

# Pharmacologic Therapy of Childhood Hypertension

**Daniel I. Feig, MD, PhD, MS**

*Division of Nephrology*

*Department of Pediatrics*

*University of Alabama, Birmingham*

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# Topics for Discussion

- **Goals of therapy**
- **How to assess insufficiency of lifestyle modification**
- **Pharmacologic Options**
- **Use of fixed combinations**
- **Areas for study**
  
- **Not going to address**
  - **Neonatal hypertension**
  - **Hypertensive emergencies**



# Goals of Pharmacologic Therapy

- **Primary**
  - Mitigate existing target organ damage
  - Prevent future target organ damage
  - Reduce long term CV risk
  - Slow progression of CKD
  - Minimize side effects
- **Secondary**
  - Control symptoms – neuropsych, subjective
  - Consider prevention of hypertension progression
- **Over-riding**
  - Provide attainable therapy (adherence, cost, etc)
  - Make the child feel better (or at least not worse)
  - ?? Data driven !!



# Organ Injury at Diagnosis

- **CARDIAC**

- **Left ventricular hypertrophy**

- **42% LVMI criteria >95<sup>th</sup> percentile (38g/m<sup>2.7</sup>)**
- **18% >99.7<sup>th</sup> percentile (51g/m<sup>2.7</sup>)**
  - Burke et al., *Circulation* 1987, 76:106

- **RENAL**

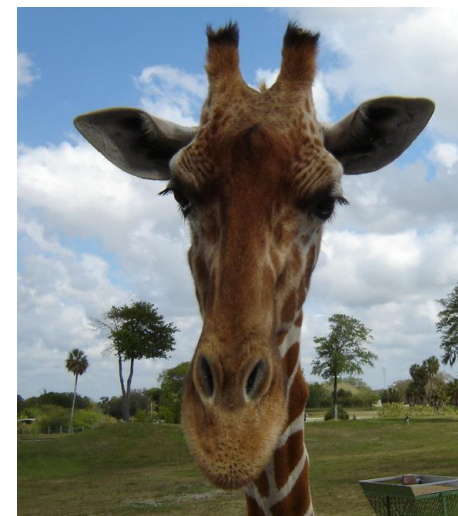
- **Proteinuria**

- **26% have urine pro/Cr >0.3**
- **14% with essential htn, pro/Cr >0.3**
  - Pontremoli et al., *Am J Hypertens* 1998, 11: 430

- **VASCULAR**

- **Accelerated atherosclerosis (autopsy data)**

- Daniels et al., *Circulation* 1999, 82:1243



# Neurocognitive Impairment in High Normal and Greater BP

- **Impaired Performance on Cognitive Tests (WISC, WRAT in NHANES III) Data**
  - 5077 kids: digit span, block design, math scores, down by 1 SD
    - Lande et al., Pediatrics 2003, 1143(6):720-724
- **Children with hypertension had impaired behavioral regulation, executive function and low transcranial Doppler-reactivity**
  - Ostrovskaya et al. J Child Neurol. 2015, 30:543-6



# Symptoms of Hypertension

	Htn	Normal BP
Headache	42%	10%
Chest Pain	14%	4.9%
Abd Pain	10%	4%
Sleep Initiation	27%	6%
Tiredness	26%	6%
Concentration	10%	5%
School Failure	10%	3%



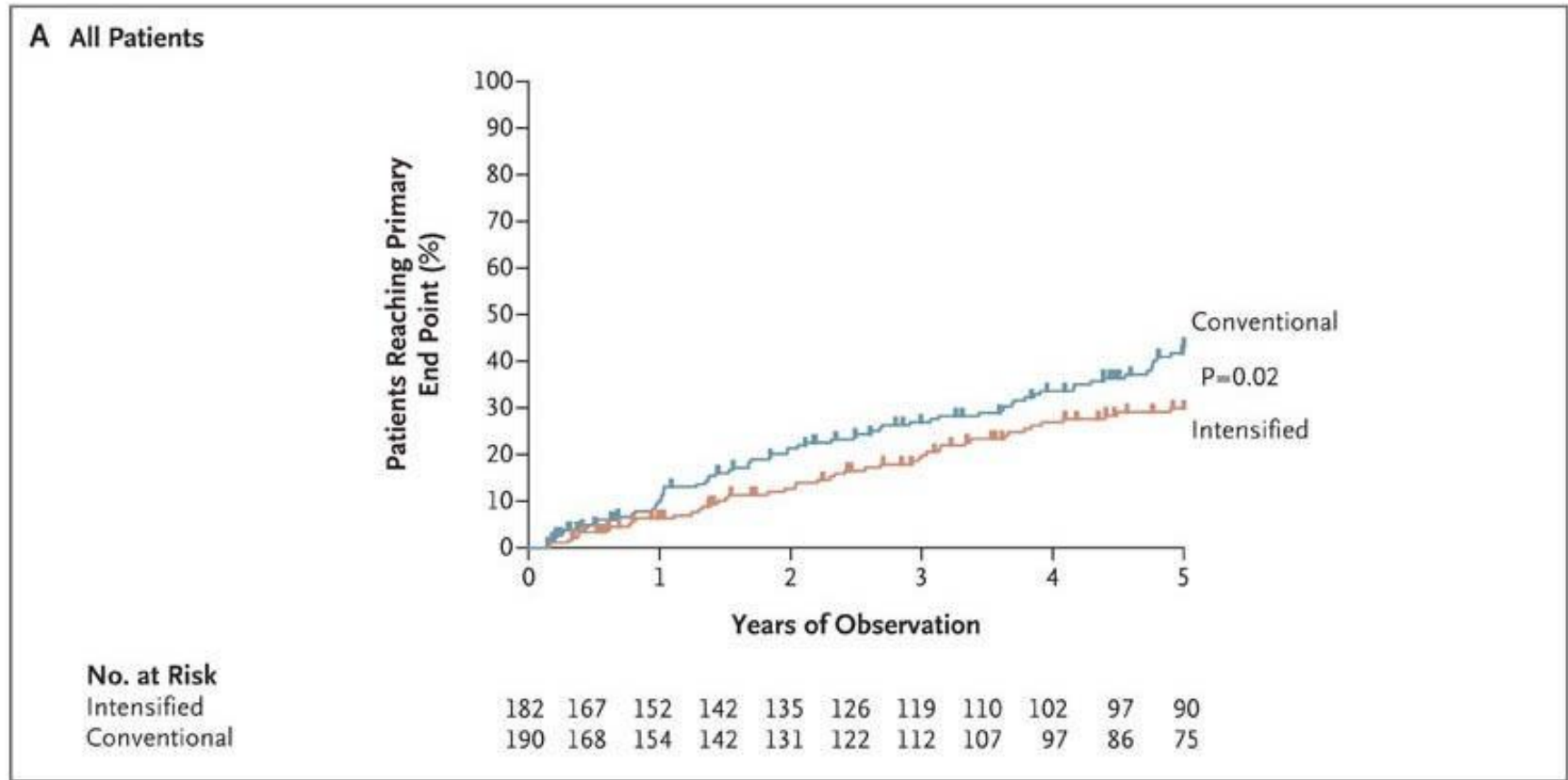
Croix et al. Ped Neph 2006; 21:527



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# Effect of intensified therapy on CKD progression (ESCAPE Trial)



ESCAPE Trial Investigators, NEJM 2009; 361: 1639



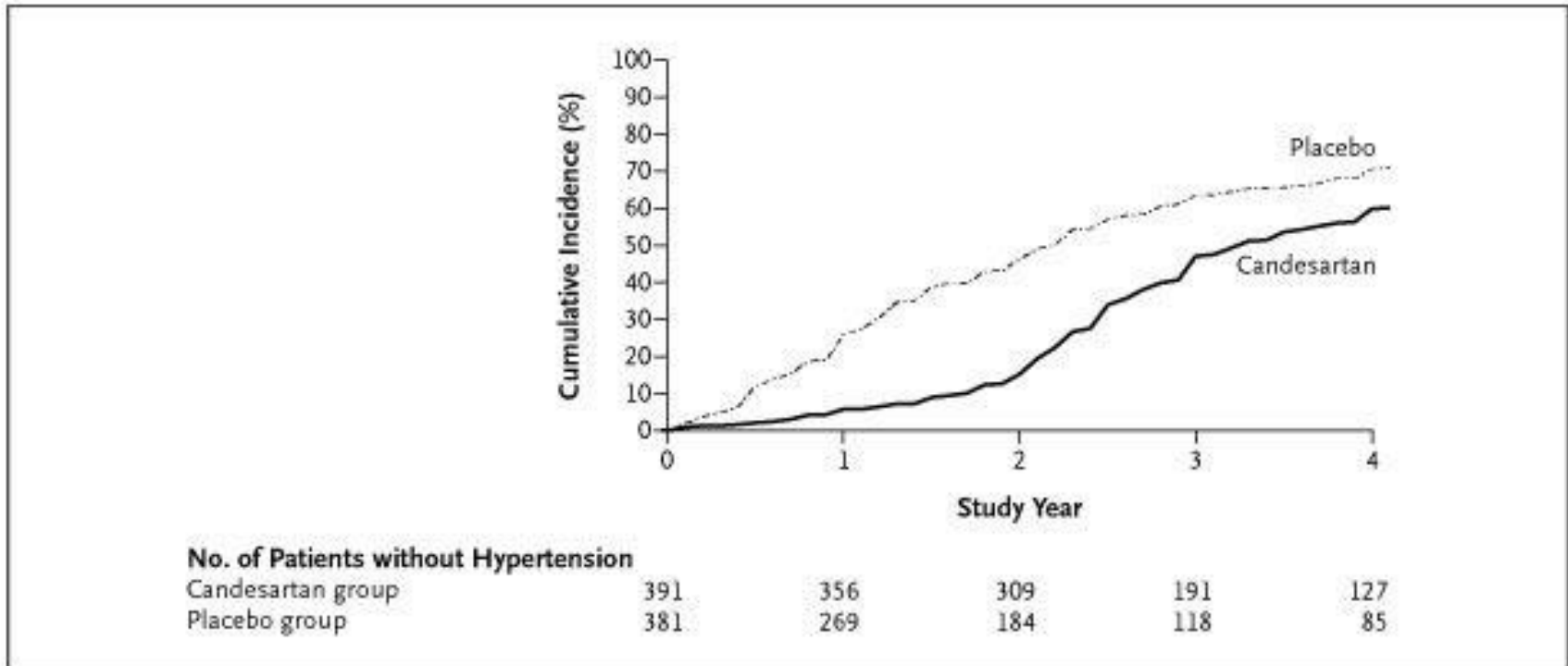
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# Treatment of High Normal BP

## TROPHY Trial



Julius et al. NEJM 2006; 354:1685



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# When to start pharmacologic therapy

- ❑ No improvement in BP after 6mo lifestyle modification
- ❑ Patient/family uninterested in lifestyle changes
- ❑ New or worsening target organ damage despite good efforts
- ❑ Stage 2 hypertension at presentation or after lifestyle efforts



# Medication Selection

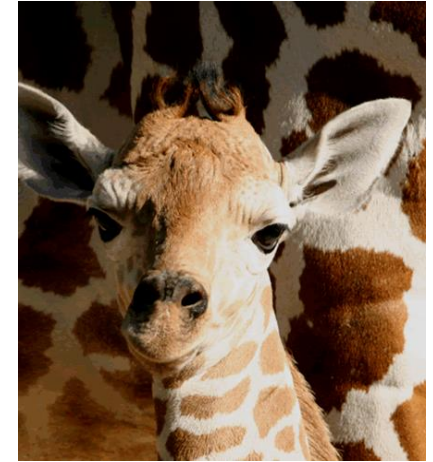
- **ACEi/ARBs**
  - **Essential or secondary hypertension**
  - **Ideal for renin dominant hypertension**
  - **Ideal CKD, DM, proteinuria**
  - **Lower efficacy for low-renin, volume**
  - **High risk in pregnancy, dehydration**
  - **Pharmacogenomic/Race issues**
  - **Monitor: Cough, K+, Cr, transaminases**
  
- **Diuretics**
  - **Good 1<sup>st</sup> line in essential hypertension**
  - **Particularly attractive in obesity hypertension**
  - **Lower effectiveness in advanced CKD**
  - **Excellent in synergy as 2<sup>nd</sup> agent**
  - **Monitor electrolytes**



# Medication Selection

- **Calcium Channel Blockers**

- **Essential or secondary hypertension**
- **Poor for renin dominant hypertension**
- **Less ideal in very obese**
- **Some issues with gingival hypertrophy**
  - **Caution with CNIs, antiepileptics**
- **Monitor edema, transaminases**



- **Beta Blockers**

- **Very effective**
- **Ideal in some cardiac disease, anxiety disorder**
- **Consider in CKD where, ACEi/ARB not tolerated (eGFR)**
- **Less optimal side effect profile especially in obese**



# Routine Medication Options

Medication	Age Tested	Dosing interval	Formulation
<b>ACE-I</b>			
Benazepril	>6yr	Daily	Tablet, Extemp liquid
Captopril	Infants/children	3-4x/d	Table, liquid
Enalapril	>1mo	1-2x/d	Tablet, liquid
Fosinopril	>6yr	Daily	Tablet
Lisinopril	>1yr	Daily	Tablet, liquid
Ramapril	>6yr	Daily	Tablet
<b>ARBs</b>			
Candesartan	>1yr	1-2x/d	Tablet, Extemp liquid
Irbesartan	>6yr	Daily	Tablet
Losartan	>6yr	Daily	Tablet
Olmesartan	>6yr	Daily	Tablet
Valsartan	>6yr	Daily	Tablet



# Routine Medication Options

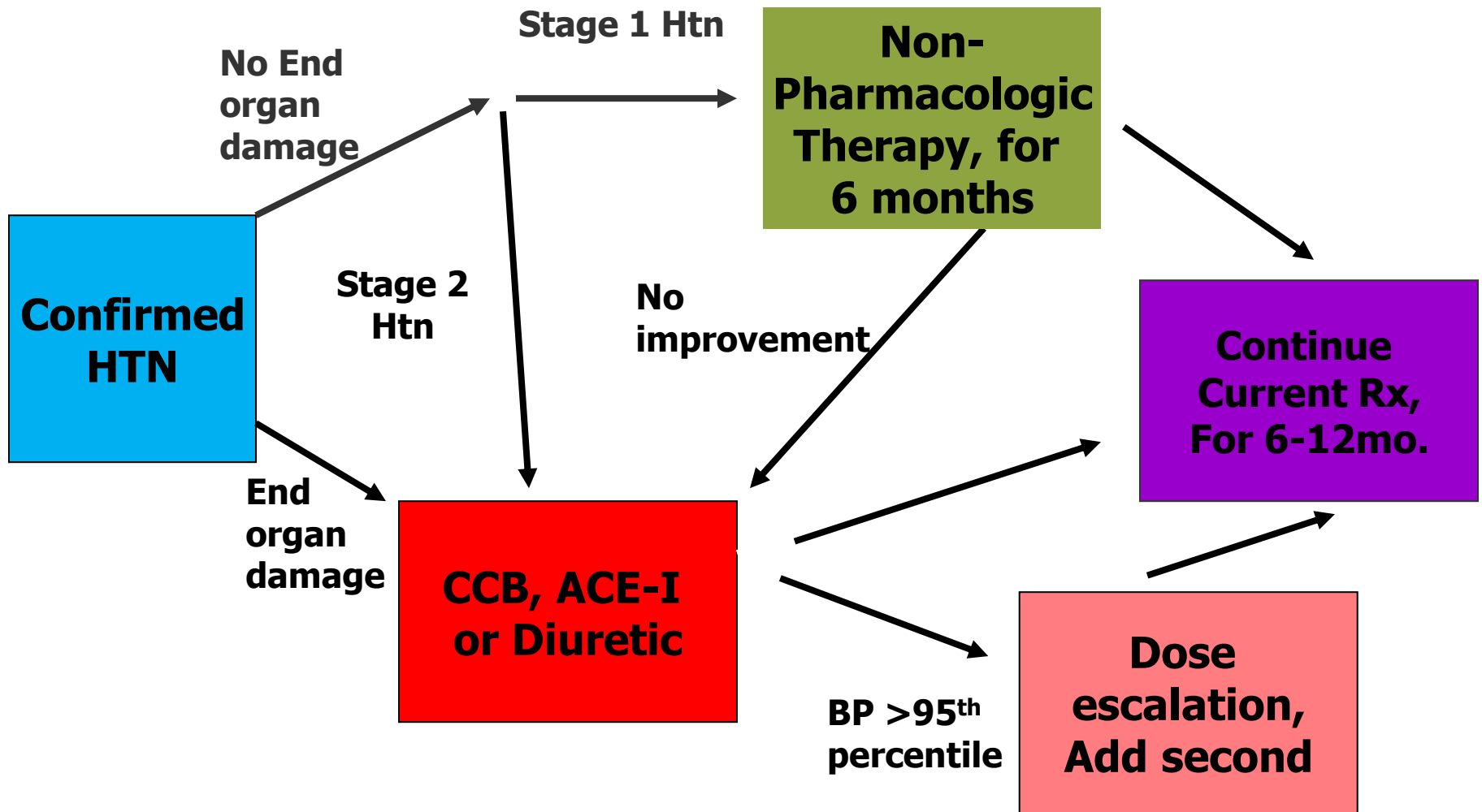
Medication	Age Tested	Dosing interval	Formulation
<b>Diuretics</b>			
Chlorthalidone	>3yr	Daily	Tablet
Chlorothiazide	Infant-child	1-2x/d	Tablet, liquid
HCTZ	Infant-child	1-2x/d	Tablet
<b>CCBs</b>			
Amlodipine	>1yr	Daily	Tablet Extemp liquid
Felodipine	>6yr	Daily	Tablet
Isradipine	>1yr	2-3x/d	Capsule
Nifedipine ER	>6yr	1-2x/d	Tablet



# Other Medication Options

Medication	Age Tested	Dosing interval	Formulation
<b>Beta-Blockers</b>			
Atenolol	>6yo	Daily	Tablet
Labetalol	Infant-child	2-4x/d	Tablet Extemp liquid
Metoprolol	>3yo	2x/d	Tablet Extemp liquid
Nebivolol	>18	Daily	Tablet
<b>ARAs</b>			
Epleronone	>6yo	Daily	Tablet Extemp liquid
Spironolactone	Infant-child	1-3x/d	Tablet Extemp liquid
<b>Others</b>			
Doxazosin	N/A	Daily	Tablet
Clonidine	Infant-child	3-6x/d OR 1x/week	Tablet, TD-Patcht
Hydralazine	Infant-child	2-4x/d	Tablet
Minoxidil	>3yo	Daily	Tablet

# Treatment Algorithm



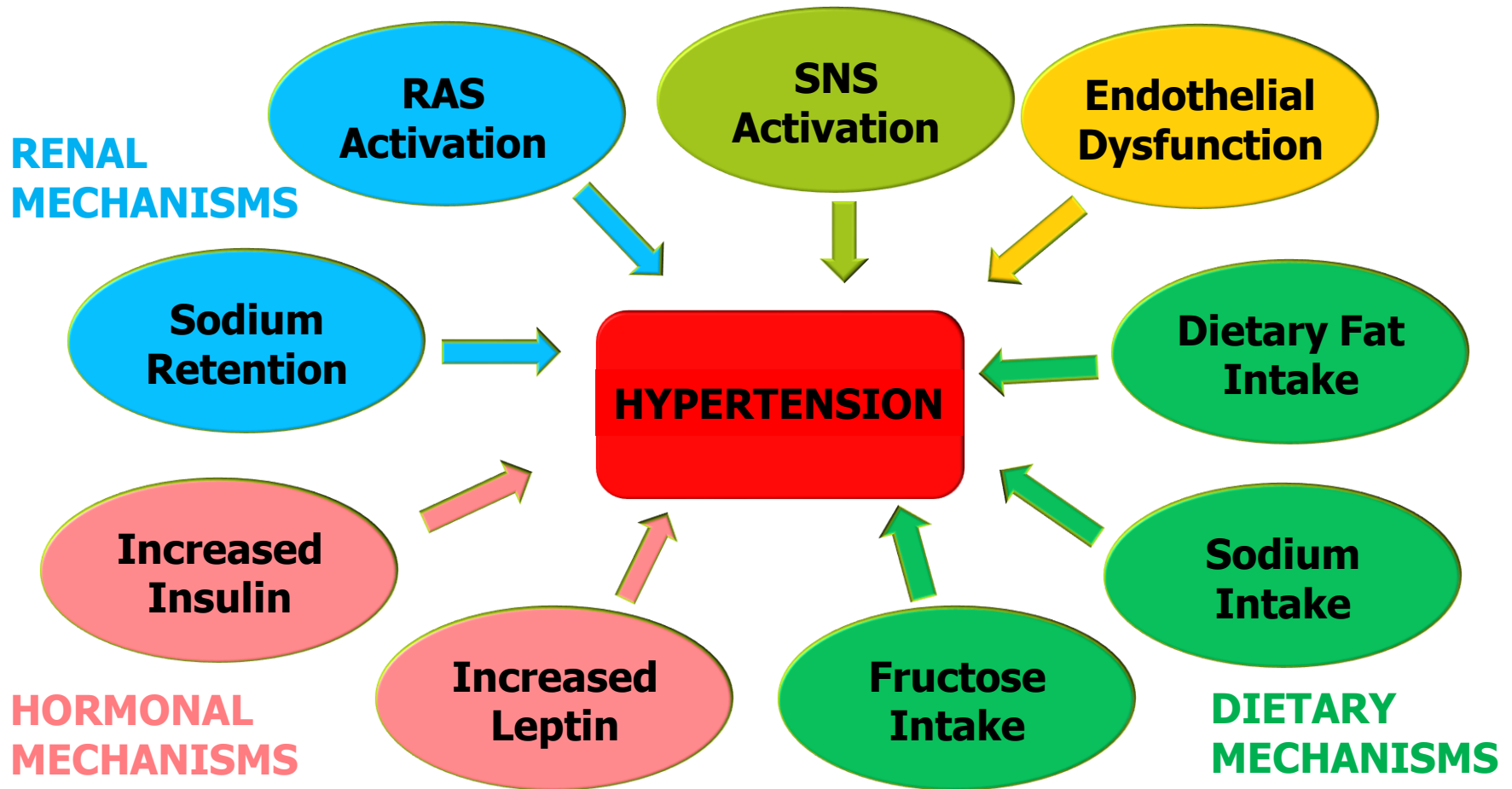
# 16yo Football Player

- **184cm, 162kg, BMI 47.8 kg/m<sup>2</sup>**
- **Casual BPs: 147/96, 145/95**
- **Confirmed hypertension by ABPM**
- **Electrolytes, Cr normal, elevated transaminases, HgbA1c 6.2**
- **Past Med history: obesity, no illnesses**
- **Family history: hypertension, early CVD**





# Mechanisms of Obesity Hypertension



# The Triumphant Return

## □ RTC Triage:

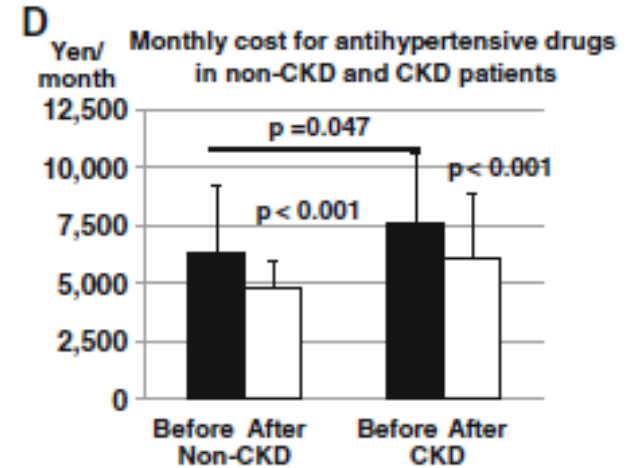
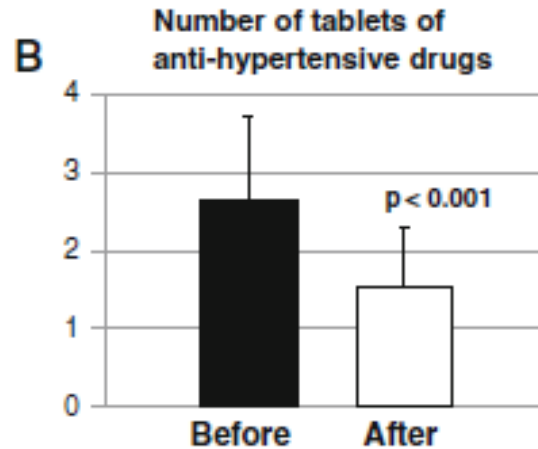
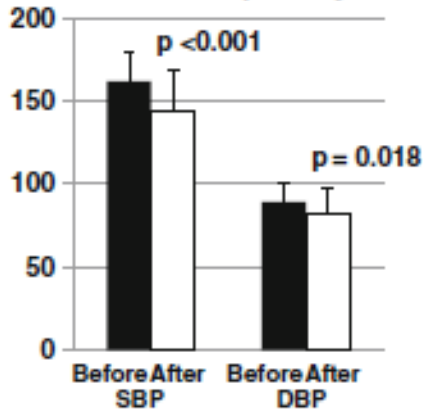
- Ht 184cm, Wt 172kg, BMI 50.4
- BP 151/94

## □ Medications

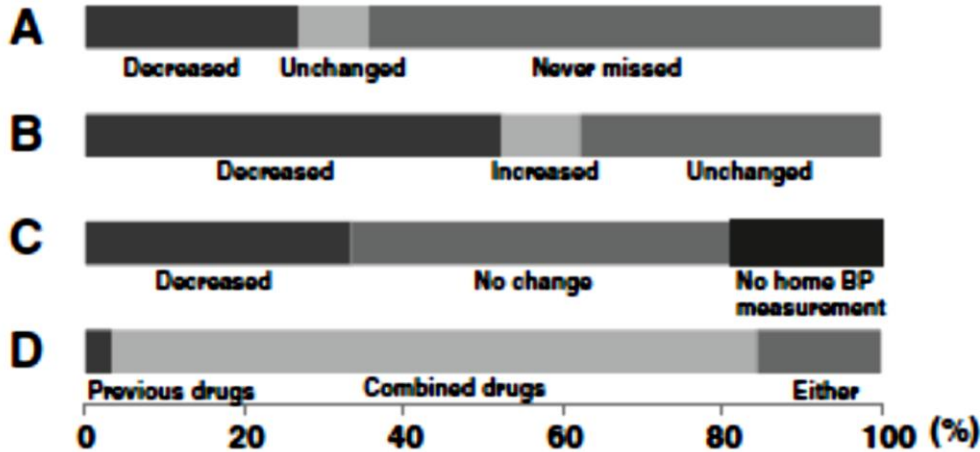
- Chlorthalidone 145/90
- +Losartan 152/94
- Losartan/HCTZ 136/85
- Valsartan/Amlodipine/HCTZ 122/78



# Impact of Fixed Combinations



## Questionnaire survey



Kato et al. Clin Exper Nephrol. 2015. 19;465.

90 patients transitioned to fixed combination tablets of same classes of medications already prescribed.

Monitor BP, tabs/d, cost



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# Adherence to Pharmacology Therapy

- Simplify, Simplify, Simplify
- Talk about it
  - “I just forget”
  - “I don’t want to take it”
  - “My coach, My friends ....”
  - “It makes me feel bad”
- Reminders – Technology is cool
- Work with parents or rewards system
- Consider inpatient observation

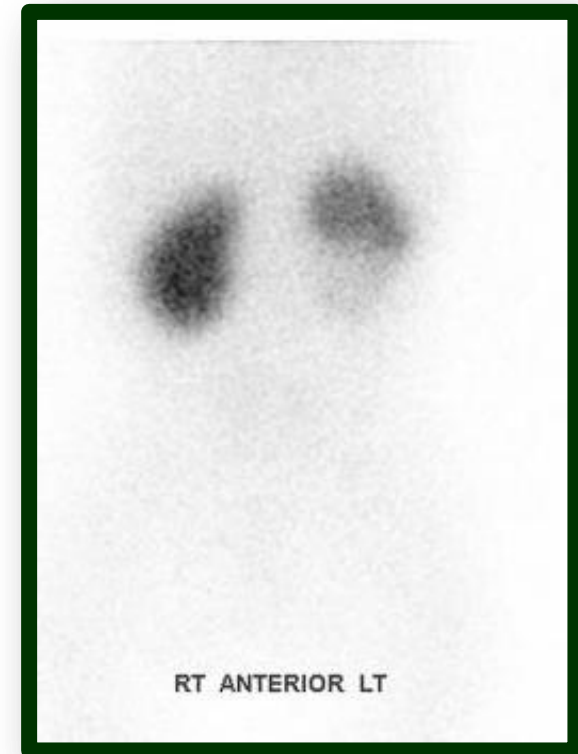


# 17yo Female Swimmer

- **Elite swimmer, told not to work out because of hypertension**
- **Medical history**
  - **BW 2100gm at 33 wks EGA, pre-eclampsia**
  - **Many ear infections, continued after PETs**
- **No meds, denies steroids, supplements**
- **BP 149/98 confirmed by ABPM**
- **BMI 22%, normal exam Na 141, K 3.3, Cl 102, HCO3 30, BUN 12, Cr 1.1**
- **Moderate LVH, LVMI 61gm/cm<sup>2.7</sup>**
- **Proteinuria, pro/Cr 0.45**

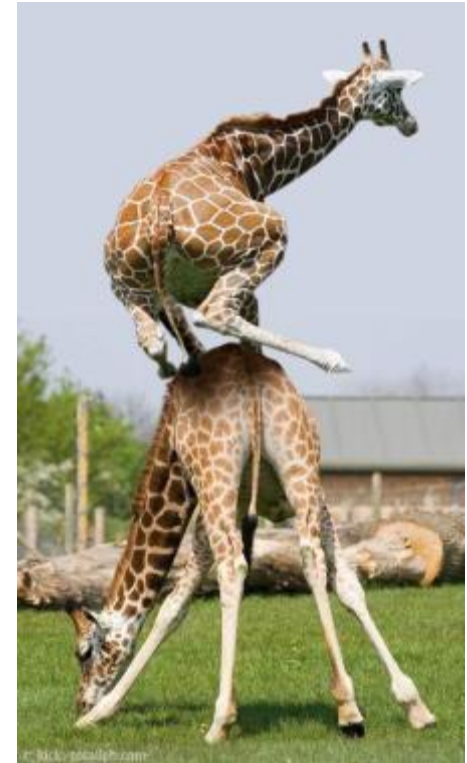


# Renal Imaging



# Hypertensive Athlete

- Renin mediated hypertension associated with renal scarring
- 1<sup>st</sup> line ACEi/ARB
  - Great BP control on Telmisartan
- Sexually active, did not want OCP
  - Issues: CKD with proteinuria, renin mediated hypertension
  - Options: CCB, Beta Blocker
  - Eventually Telmisartan/OCP



# Pheochromocytoma

- **14yo boy, competitive gymnast until 12 months ago**
- **Symptoms: vomiting during exertion, anxiety depression**
- **Developed: Weight loss, headaches, auditory hallucinations**
- **Denied: palpitations, diaphoresis, flushing**
- **BP 142/86 in Outpatient Psychiatry**
- **Work-up**
  - **ABPM demonstrated volatile hypertension**
  - **Echo moderate LVH**
  - **Plasma normetanephrine 1239mg/dL (45-120),**
  - **Plasma metanephrine 216mg/dL (92-250)**
  - **24hr urine (epi, norepi, dopamine, VMA) normal**





# Pre-Op for Pheo Resection

- UAB/Baylor Protocol
- Alpha blockade (phenoxybenzamine, doxazosin) dose escalation over 2wks
- Aggressive Na and Volume loading
- Add Tyrosine hydroxylase inhibitor (metyrosine) for 2<sup>nd</sup> week
- If symptomatic tachycardia that is volume nonresponsive then beta blocker can be added
- OR on day 14
- Immediate withdrawal of phenoxybenzamine, metyrosine post-op
- 50% require vasopressin for 4-8hrs



# Summary

- ❑ **Antihypertensive medications should be started**
  - ❑ Essential hypertension non-responsive to Non-Pharm
  - ❑ Persistent stage 2 hypertension
  - ❑ Evidence of target organ damage
  - ❑ Secondary hypertension with a direct therapy
- ❑ **Primary**
  - ❑ Mitigate existing target organ damage
  - ❑ Prevent future target organ damage
  - ❑ Reduce long term CV risk
  - ❑ Slow progression of CKD
  - ❑ Minimize side effects
- ❑ **Secondary**
  - ❑ Control symptoms – neuropsych, subjective
  - ❑ Consider prevention of hypertension progression
- ❑ **Over-riding**
  - ❑ **Provide attainable therapy (adherence, cost, etc)**
  - ❑ **Make the child feel better (or at least not worse)**
  - ❑ **?? Data driven !!**



# The End



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[dfeig@peds.uab.edu](mailto:dfeig@peds.uab.edu)

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