Management of Hypertension

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Disturbing Trends in Hypertension

- HTN awareness, treatment and control rates are decreasing
- Age adjusted mortality rates for stroke and CHD appear to be either rising or leveling of
- The incidence of ESRD and the prevalence of CHF is increasing
- HTN related complications are a public health concern
- Treatment of HTN is a worldwide failure!

Mechanics of Hypertension

- Primary salt factor:
  suppressed renin
  good response to a diuretic
- Primary Renin Angiotensin factor:
  elevated renin
  good response to antirenin-angiotensin type medication

Blood Pressure and Cardiovascular Risk

Relationship between BP and Cardiovascular risk

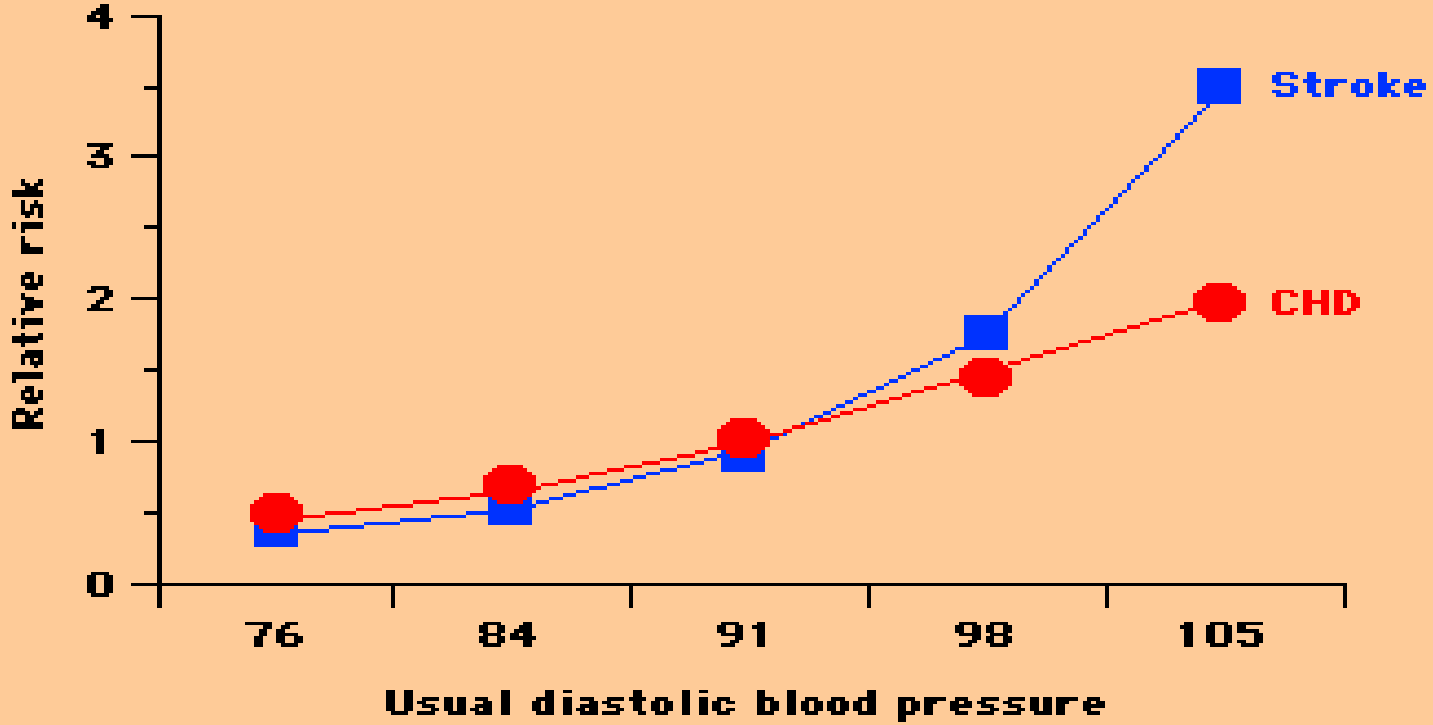
- Strong
- Continuous
- Graded
- Consistent
- Independent
- Predictive
- Etiologically significant

Why treat?

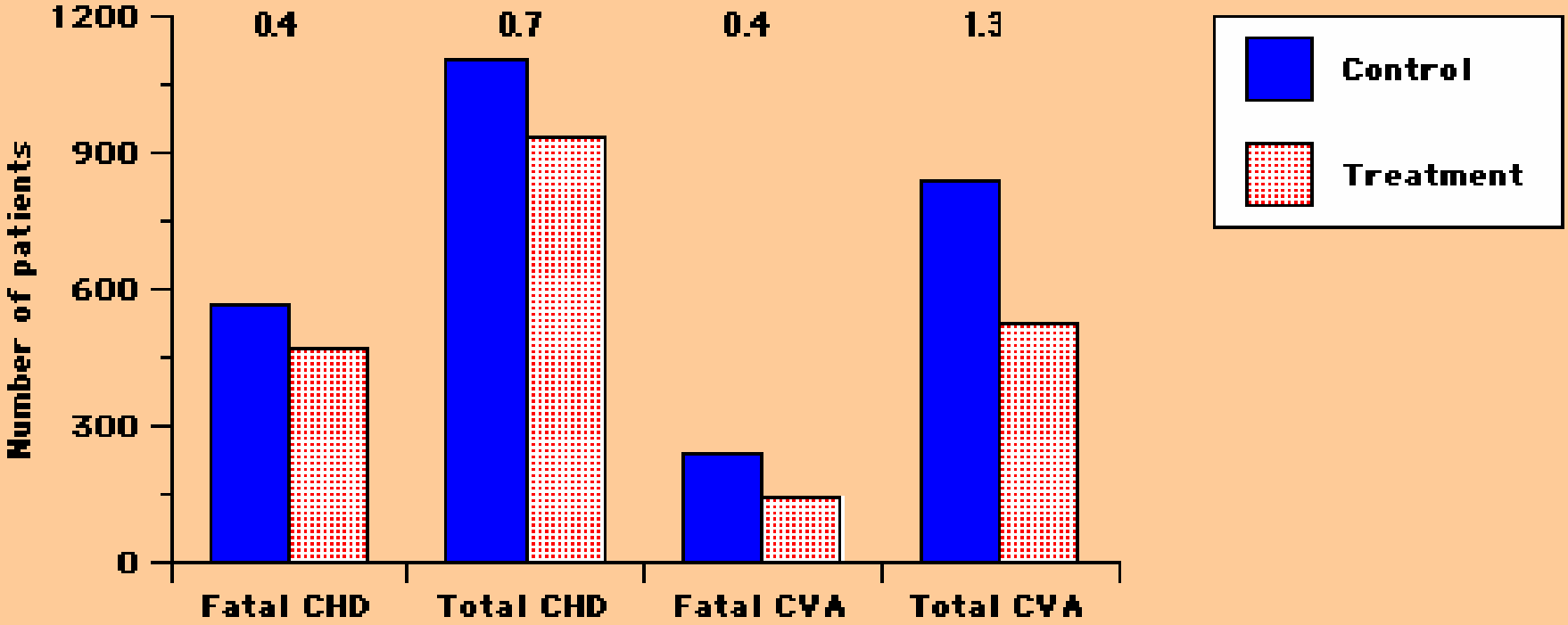
- Hypertension is deleterious to the vascular health
- **Evidence** from natural experiments in humans: Unilateral RVD

  Coarctation of aorta

  Pulmonary hypertension
- **Evidence** from animal experiments
- **Evidence** from Clinical trials



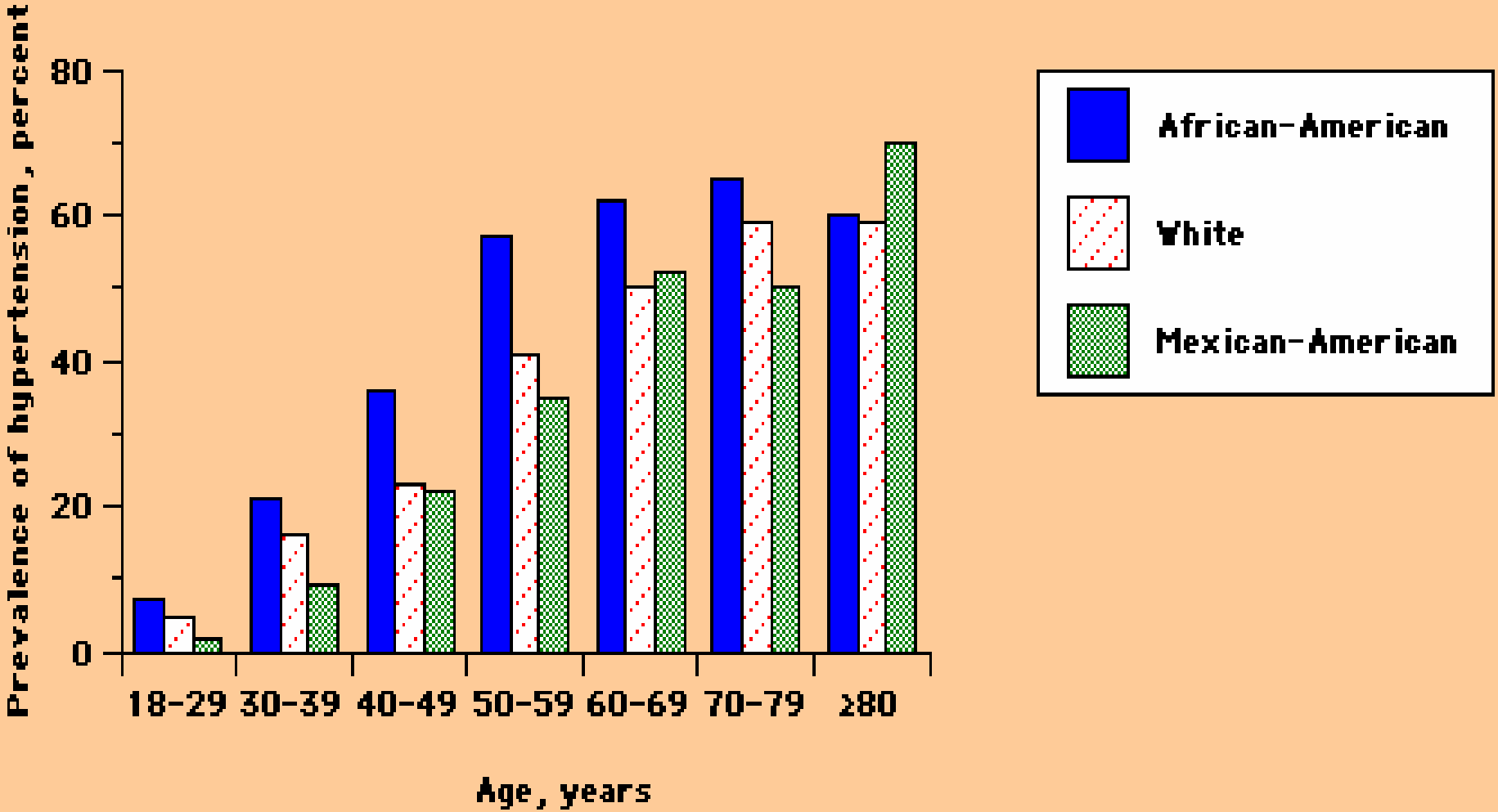
Relation between diastolic pressure and cardiovascular disease Increasing relative 10-year risk of stroke and coronary heart disease (CHD) at higher usual diastolic blood pressures in nine studies of untreated subjects. These observations, however, do not necessarily mean that the blood pressure was responsible for the cardiovascular disease or that the risk could be reduced at all levels of diastolic pressure with antihypertensive medications. (Data from MacMahon, S, Peto, R, Cutler, J, et al, Lancet 1990; 335:765.)



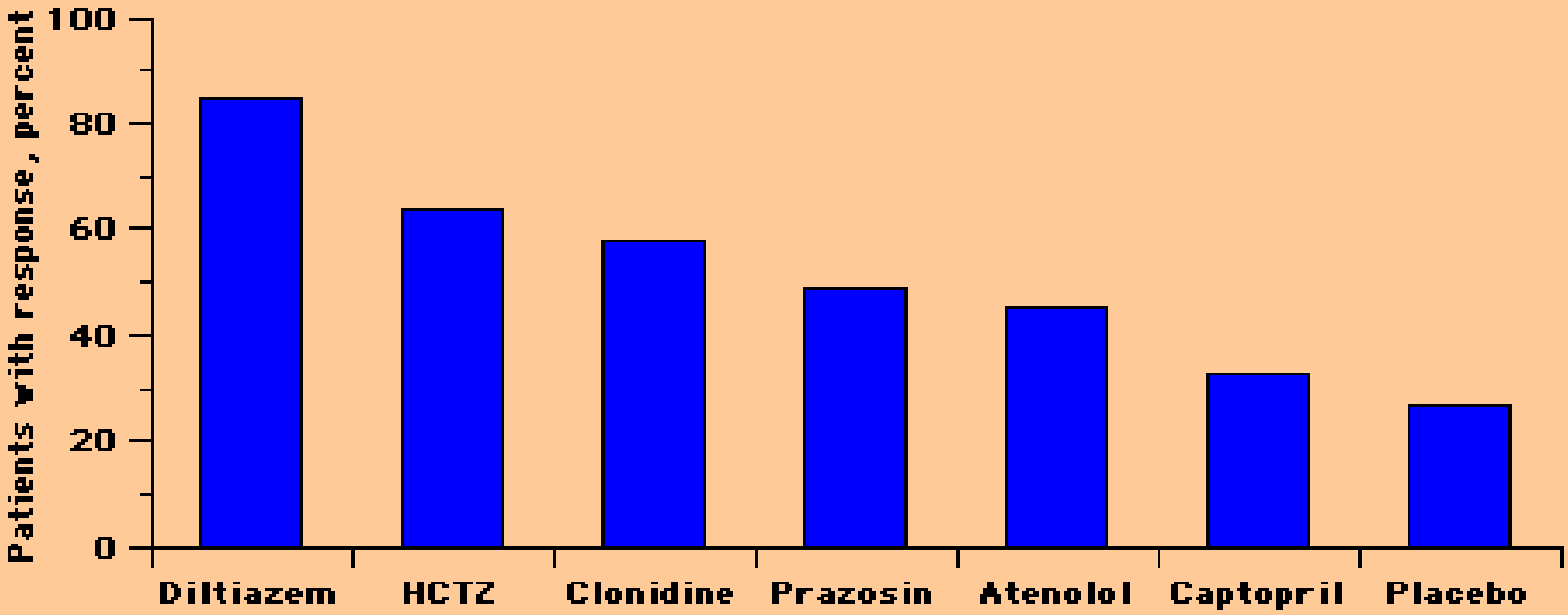
Cardiovascular benefit of treating mild hypertension Reduced incidence of fatal and total coronary heart disease (CHD) events and strokes following antihypertensive therapy in 17 controlled studies involving almost 48,000 patients with mild to moderate hypertension. The number of patients having each of these events is depicted, with active treatment lowering the incidence of coronary events by 16 percent and stroke by 40 percent. However, the absolute benefit – as shown, in percent, by the numbers at the top of the graph – was much less. Treatment for approximately 4 to 5 years prevented a coronary event or a stroke in two percent of patients (0.7 + 1.3), including prevention of death in 0.8 percent. (Data from Hebert, PR, Moser, M, Mayer, J, et al, Arch Intern Med 1993; 153:578.)

Variables in Treatment and/or Response

- Race / ethnicity
- Age
- Sex
- Co-morbidity
- Co-treatment



Prevalence of hypertension in men in the United States Prevalence of hypertension in men according to age and race/ethnicity in the United States from the NHANES-III survey. Hypertension occurs earlier and more frequently in African-American men. (Data from Burt, VL, Whelton, P, Roccella, EJ, et al, Hypertension 1995; 25:305.)



Antihypertensive response to different drugs in blacks Response rates to single drug therapy for hypertension in blacks over the age of 60. The highest response was seen with diltiazem and hydrochlorothiazide (HCTZ) and the lowest with captopril. A response was defined as a diastolic pressure below 90 mmHg at the end of the titration phase and below 95 mmHg at one year. The pattern of response was similar but the success rate for each drug was reduced by five to 15 percent if goal diastolic pressure were less than 90 mmHg at one year. There were between 42 and 53 patients in each group. (Data from Materson, BJ, Reda, DJ, Cushman, WC, et al, N Engl J Med 1993; 328:914. Correction and additional data: Am J Hypertens 1995; 8:189.)

Components of Cardiovascular Risk Factors in Patients with Hypertension[†]

Major risk factors

- Smoking
- Dyslipidemia
- Diabetes mellitus
- Age older than 60 years
- Sex – men and postmenopausal women
- Family history of cardiovascular disease
  - Men under age 55
  - Women under age 65

Target organ damage/ clinical cardiovascular disease

- Heart diseases
  - Left ventricular hypertrophy
  - Angina or prior myocardial infarction
  - Prior coronary revascularization
  - Heart failure
- Stroke or transient ischemic attack
- Nephropathy
- Peripheral arterial disease
- Retinopathy

[†]Data from Joint National Committee. The sixth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1997; 157:2413.

Management Objectives

- Identify **Cause**
- Identify other **Cardiovascular Risk Factors**
- Assess **Target Organ Damage**
- Assess **Cardiovascular Disease.**

Classification of Hypertension in adults (>18years)

BP Classification	Systolic BP, mm Hg*		Diastolic BP, mm Hg*	Management*		
				Lifestyle Modification	Initial Drug Therapy	
					Without Compelling Indication	With Compelling Indications†
Normal	<120	and	<80	Encourage		
Prehypertension	120-139	or	80-89	Yes	No antihypertensive drug indicated	Drug(s) for the compelling indications‡
Stage 1 hypertension	140-159	or	90-99	Yes	Thiazide-type diuretics for most; may consider ACE inhibitor, ARB, β-blocker, CCB, or combination	Drug(s) for the compelling indications Other antihypertensive drugs (diuretics, ACE inhibitor, ARB, β-blocker, CCB) as needed
Stage 2 hypertension	≥160	or	≥100	Yes	2-Drug combination for most (usually thiazide-type diuretic and ACE inhibitor or ARB or β-blocker or CCB)§	Drug(s) for the compelling indications Other antihypertensive drugs (diuretics, ACE inhibitor, ARB, β-blocker, CCB) as needed

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; BP, blood pressure; CCB, calcium channel blocker.

*Treatment determined by highest BP category.

†See Table 6.

‡Treat patients with chronic kidney disease or diabetes to BP goal of less than 130/80 mm Hg.

§Initial combined therapy should be used cautiously in those at risk for orthostatic hypotension.

Identifiable causes of Hypertension

- **Sleep Apnea**
- **Drug induced/related**
- **Chronic Kidney Disease**
- **Primary aldosteronism**
- **Renovascular disease**
- **Cushings/chronic steroid therapy**
- **Pheochromocytoma**
- **Coarctation of aorta**
- **Thyroid or hyperparathyroid disease**

Lifestyle modifications for Hypertension

Modification	Recommendation	Approximate Systolic BP Reduction, Range
Weight reduction	Maintain normal body weight (BMI, 18.5-24.9)	5-20 mm Hg/10-kg weight loss[23,24]
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat	8-14 mm Hg[25,26]
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mEq/L (2.4 g sodium or 6 g sodium chloride)	2-8 mm Hg[25-27]
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)	4-9 mm Hg[28,29]
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks per day (1 oz or 30 mL ethanol [eg, 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey]) in most men and no more than 1 drink per day in women and lighter-weight persons	2-4 mm Hg[30]

Abbreviations: BMI, body mass index calculated as weight in kilograms divided by the square of height in meters; BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension.

*For overall cardiovascular risk reduction, stop smoking. The effects of implementing these modifications are dose and time dependent and could be higher for some individuals.

Renal Diseases in Hypertension
Core Concepts of Treatment

- Hypertension is an independent variable that predicts long-term decline in renal function
- Proteinuria is also an independent variable that predicts long-term decline in renal function
- Reduction of blood pressure reduces both cardiovascular and renal risk
- Reduction of proteinuria may reduce both cardiovascular and renal risk
- Relative renal hypoperfusion during initial stages of therapy for hypertension is associated with a transient limited rise in serum creatinine and is not a reason to stop therapy

The Dual Significance of Proteinuria

- Proteinuria (albuminuria) results from injury to glomerular circulation
  - Increased proteinuria (albuminuria) is associated with progressive kidney disease
- In diabetes and hypertension, proteinuria (albuminuria) is also an indicator of injury in the systemic circulation
  - Proteinuria (albuminuria) is associated with increased cardiovascular risk

Definitions of Microalbuminuria and Macroalbuminuria

Parameter	Normal	Micro-albuminuria	Macro-albuminuria
Urine AER (μg/min)	< 20	20 - 200	>200
Urine AER (mg/24h)	< 30	30 - 300	>300
Urine albumin/ Cr# ratio (mg/gm)	< 30	30 - 300	>300

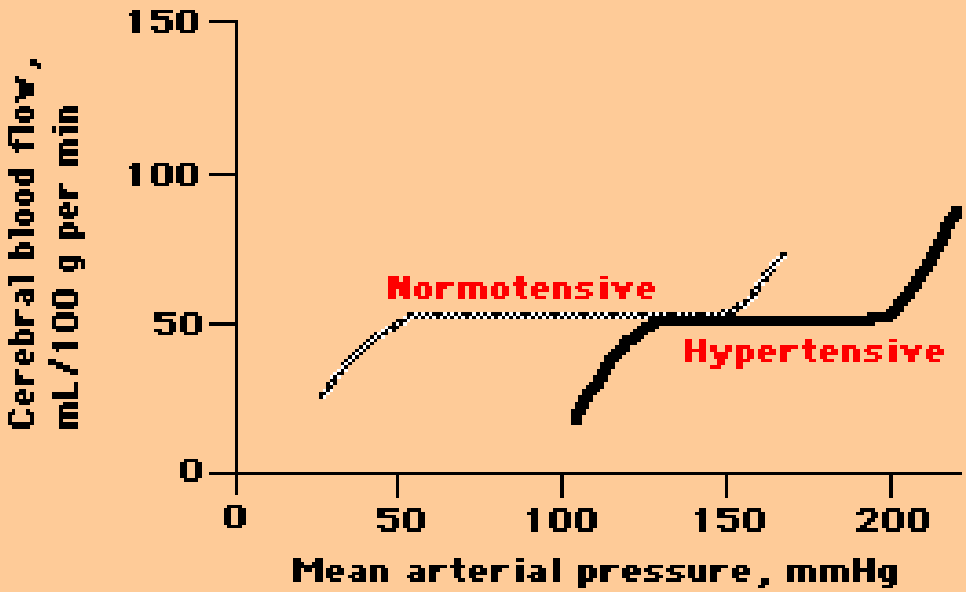
AER=Albumin excretion rate CR# =creatinine

Goal BP Recommendations for Patients with DM or Renal Disease

Organization	Year	Systolic BP	Diastolic BP
American Diabetes Association	2001	<130	<80
National Kidney Foundation	2000	<130	<80
Canadian Hypertension Society	1999	<130	<80
British Hypertension Society	1999	<140	<80
WHO & International Society of Hypertension	1999	<130	<85
Joint National Committee (JNC VI)	1997	<130	<85

Drug Therapy

- Avoid overdosing
- Avoid Quick Fix (cerebral and coronary hypoperfusion may result)
- Aim for 24 hour coverage



Cerebral autoregulation in hypertension Schematic representation of autoregulation of cerebral blood flow in normotensive and hypertensive subjects. In both groups, initial increases or decreases in mean arterial pressure are associated with maintenance of cerebral blood flow due to appropriate changes in arteriolar resistance. More marked changes in pressure are eventually associated with loss of autoregulation, leading to a reduction (with hypotension) or an elevation (with marked hypertension) in cerebral blood flow. These changes occur at higher pressures in patients with hypertension, presumably due to arteriolar thickening. Thus, aggressive antihypertensive therapy will produce cerebral ischemia at a higher mean arterial pressure in patients with underlying hypertension. (Redrawn from Kaplan, NM, Lancet 1994; 344:1335.)

Drug Therapy

- Minimize Side Effects
- Establish goal
- Educate
- Maintain contact
- Keep care inexpensive
- Favor longer acting medications
- Be willing to change

Anti-Hypertensive Drugs: Sites of Action

Blood Pressure = **Cardiac Output** X **Total Peripheral Resistance**

Cardiac Output	Total Peripheral Resistance
β-Blockers	ACE Inhibitors
CCBs*	AT_1 Blockers
Diuretics	a-Blockers
	a_2-Agonists
	CCBs
	Diuretics
	Sympatholytics
	Vasodilators

* = non-dihydropyridine CCBs

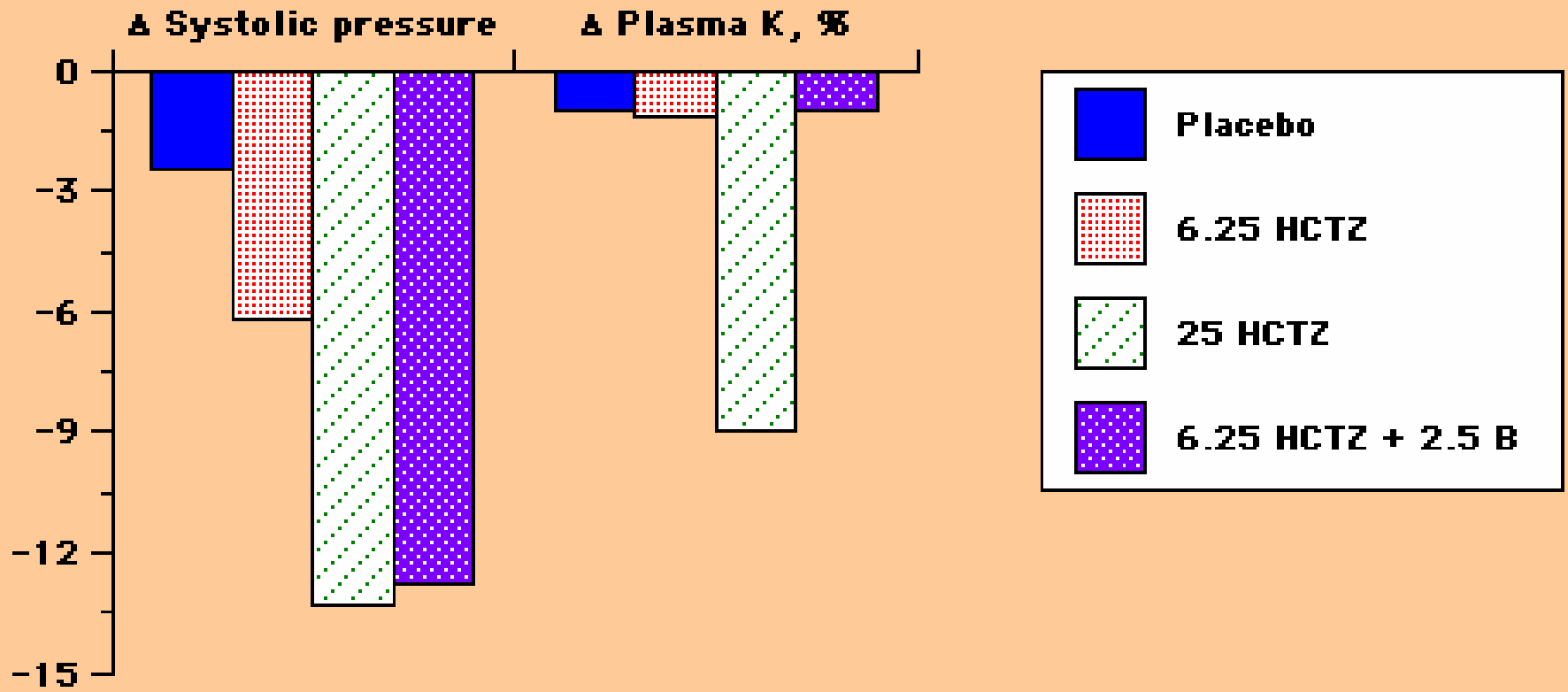
Average Number of Anti-Hypertensive Agents Used to Achieve Target BP

	MDRD	ABCD	HOT	UKPDS
Goal BP	<92 mmHg MAP*	<75 mmHg DBP	<80 mmHg DBP	<85 mmHg DBP
Achieved BP	93	~75	81	82
Avg # of drugs per patient	3.6	2.7	3.3	2.8

*The goal mean arterial pressure (MAP) of <92 mmHg specified in the MDRD trial corresponds to a systolic/diastolic blood pressure of approximately 125/75 mmHg.

Diuretics

- **Action**: Decrease plasma volume and TPR.
- **Effect**: Decrease overall CV mortality.
- **Side effects**: Mainly metabolic
- Start with a thiazide diuretic (low dose combinations)
- Loop diuretics required if serum Cr > 2.5 mg/dl



Efficacy of very low dose hydrochlorothiazide Comparison of fall in systolic pressure and change in plasma potassium concentration induced by placebo, 6.25 mg/day of hydrochlorothiazide (HCTZ), 25 mg/day of HCTZ, and 6.25 mg/day of HCTZ plus a very low dose (2.5 mg/day) of the ß-blocker bisopropol (B). 6.25 mg/day of HCTZ was less effective than the higher dose. However, combination therapy was as effective as 25 mg/day of HCTZ alone and had the advantage of producing no significant reduction in the plasma potassium concentration. (Data from Frishman, WH, Bryzinski, BS, Coulson, LR, et al, Arch Intern Med 1994; 154:1461.)

β Blockers

- ↓ Reduce CO, ↓ Sympathetic outflow, ↓ Renin release
- Indications:
  - Young,
  - Middle aged, Caucasian
  - Post MI
  - Increased level of stress
- Lipid solubility
- Cardio-selectivity
- Intrinsic sympathomimetic activity

Calcium Channel Blockers

- Dihydropyridines : vasodilators
- Short acting CCB are contraindicated
  - Post MI
  - HT emergencies
- Non dihydropyridines:
  - Depress cardiac contractility
  - Inhibit AV node
  - Induce vasodilatation.
- Elderly and Black patients respond better

ACE inhibitors

- Main action is to block conversion of ATI to ATII
- Protect the heart and the kidneys
- Diuretics enhance ACEI response
- Use with caution in Renovascular HTN
- Hyperkalemia and Cough are common
- Contraindicated in Pregnancy

Inadequate Response

- Pseudo-resistance
- Non adherence
- Volume overload
- Drug Related Causes/Interactions (NSAIDS, Cyclosporin, Epogen, Cold remedies, Caffeine, Cocaine)
- Associated Conditions (Smoking, Obesity, Alcohol, OSA, Chronic pain)
- Secondary Causes

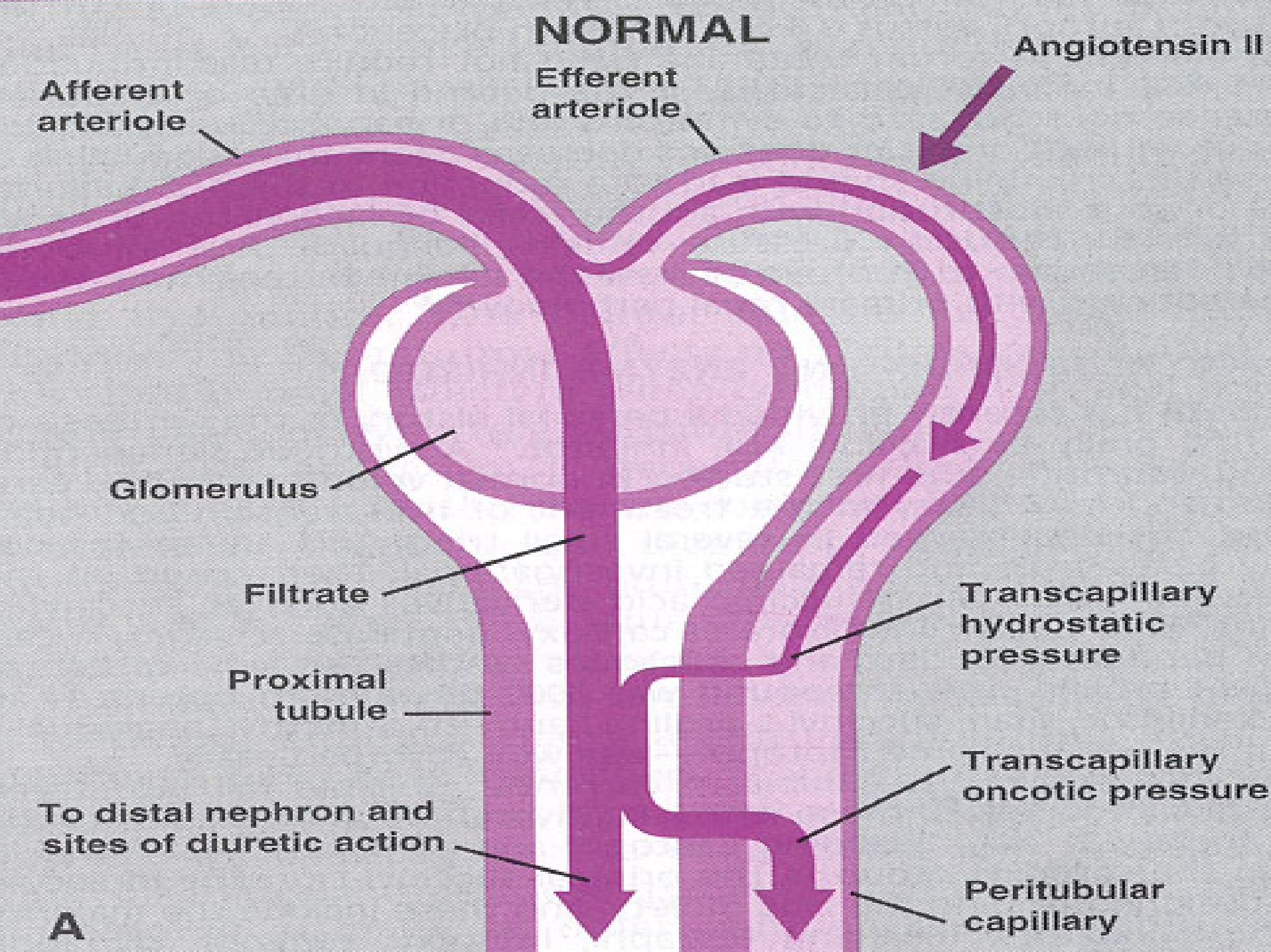
Case 1

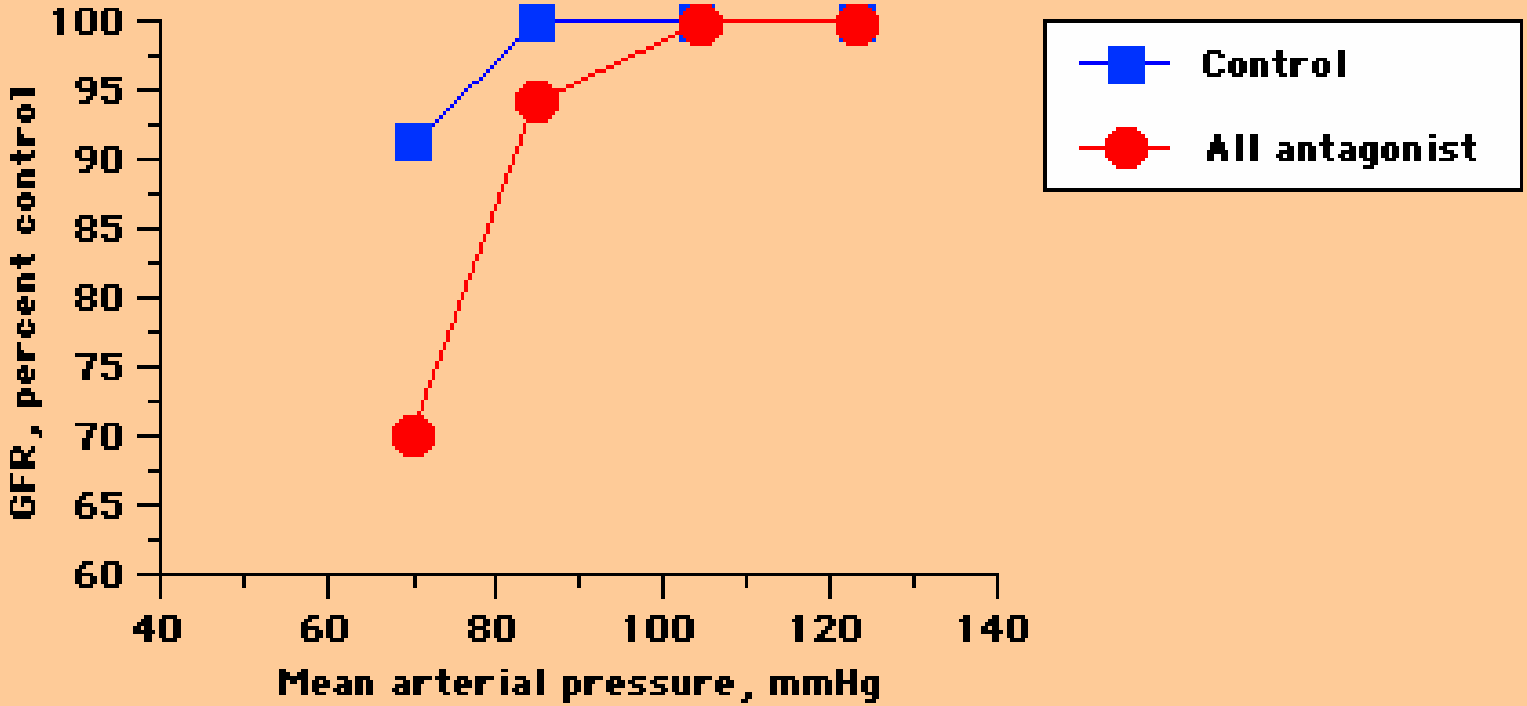
- 65 y/o m with 20 y h/o mild HTN. BP was well controlled with medications that were discontinued after Cardiac Cath for Angina. BP gradually drifted up in the next 1-2 years. Patient was started on ACEI with a sharp fall in BP, and a rise in S Cr. from 2 to 6.0 mg/dl.

- What is the mechanism of HTN?
- Why did renal function deteriorate?
- What alternative therapies are available?

Clinical clues of Renovascular Disease

- Age of Onset
- Abdominal Bruit
- Accelerated or resistant Hypertension
- Flash Pulmonary Edema
- Renal Failure of uncertain etiology
- Widespread Vascular disease
- ARF precipitated by ACEI
- Asymmetric Kidneys


NORMAL
Angiotensin II
Afferent arteriole
Efferent arteriole
Glomerulus
Filtrate
Transcapillary hydrostatic pressure
Proximal tubule
Transcapillary oncotic pressure
To distal nephron and sites of diuretic action
Peritubular capillary
A



Role of angiotensin II in autoregulation of GFR Effect of reducing renal artery pressure (from a baseline value of about 125 mmHg) on GFR, expressed as a percentage of control values in dogs fed a normal sodium diet. The blue squares represent control animals in which both GFR was maintained until the pressure was markedly reduced. The red circles represent animals given an intrarenal infusion of an angiotensin II antagonist; autoregulation of GFR was less well regulated. Although not shown, autoregulation also applies to GFR when the renal artery pressure is initially raised and to renal blood flow; which is not impaired by inhibiting the activity of angiotensin II. (Data from Hall, JE, Guyton, AC, Jackson, TE, et al, Am J Physiol 1977; 233:F366.)

Renal artery stenosis Aortogram shows a focal stenosis of the left renal artery with poststenotic dilatation (arrow). The right renal artery has a normal caliber and is delivering contrast to the right kidney well before the left kidney recieves contrast. Courtesy of Jonathan Kruskal, MD.

Hypertension & Diabetes Mellitus

- Measure BP in all 3 positions
- Aim for 125/75 mm Hg
- Preferably use ACEI, ARB
- Supplement Treatment with life style modifications

HTN and Renal Parenchymal Disease

- HT nephrosclerosis is a very common cause of CKD in African Americans
- Aim for 130/80 or lower especially in those with proteinuria
- Adequate control is more important than type of therapy

Case 2

82 y/o male with long standing systolic HTN.

BP is recorded at 220/70 mm Hg.

- What is the mechanism of Hypertension?
- Is there value of lowering BP in this individual?
- What agents would you consider as initial therapy?

Hypertension in the elderly

- Extremely common in older Americans
- Elevated SBP and/or Pulse Pressure is a better adverse event predictor in this age group
- Primary HTN is the commonest etiology.
- Pseudo HTN and White coat HTN is common
- Orthostatic Hypotension is commoner

Hypertension in the elderly

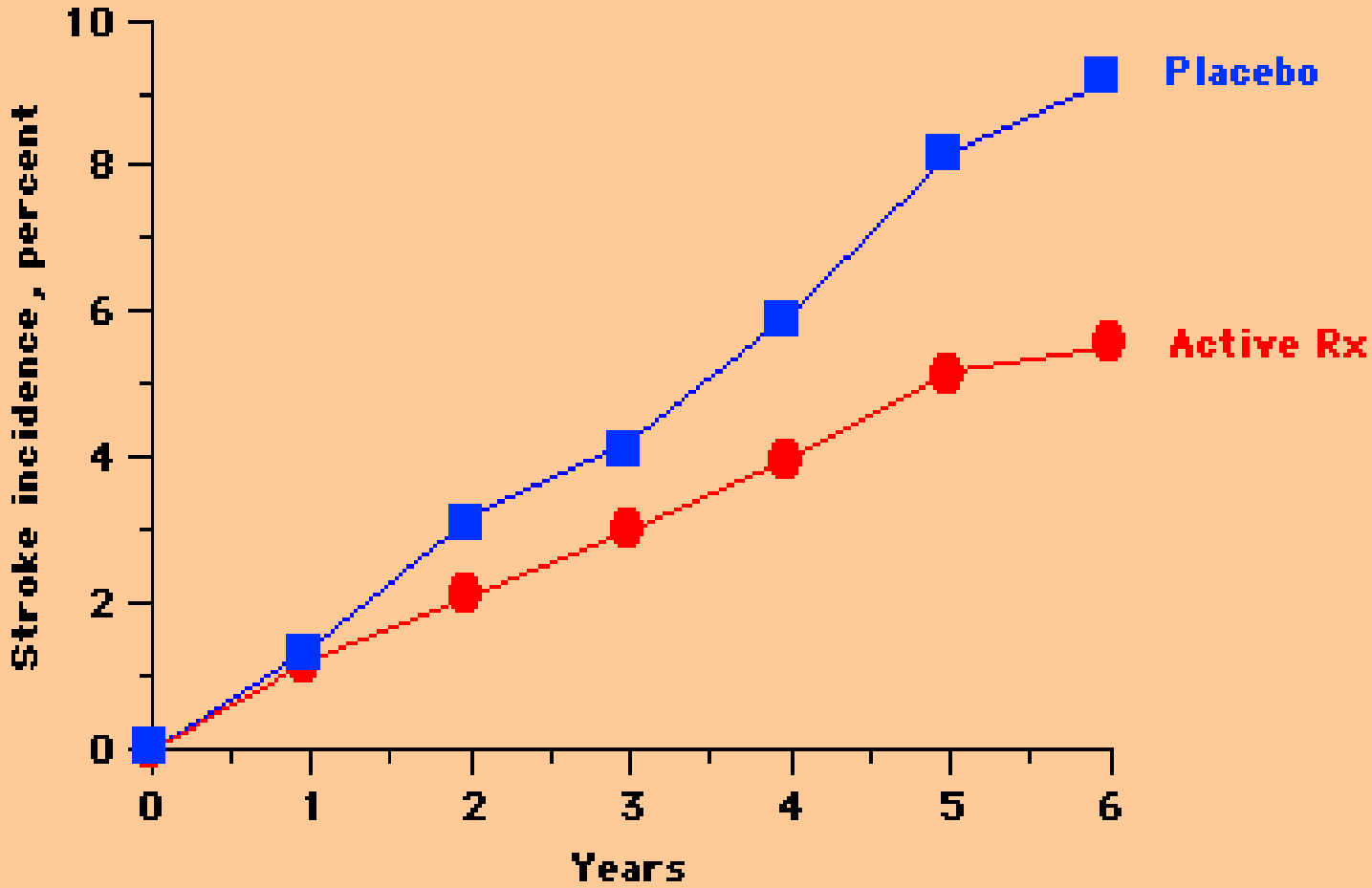
Should we treat?

What is the goal BP?

What medications to use?

Should we Treat Hypertension in the elderly?

- Treatment reduces CVD/CHD morbidity and mortality
- Any reduction in BP confers benefit
- The closer to normal blood pressure, the greater the benefit



Benefit of treating isolated systolic hypertension idence of stroke in elderly patients with isolated systolic hypertension treated with antihyperte drugs or placebo. At six years, active therapy prevented strokes in 4 percent patients compared to the placebo group. (Data from SHEP Cooperative Researc Group, JAMA 1991; 265:3255.)

What medications?

- For Isolated SHTN use

  Diuretics

  Calcium channel blockers

- β blockers and ACEI may be added if needed

GOAL BP in Elderly

- DBP <85-90 and
- SBP <160 (if initial SBP>180)
  or 20mm below baseline if initial SBP
  was between 160-180

Management of hypertension
Key points

- Risk Stratify
- Try Life Style Modifications
- Individualize Drug therapy

Management of Hypertension Key points

- Try once daily drugs or pharmacologically complementary combinations
- Apply redefined targets for special subsets of patients
- Try once daily drugs or pharmacologically complementary combinations in the elderly.

The overriding issue

Lower the Blood Pressure to maximally reduce cardiovascular risk without decreasing and perhaps even improving the enjoyment of life!