
N	No recommendation for or against ("There is insufficient evidence or evidence is unclear or conflicting.") Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, and the Panel thought no recommendation should be made. Further research is recommended in this area.	0

Recommendation #1

1. In patients aged ≥ 60 years, initiate pharmacologic treatment in systolic BP ≥ 150 mmHg or diastolic BP ≥ 90 mmHg and treat to a goal systolic BP < 150 mmHg and goal diastolic BP < 90 mmHg.

(Strong Recommendation – Grade A)

In other words:

**Ease up on Hypertension
Treatment in Older Adults (60
years of age or older)**

**Treat if BP $\geq 150/90$
Aim for $< 150/90$**

**"Antihypertensive agents produce no
obvious benefit in patients over 65"**

Fry J, Lancet 1974

**"Hypertensive drugs should probably not
be given (in the elderly) unless the blood
pressure is more than 200/110 mm Hg."**

Editorial, Br Med J, 1978

HYVET Trial: Study Design

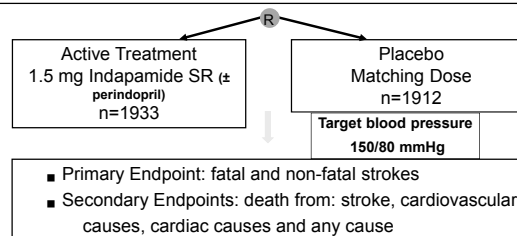
Prospective, Double Blind, Placebo controlled RCT. 3845 patients ≥ 80 years with standing SBP ≥ 160 mm Hg; Mean follow-up 1.8yrs; **BP GOAL** $< 150/80$

Inclusion Criteria:

Aged 80 or more,
Systolic BP: 160 -199 mmHg
+ diastolic BP; < 110 mmHg,

Exclusion Criteria:

Standing SBP < 140 mmHg
Stroke in last 6 months
Dementia; Need for daily nursing care



N Engl J Med 2008;358:ACC 2008

Hypertension in the Elderly

- Two "treat-to-target" trials in the elderly
 - Japanese Trial to Assess Optimal SBP (JATOS)
 - 4416 patients aged 65-85 (average age of 74)
 - Randomized to SBP < 140 vs. SBP 140-160
 - Achieved BP of 136/75 vs. 146/78
 - No difference in CV events or renal failure ($p=0.99$)
 - VALISH trial
 - 3079 patients aged 70-84 (average age of 76)
 - Randomized to SBP < 140 or SBP 140-149
 - No significant reductions in stroke, CV events, or renal failure

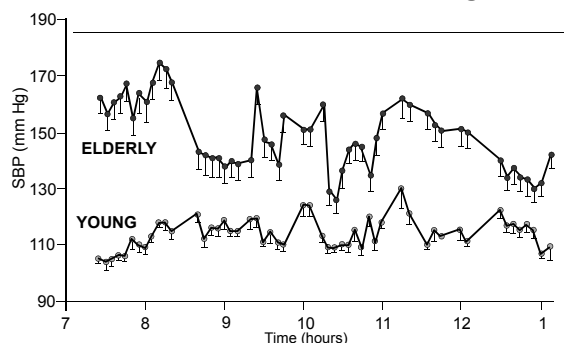
JATOS Study Group. *Hypertens Res* 2008;31:2115-27.
Ogihara T et al. *Hypertension* 2010;56:196-202.

Antihypertensive Use Linked to Serious Fall Risk in Elderly Patients

- 4961 hypertension patients enrolled in Medicare interviewed about number and dose of antihypertensive medications
- Followed for 3 years, using claims data to track fall injuries
- 446 (9%) had a serious fall; 837 (16.9%) died during f/u
- In multivariate analysis, patients with more antihypertensive medication had more serious falls compared to patients without antihypertensive medications
 - hazard ratio 1.4 for high intensity antihypertensive therapy
 - hazard ratio 1.28 for moderate intensity antihypertensive therapy
 - Among the 503 participants with a prior serious fall, the hazard ratios was 2.31

JAMA Intern Med. 2014;174(4):588-595.

Postural Changes in Blood Pressure are more common as we Age



How the Guidelines Compare...

	2014 HTN (JNC 8)	2014 ASH/ISH	2013 CHEP	2013 ESH/ESC	2013 ADA
General BP goal	140/90	140/90	140/90	140/90	140/80
BP goal (elderly)	150/90 (60 yrs)	150/90 (80 yrs)	150/90 (80 yrs)	150/90 (80 yrs)	---
BP Tx - Blacks	CCB or thiazide	CCB or thiazide	---	---	---
BP goal CKD	140/90	140/90 130/90*		140/90 130/90*	140/90
BP goal DM	140/90				140/80
Initial drug choice for most	Thiazide ACE / ARB CCB	ACE / ARB If < 60 CCB or thiazide if >60	Thiazide ACE / ARB BB	Thiazide ACE / ARB CCB, BB	ACE / ARB

* With proteinuria

Not even all JNC 8 Authors Agreed with easing up at age 60

14 January 2014

Evidence Supporting a Systolic Blood Pressure Goal of Less Than 150 mm Hg in Patients Aged 60 Years or Older: The Minority View (6/17 JNC 8 panel members)

Jackson T. Wright Jr., MD, PhD; Lawrence J. Fine, MD, DrPH; Daniel T. Lackland, PhD; Gbenga Ogedegbe, MD, MPH, MS; and Cheryl R. Dennison Himmelfarb, PhD, RN, ANP

Recommendations #2 and #3

2. In patients aged <60 years, initiate pharmacologic treatment at DIASTOLIC BP ≥ 90 mmHg and treat to a goal <90mmHg.

For ages 30–59 years, Strong Recommendation–Grade A

For ages 18–29 years, Expert Opinion–Grade E

3. In patients aged <60 years, initiate pharmacologic treatment at SYSTOLIC BP ≥ 140 mmHg and treat to a goal <140mmHg.

Expert Opinion–Grade E

For Adults under 60 years of age

Treat if BP $\geq 140/90$; Aim for <140/90

There's strong evidence for treating high diastolic BP in patients 30–59 years of age. Everything else is "Expert Opinion"

What???? You mean treating SBP ≥ 140 mm Hg is only "Expert Opinion"?

- Prior guidelines relied on epidemiologic evidence and observational studies that noted that the risks for cardiovascular events in untreated adults increased rapidly as SBP increased above 140 mm Hg
- Older trials actually used a DBP goal rather than a SBP goal
- The older trials that did use a SBP goal, targeted < 160
- So, direct RCT evidence to support this threshold is limited. JNC 8 acknowledges this limitation

Recommendations # 4 & 5

5. In patients aged ≥ 18 years with diabetes mellitus initiate pharmacologic treatment at systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg and treat to goal systolic BP <140mmHg and goal diastolic BP <90mmHg. (Expert Opinion–Grade E)

Earlier HTN guidelines lowered treatment goals for adults with CKD and DM; but JNC 8 gives the same BP goals in these patients as in the general population.
BP goal <140/90

Hypertension in CKD

Modification of Diet in Renal Disease (MDRD)

- Randomized to a MAP < 93 (120/80) vs MAP < 107 (140/90)
- **RESULT: No CV or renal benefit**

African American Study of Kidney Disease

- randomized to a MAP < 93 vs MAP 102-107; Achieved BP 130/78 vs 141/86
- **RESULT: No CV or renal benefit**

Klahr S, Levey AS, Beck GJ, Caggiula AW, Hunsicker L et. al. N Engl J Med 330:887-884, 1994
Wright JT Jr et. al. Arch Intern Med. 2002;162:1636-1643.

Action to Control Cardiovascular Risk in Diabetes (ACCORD) Trial

■ NHLBI 10,251 Type 2 diabetics

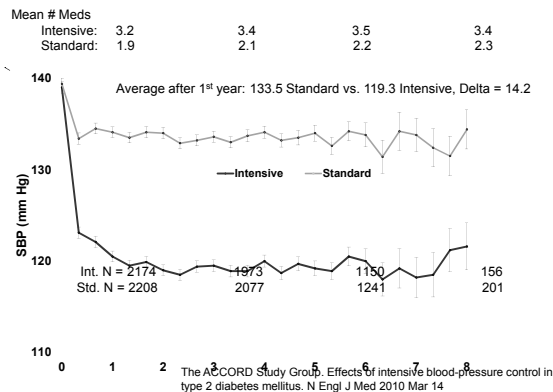
■ Three Trial arms

- Glycemic control
- BP
- Lipids

■ BP arm 4,773 randomized to SBP<120 or <140

The ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med 2010 Mar 14

ACCORD Trial: Blood Pressures



ACCORD Trial: Adverse Events

	Intensive N (%)	Standard N (%)	P
Serious AE	77 (3.3)	30 (1.3)	<0.0001
Hypotension	17 (0.7)	1 (0.04)	<0.0001
Syncope	12 (0.5)	5 (0.2)	0.10
Bradycardia or Arrhythmia	12 (0.5)	3 (0.1)	0.02
Hyperkalemia	9 (0.4)	1 (0.04)	0.01
Renal Failure	5 (0.2)	1 (0.04)	0.12
eGFR ever <30 mL/min/1.73m ²	99 (4.2)	52 (2.2)	<0.001
Any Dialysis or ESRD	59 (2.5)	58 (2.4)	0.93
Dizziness on Standing	217 (44)	188 (40)	0.36

The ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med 2010 Mar 14

Recommendations #6

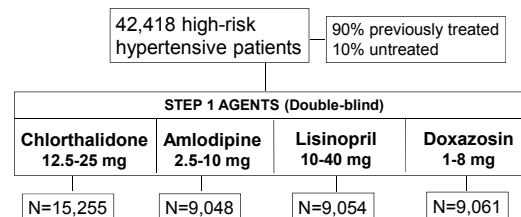
6. In the general nonblack population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, CCB, ACE inhibitor, or ARB. (Moderate Recommendation-Grade B) This recommendation is different from the JNC 7 in which the panel recommended thiazide-type diuretics as initial therapy for most patients.

While JNC 7 recommended thiazide-type diuretics as the initial antihypertensive choice for all, JNC 8 broadens the choices to also include CCB, ACE-I, and ARBs along with thiazide-type diuretics.

NOTE: β blockers are OUT

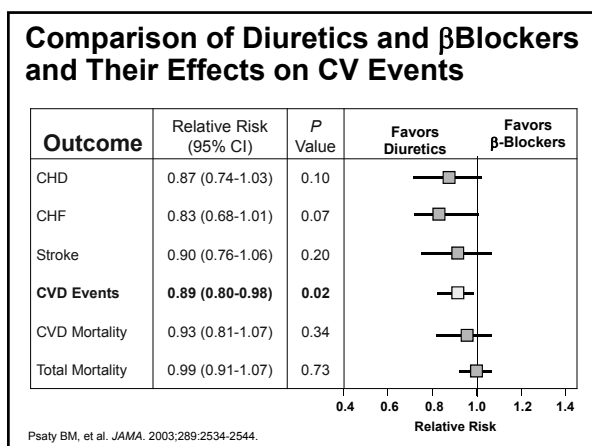
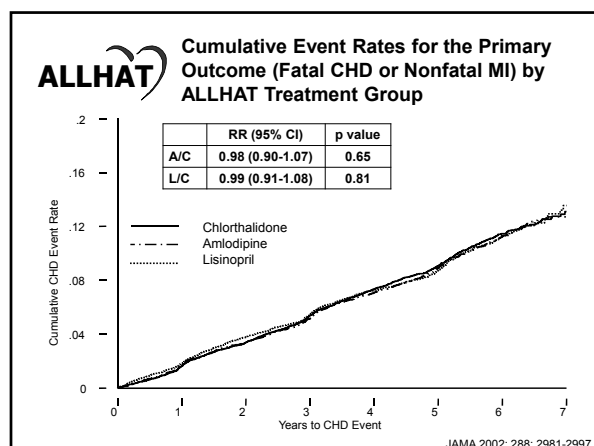
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ALLHAT Hypertension Trial



Step 1 agents titrated and atenolol, clonidine, reserpine, and/or hydralazine added as needed to achieve BP goal

JAMA 2002; 288: 2981-2997



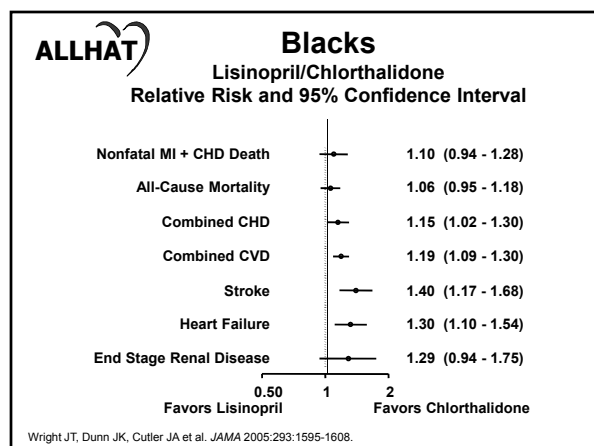
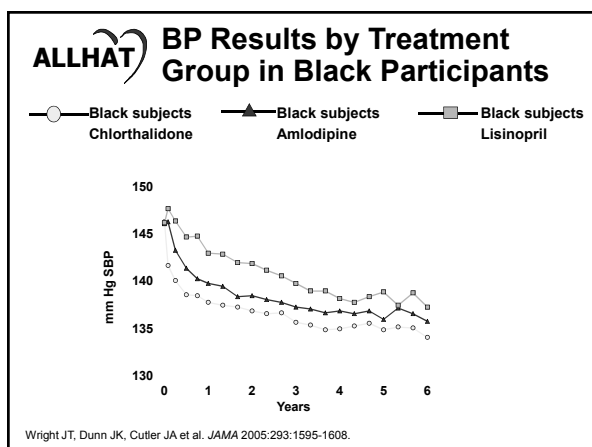
Recommendations #7

7. In the general black population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic or CCB.

For general black population Moderate Recommendation - Grade B

For black patients with diabetes: Weak Recommendation - Grade C

JNC 8 recommends a thiazide-type diuretic or CCB as the initial choice in African Americans, but there's less certainty about African Americans with diabetes due to lack of data (they were torn about not including ACE/ARB)



Recommendation # 8

8. In the population aged ≥ 18 years with chronic kidney disease, initial (or add-on) antihypertensive treatment should include an ACE inhibitor or ARB to improve kidney outcomes. (Moderate Recommendation - Grade B)

In adult patients with CKD, make sure an ACE-I or an ARB is part of the antihypertensive regimen

ACE-I or ARB in CKD reduces progression of kidney disease

Study	Pts	Design	RR for kidney disease progression
Maschio et al 1996	583	Benazapril v. placebo	53%
Gisen group 1997	166	Ramapril v. placebo	48%
Hou et al 2006	224	Benazapril v placebo	43%
Brenner et al 2001	1513	Losartan v. placebo	22%

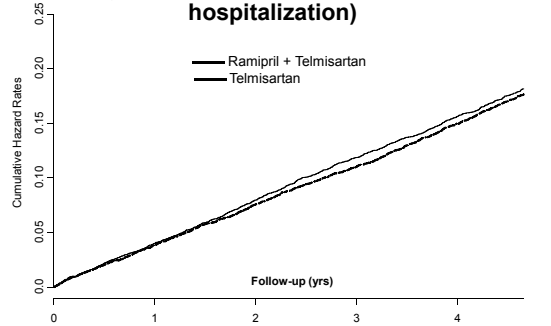
Recommendation # 9 Thiazide-type diuretic, CCB, ACE-I or ARB

9. If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a second drug from one of the classes in Recommendation 6. If goal BP cannot be reached with two drugs, add and titrate a third drug from the list provided. Do not use an ACEI and an ARB together in the same patient. If goal BP cannot be reached using only the drugs in Recommendation 6 ... antihypertensive drugs from other classes can be used. (Expert Opinion–Grade E)

Don't dilly dally. If BP is not at goal within a month, use one of these 3 strategies :

1. Increase the dose of the initial drug
2. Add a 2nd, then a 3rd drug (Rec #6)
(Not an ACE + ARB together)
3. Add a drug from other classes

Telmisartan vs. Telmisartan + Ramipril: Primary Outcome (MI, Stroke, CV death, CV hospitalization)



The ONTARGET Investigators N ENGL J MED 2008; 358:1547-1559 April 10, 2008

Adverse Events with Ramipril + Telmisartan

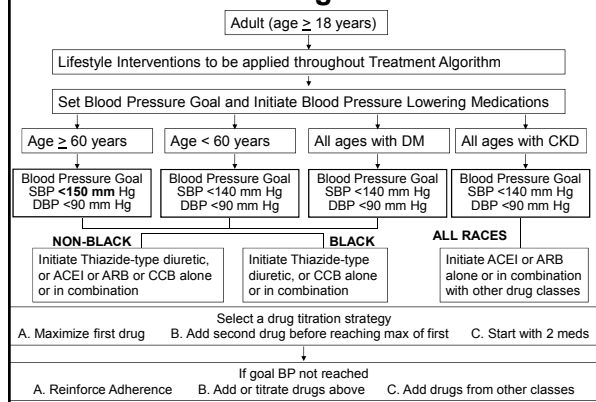
	Ram N=8576	Ram + Tel N=8502	RR	P
Hypotension	149	406	2.75	<0.0001
Syncope	15	29	1.95	0.032
Cough	360	392	1.10	0.1885
Diarrhea	12	39	3.28	0.0001
Angioedema	25	18	0.73	0.30
Renal Impairment	60	94	1.58	0.0050
Any Discontinuation	2099	2495	1.20	<0.0001

The ONTARGET Investigators N ENGL J MED 2008; 358:1547-1559 April 10, 2008

JNC 8 in a nutshell

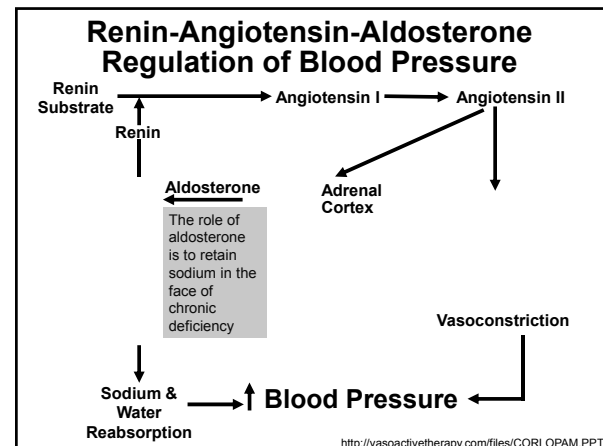
- Ease up on hypertension treatment in older adults (Adults over 60 years goal < 150/80)
- In all others blood pressure goal < 140/90
 - Including those with diabetes and CKD
- Initial antihypertensive therapy can be a thiazide-type diuretic, CCB, ACE inhibitor, or ARB
 - In black patients initial therapy should be with a CCB or thiazide-type diuretics
- In adults with CKD, make sure an ACE-I or an ARB is part of the antihypertensive regimen
- Don't dilly dally

JNC 8 Algorithm

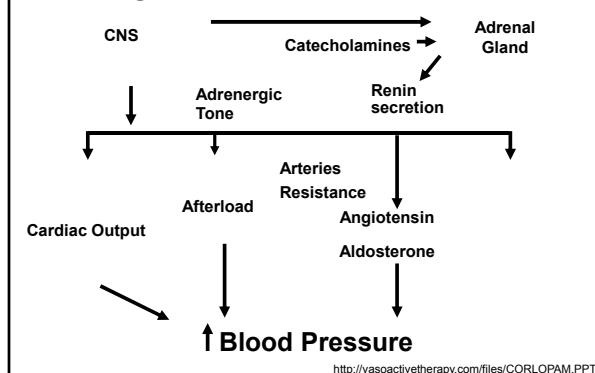


CLINICAL PEARL # 1

Two main physiologic systems control blood pressure



Sympathetic Nervous System Regulation of Blood Pressure



Most cases of Resistant Hypertension are caused by:

- Sodium excess
- Extracellular volume expansion
- Sympathetic overactivation

Too Much Salt (Na⁺)
Too Much Water
Too Much Sympathetic Activity

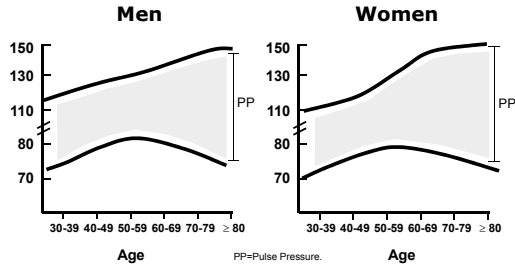
CLINICAL PEARL # 2

There is a characteristic circadian rhythm to blood pressure

CLINICAL PEARL # 3

There is a characteristic life-cycle pattern to blood pressure

Blood Pressure Distribution in the Population According to Age

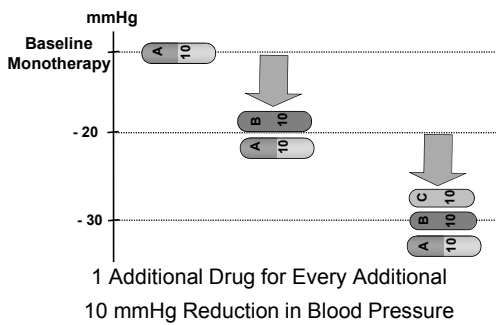


Adapted from : Third National Health and Nutrition Examination Survey, *Hypertension* 1995;25:305-13

CLINICAL PEARL # 4

Failure to use enough medication is a common cause of “resistant” hypertension

“Rule of TENS for SBP”



Cushman W and Basile J. of Clinical Hypertension

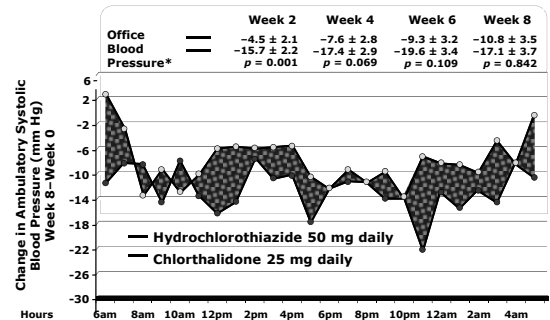
Diuretics and BP Control

- In states of sodium (and water) excess, diuretics are essential
- Most classes of antihypertensive agents lead to sodium retention, as compensation for lower BP
- JNC 8 recommends a thiazide-type diuretic, as one of four initial antihypertensive choices in the general population
- JNC 8 recommends a thiazide-type diuretic, as one of two initial antihypertensive choices in the Black patients

CLINICAL PEARL # 5

In many patients with HTN, adequate diuresis is **ESSENTIAL** for BP control

Thiazide Diuretics Differ in Their Antihypertensive Effects



Ernst ME, et al. *Hypertension*. 2006;47:352-358.

CLINICAL PEARL # 6

In patients with Resistant Hypertension switching the diuretic from HCTZ to Chlorthalidone may improve BP control (but watch electrolytes!)

Hypertension 2014

- Hypertension is common and will likely affect most individuals at some point in their lifetime
- Guidelines on how best to treat hypertension are evolving and sometimes contradictory
- For information on prevention, detection and evaluation of hypertension, JNC 7 and international guidelines offer guidance
- Inadequate treatment is also a common cause of resistant HTN (rule of 10s)
- Potassium sufficiency is critical to BP control