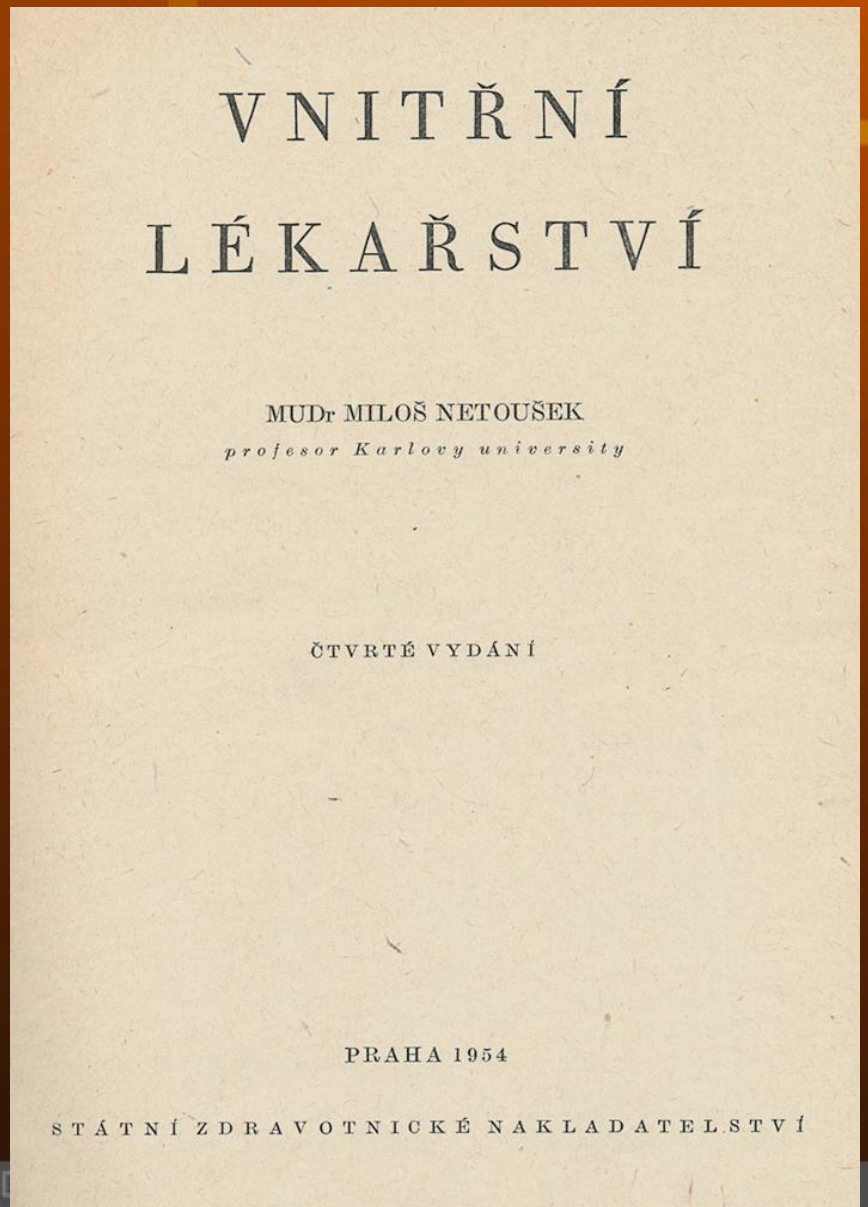
HYPERTENSION

M. Kozák, IKK, FN Brno

HT THERAPY - HISTORY


VNITŘNÍ

LÉKAŘSTVÍ

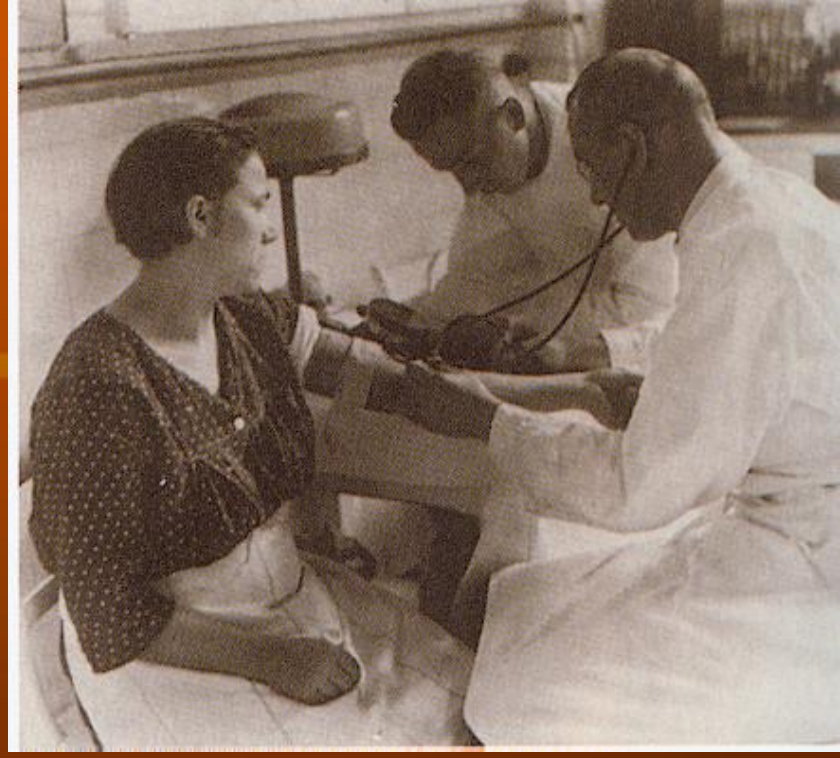
MUDr MILOŠ NETOUŠEK

profesor Karlovy university

ČTVRTÉ VYDÁNÍ

PRAHA 1954

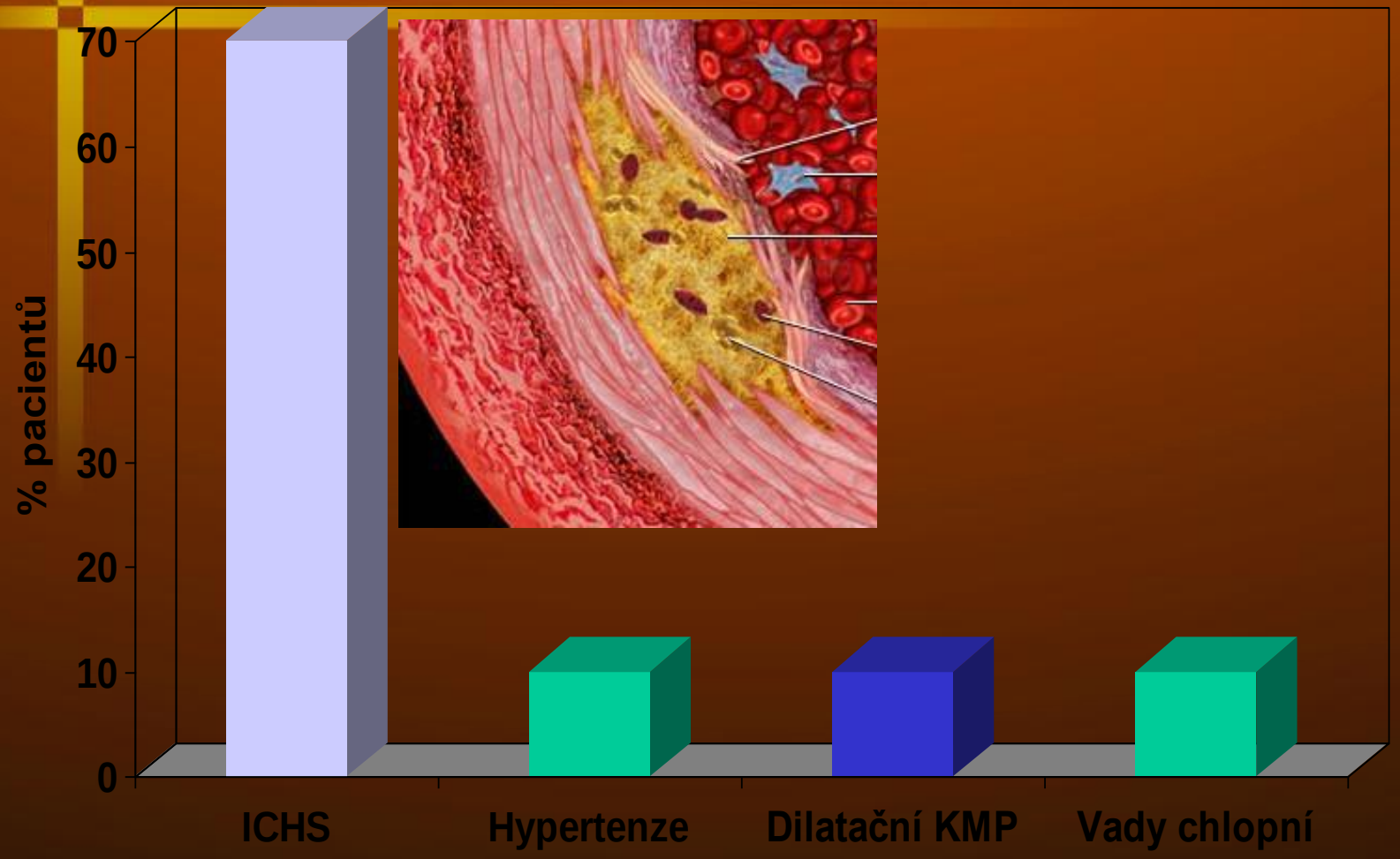
STÁTNÍ ZDRAVOTNICKÉ NAKLADATELSTVÍ



- life regime
- gymnastics
- eating moderation
- salt reducing
- nonsmoking
- analgetics
- physical th.
- liquor drenaige
- iodids
- rhodanid
- Ca
- NTG

ETIOLOGY CHF - Framingham st. 1950 -70

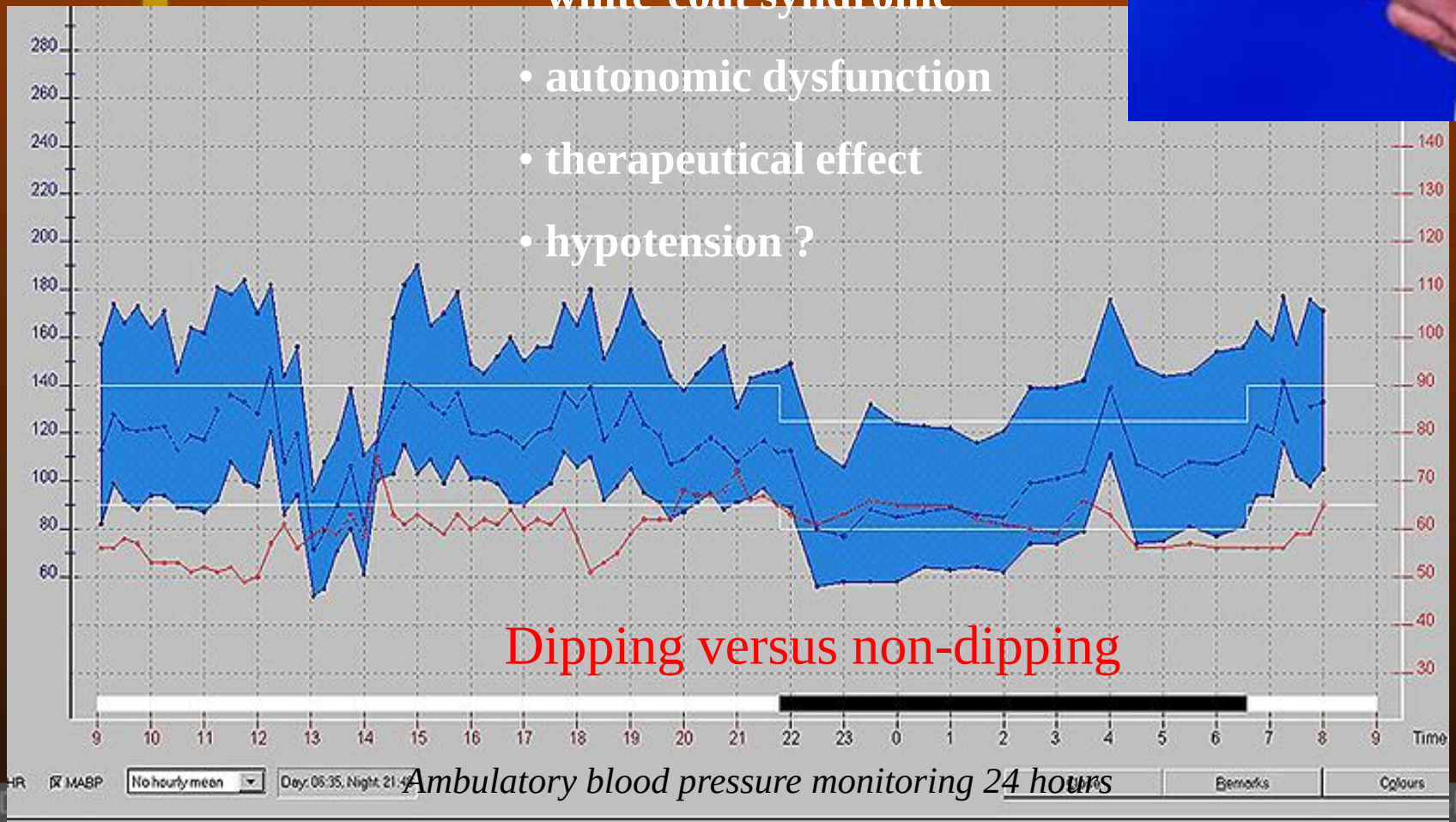
ETIOLOGY CHF - European data 1990 - 2000



BP MEASUREMENT - HOLTER

INDICATIONS

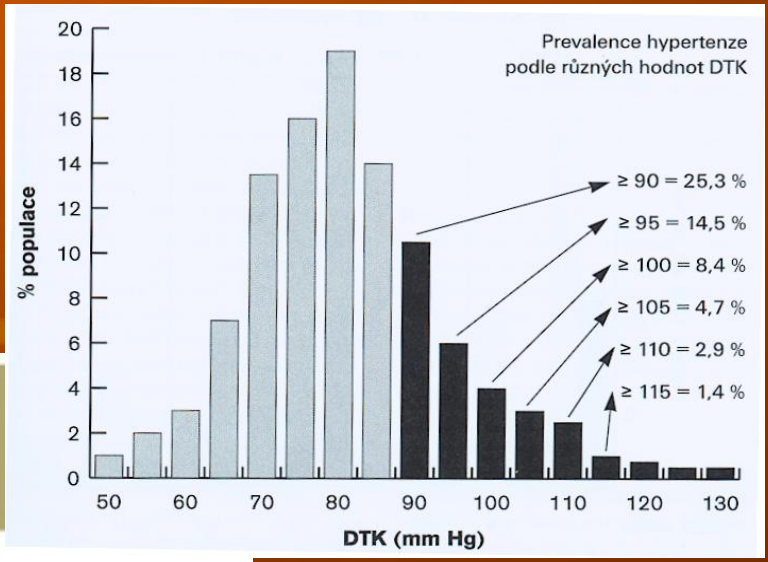
- diagnostic - hypertension
- epizodic HT
- white-coat syndrome
- autonomic dysfunction
- therapeutical effect
- hypotension ?

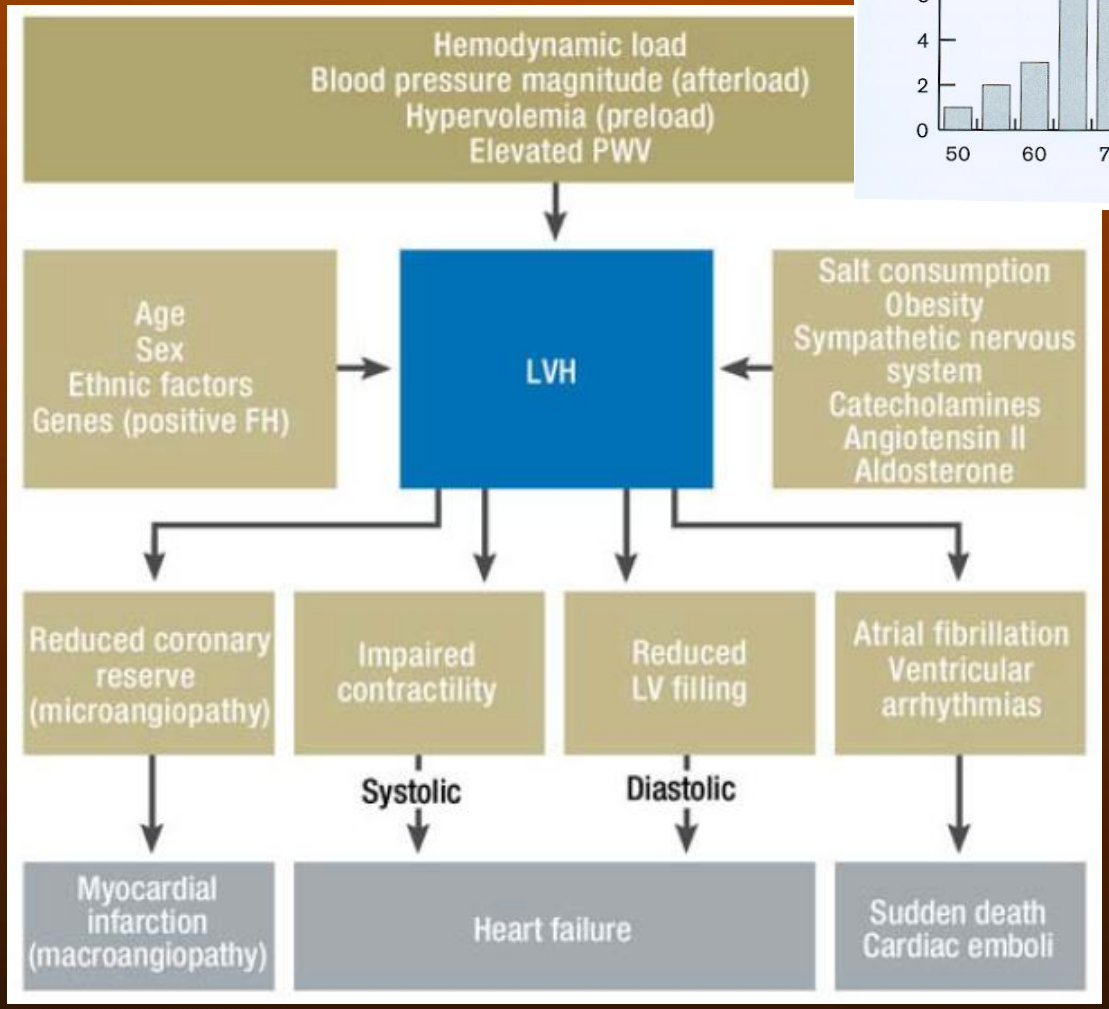


Dipping versus non-dipping

Ambulatory blood pressure monitoring 24 hours

HT IMPACTS

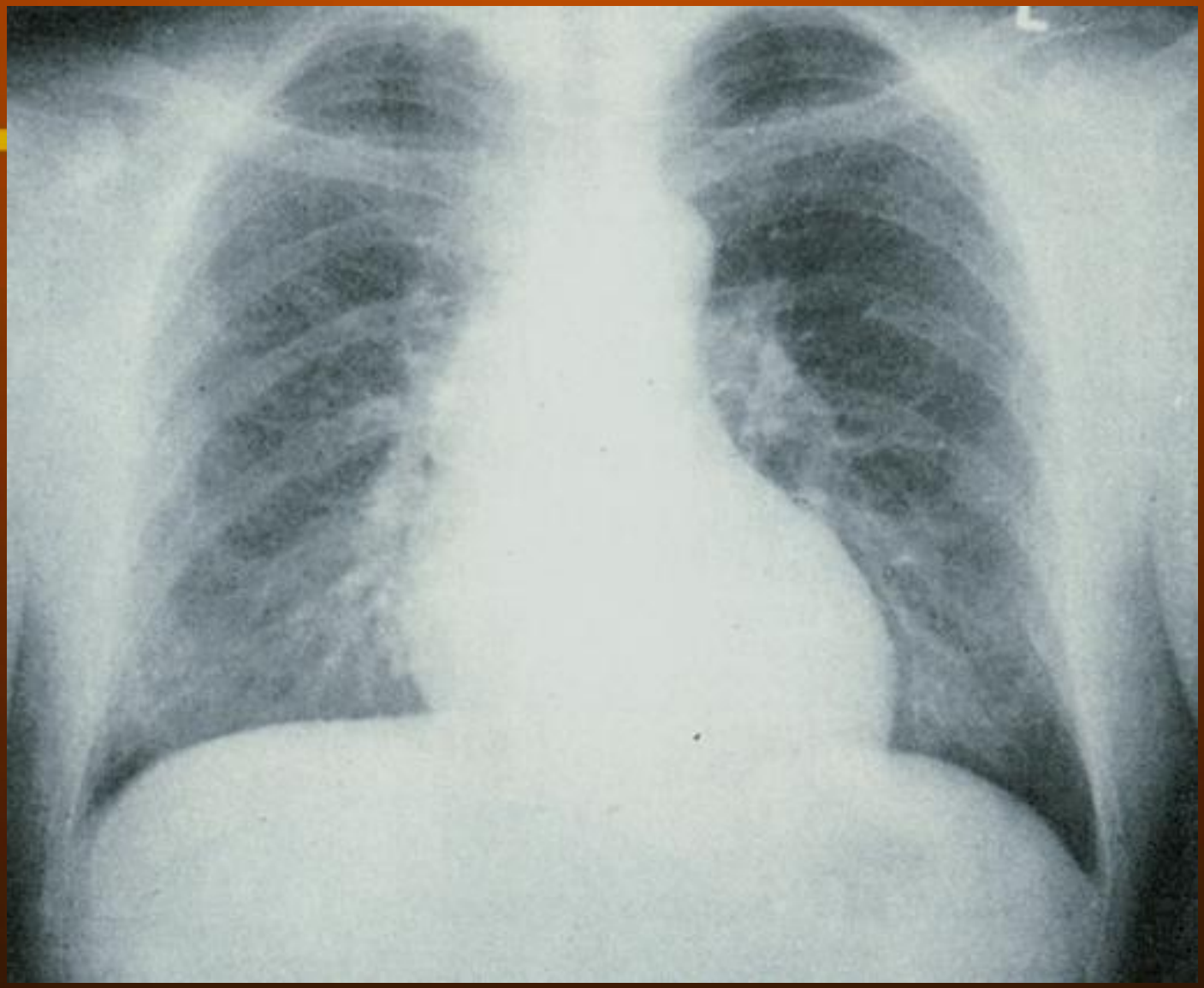

Prevalence hypertenze
podle různých hodnot DTK
% populace
DTK (mm Hg)
≥ 90 = 25,3 %
≥ 95 = 14,5 %
≥ 100 = 8,4 %
≥ 105 = 4,7 %
≥ 110 = 2,9 %
≥ 115 = 1,4 %


Hemodynamic load
Blood pressure magnitude (afterload)
Hypervolemia (preload)
Elevated PWV
Age
Sex
Ethnic factors
Genes (positive FH)
LVH
Salt consumption
Obesity
Sympathetic nervous system
Catecholamines
Angiotensin II
Aldosterone
Reduced coronary reserve (microangiopathy)
Impaired contractility
Reduced LV filling
Atrial fibrillation
Ventricular arrhythmias
Systolic
Diastolic
Myocardial infarction (macroangiopathy)
Heart failure
Sudden death
Cardiac emboli

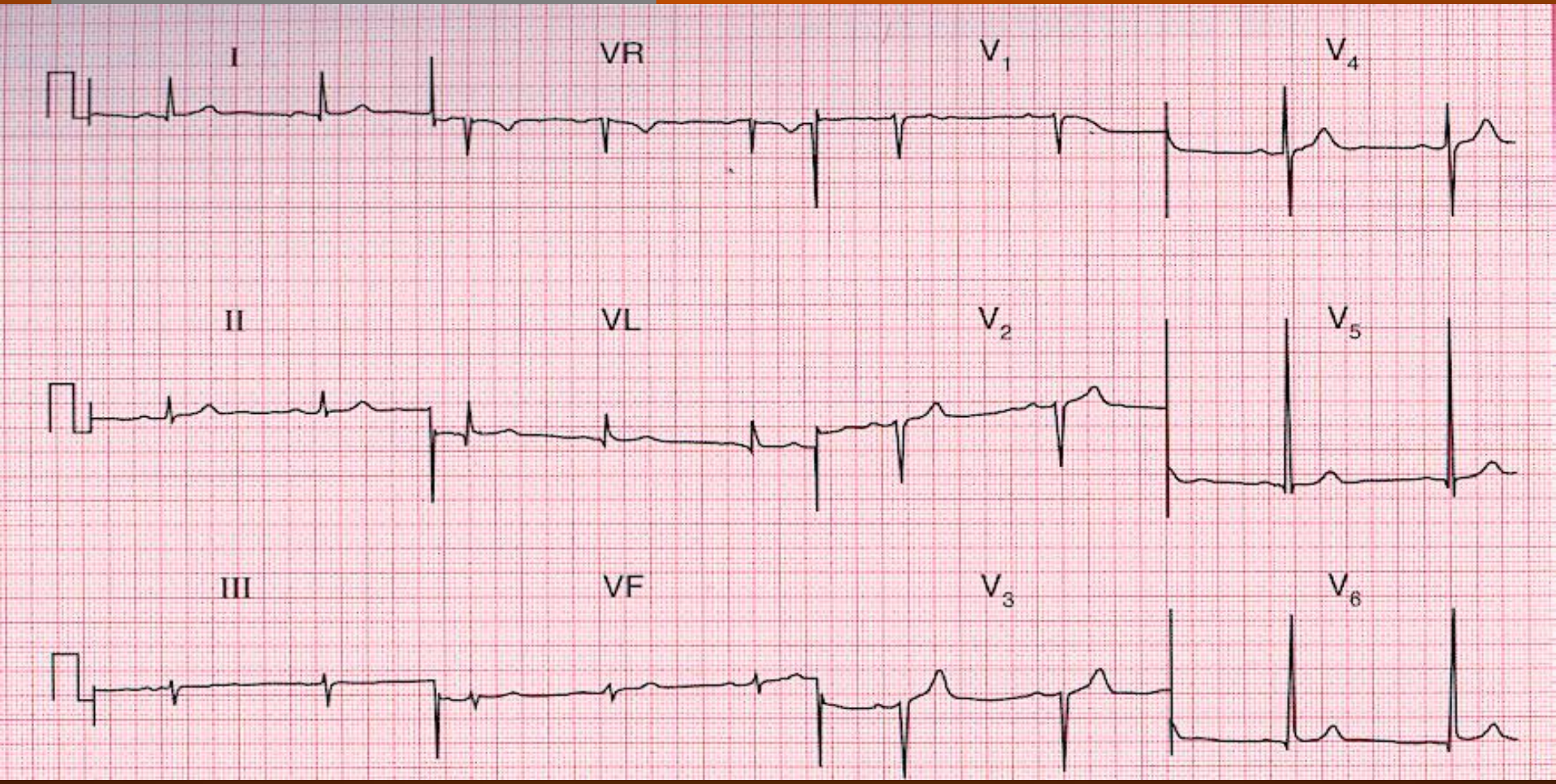
BP VALUES ACC/AHA 2018

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

X RAY CORRELATION

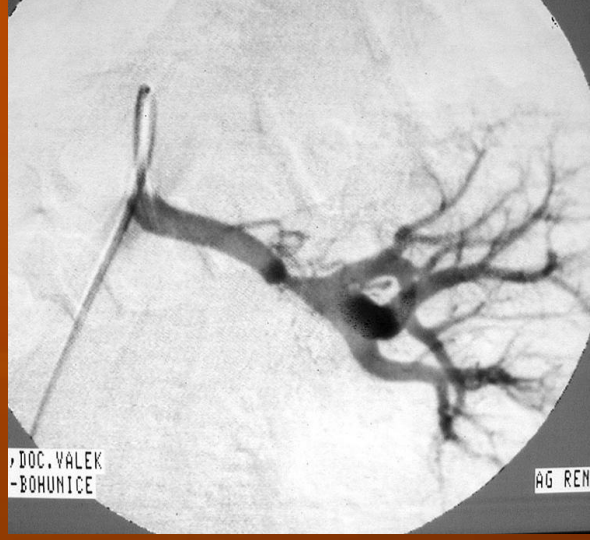


ECG CORRELATION



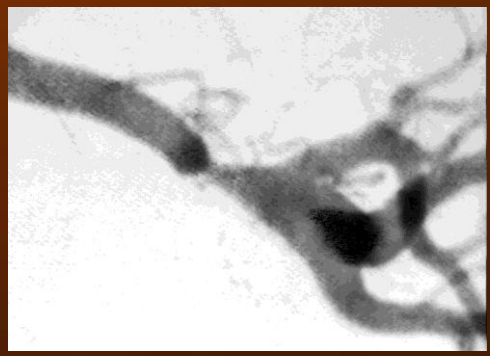
- McPhie - SVmax + RVmax over 40 mm
- Sokolov/Lyon - SV1 + RV5,6 over 35 mm

ETIOLOGY



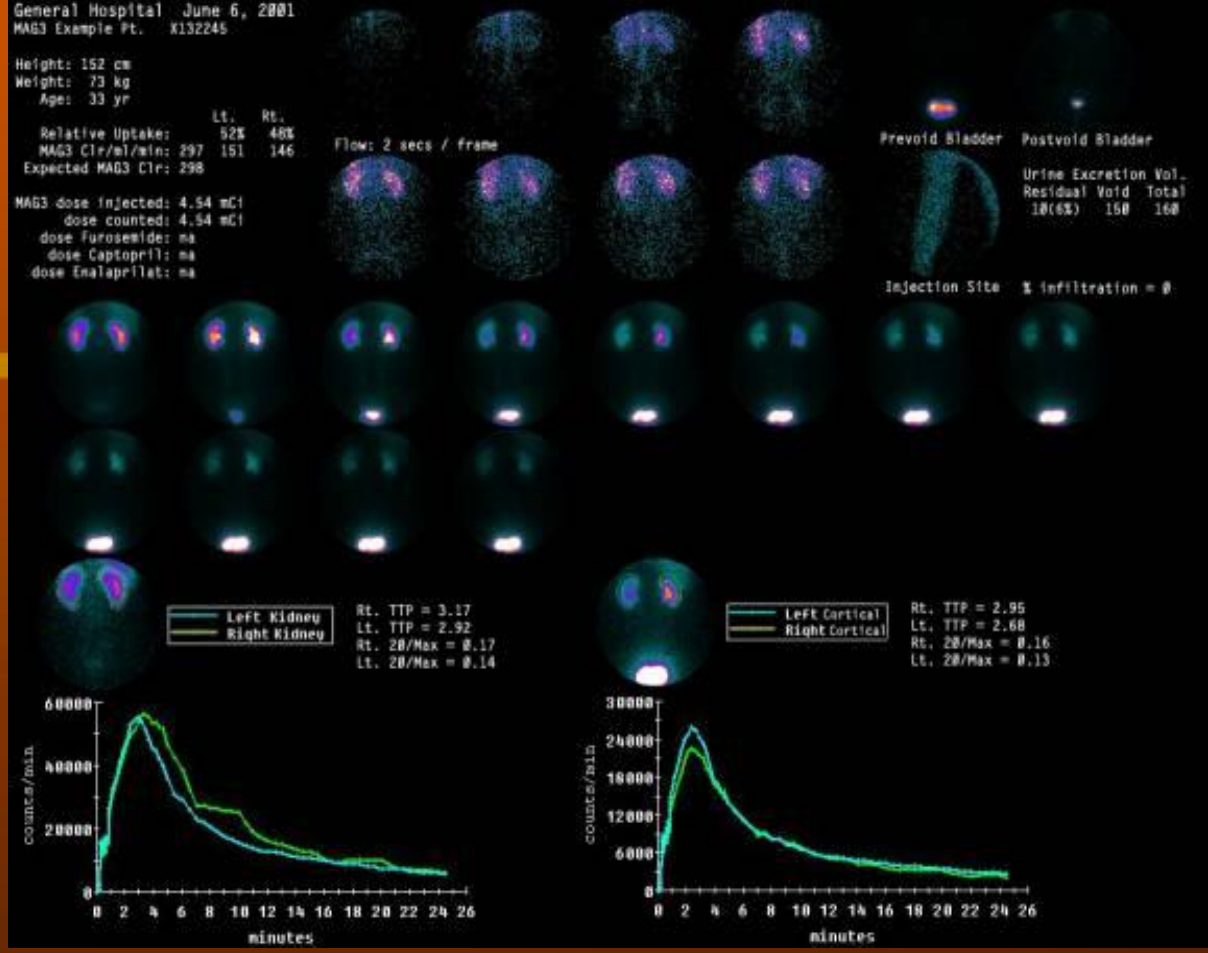
- essential HT(primary, idiopathic)
- secondary HT (10%)

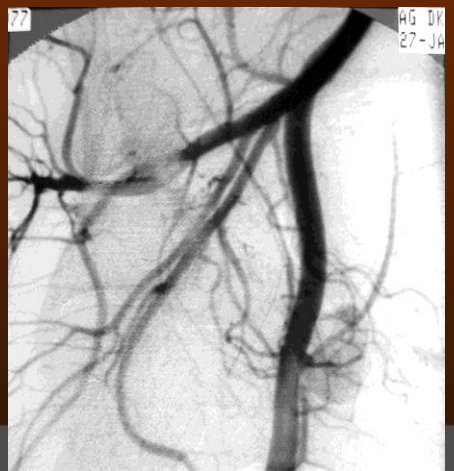
- renal (acute, chronic dissease)
- renovascular
- endocrine (hyperA, hyperK, feochromocytom, acromegaly, hyperparathyreozis)



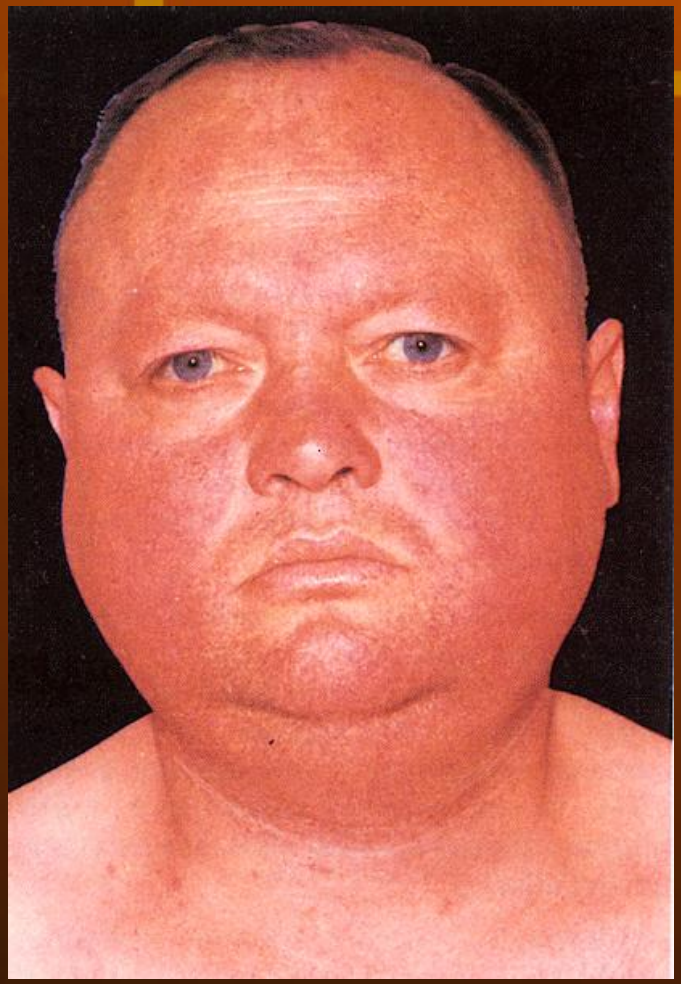
- neurogenic (Tu, injuries)
- coarctation ao
- sleeping apnoe
- iatrogenic (contraceptives, steroids, cocain, liquorice)

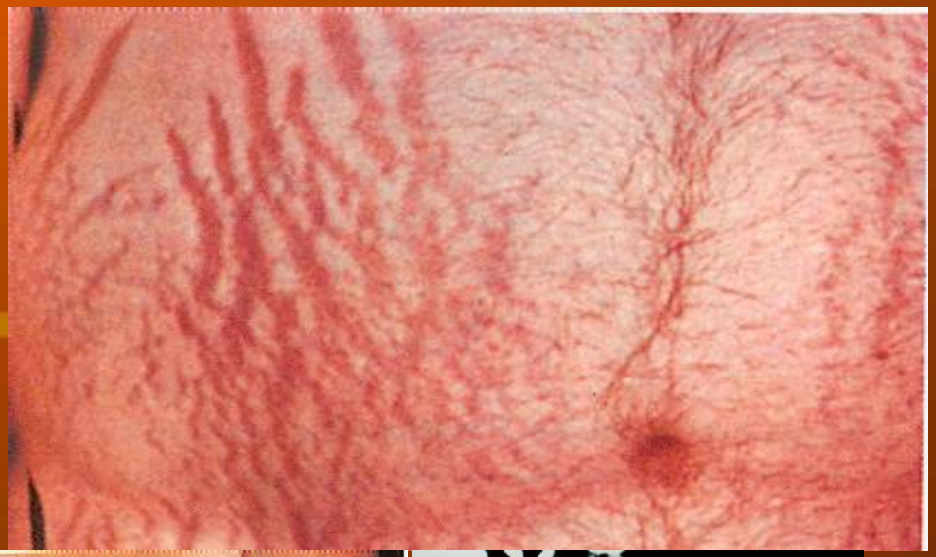
ETIOLOGY

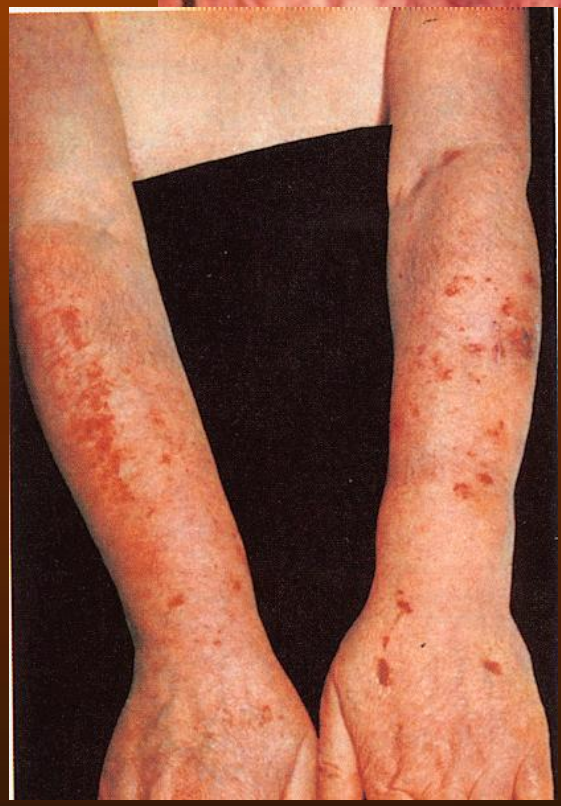

General Hospital June 6, 2001
MAG3 Example Pt. X132245
Height: 152 cm
Weight: 73 kg
Age: 33 yr
Lt. Rt.
Relative Uptake: 52% 48%
MAG3 Clr/ml/min: 297 151 146
Expected MAG3 Clr: 298
MAG3 dose injected: 4.54 mCi
dose counted: 4.54 mCi
dose Furosemide: na
dose Captopril: na
dose Enalaprilat: na
Flow: 2 secs / frame
Prevoid Bladder
Postvoid Bladder
Urine Excretion Vol.
Residual Void Total
10(6%) 150 160
Injection Site % infiltration = 0
Left Kidney
Right Kidney
Rt. TTP = 3.17
Lt. TTP = 2.92
Rt. 20/Max = 0.17
Lt. 20/Max = 0.14
counts/min
minutes
Left Cortical
Right Cortical
Rt. TTP = 2.95
Lt. TTP = 2.68
Rt. 20/Max = 0.16
Lt. 20/Max = 0.13
counts/min
minutes

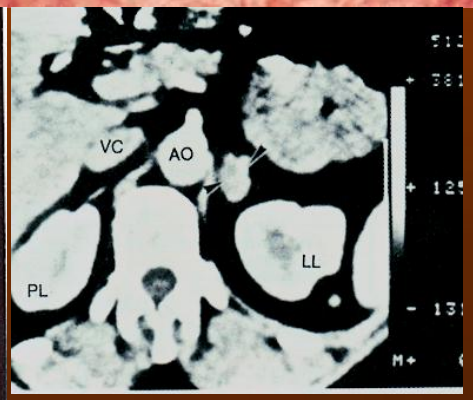


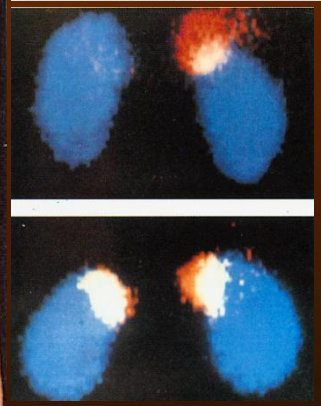
MORBUS CUSHING





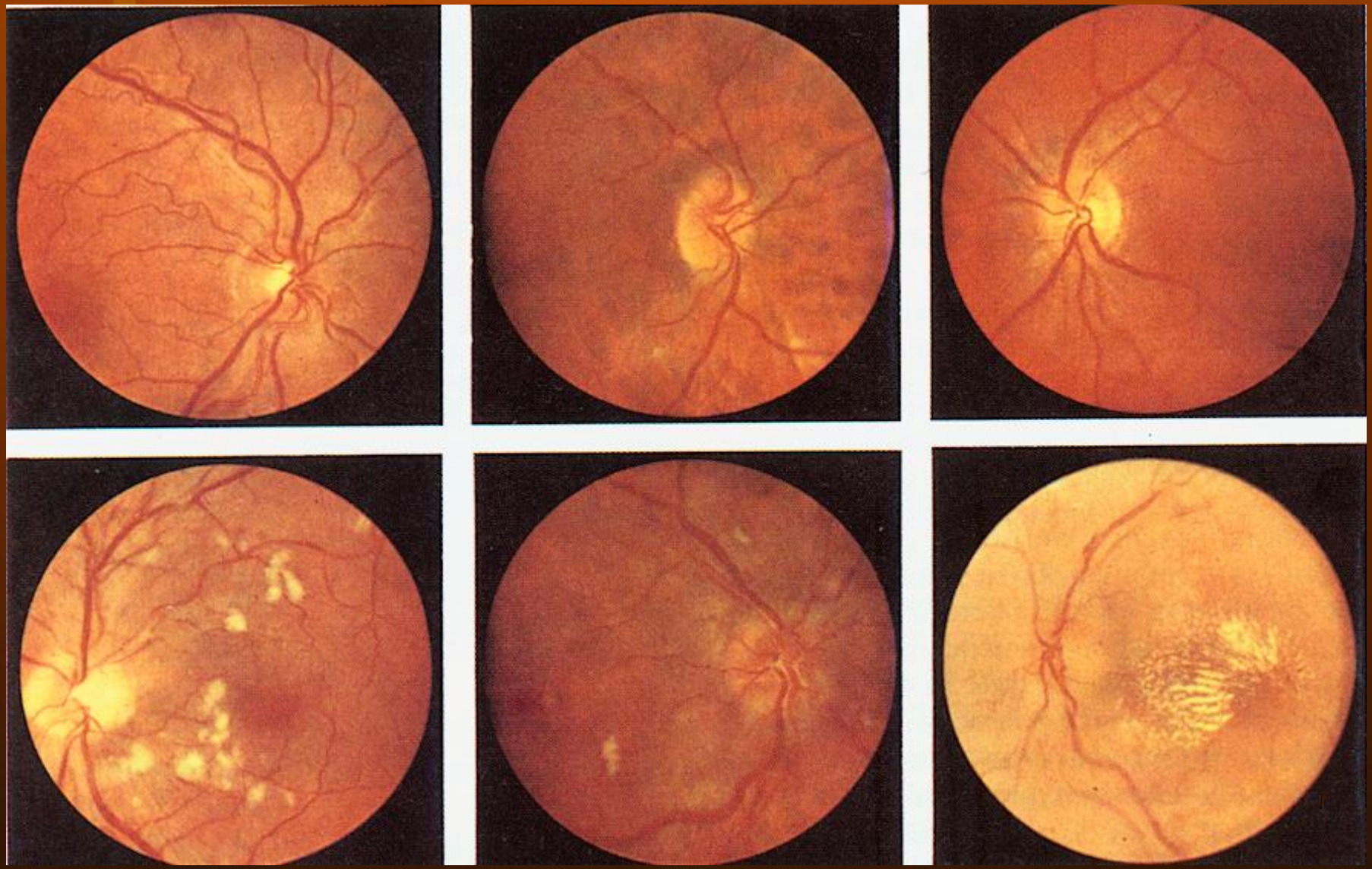




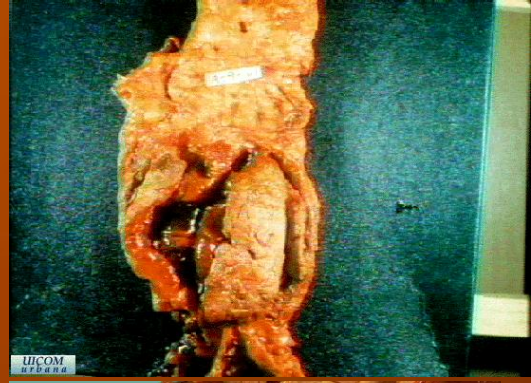


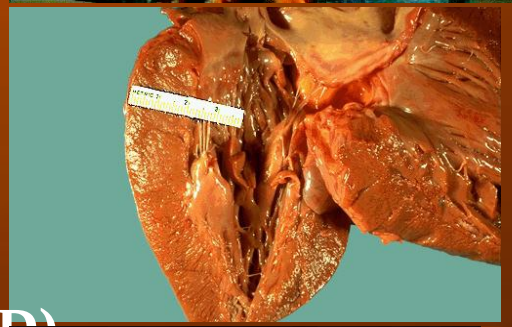
FUNDUSCOPIC CORRELATION

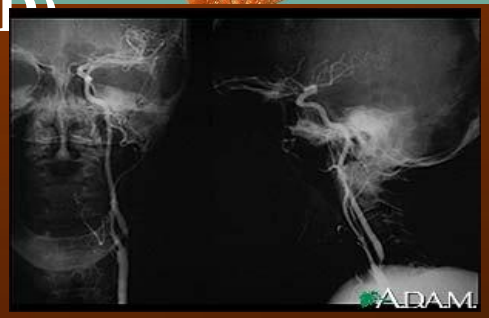
Arteriosclerotic and hypertensive retinopathy



HT IMPACTS







1. **Hypertensive**

- **Left ventricular hypertrophy**
- **Heart failure**
- **Intracerebral bleeding, ischemic stroke**
- **Renal insuficiency (Na retention, MAU, CKD)**
- **Hypertonic retinopathy**
- **Hypertonic crisis with encephalopathy**
- **Aneurysma dissecans**

2. **Atherosclerotic**

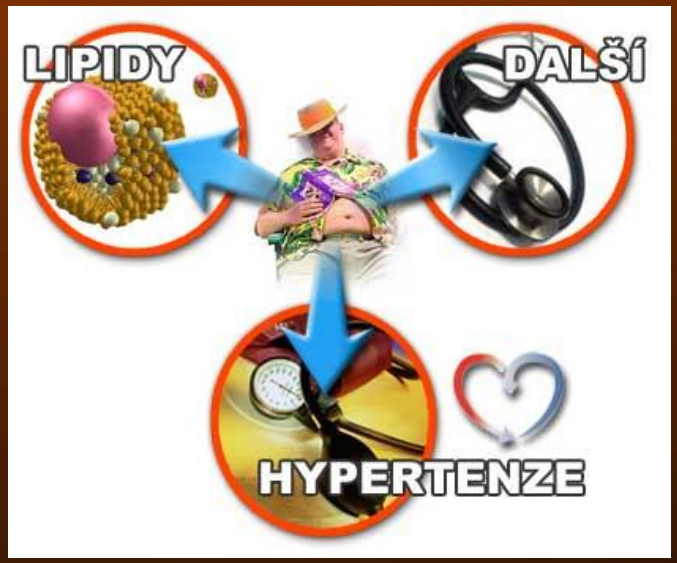
- **CAD (AP, IM, SCD)**
- **CVD (stroke, TIA, aneurysm, vascular malf.)**
- **Aortic aneurysm**
- **PAD, CLTI – chron. limb threateing, CLI – critical**

HYPERTENSION + METABOLIC SYNDROM

•**Reaven´s sy (1996) : hypertension in pt with obesity, hyperglycemia (insulin resistance)**

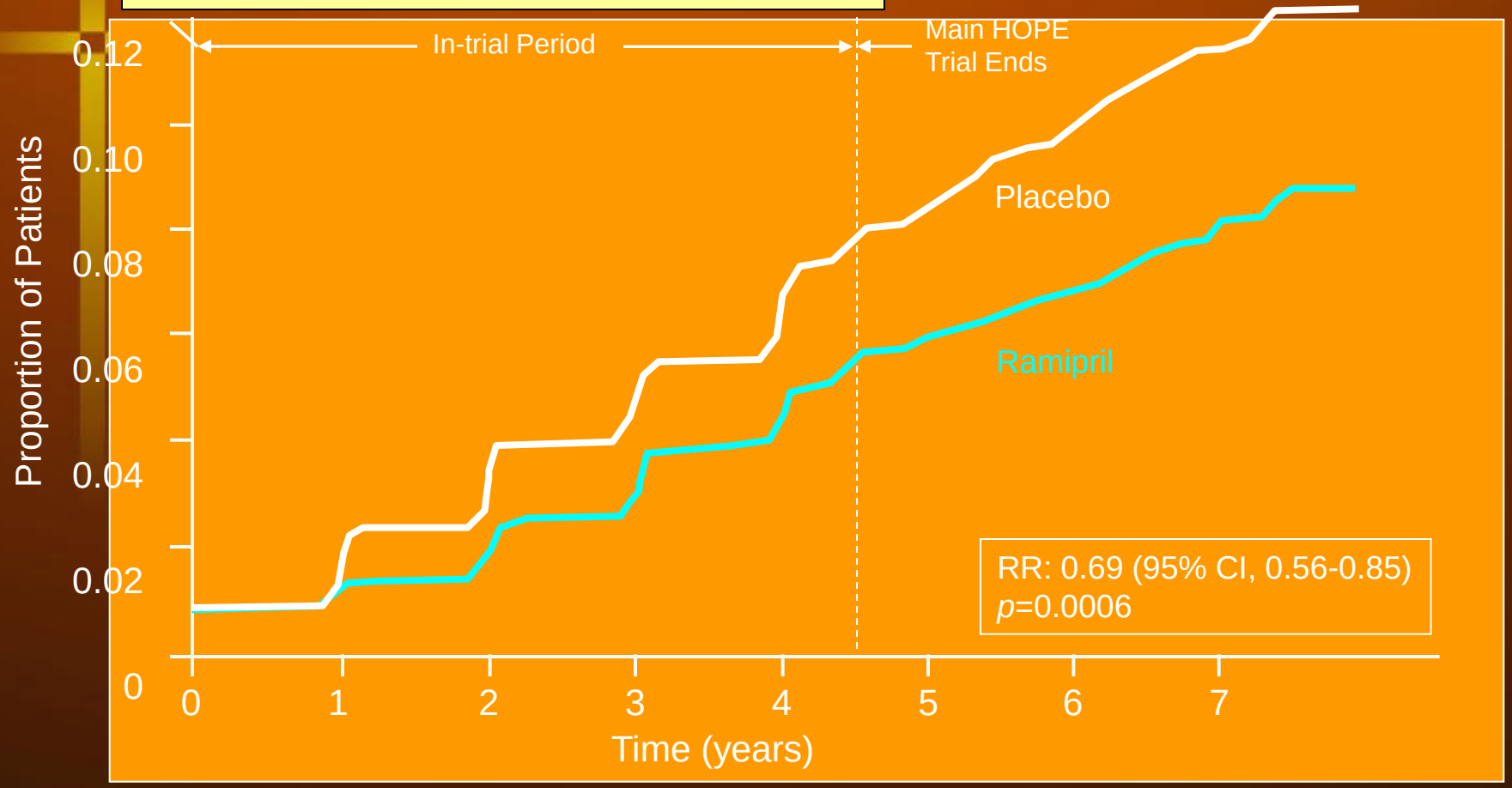
ATP III (Adult Treatment Panel) 2001 - 3 or more from:

- **obezity**
- **TG ↑**
- **HDL ↓**
- **hypertension**
- **hyperglycemia**



Hope

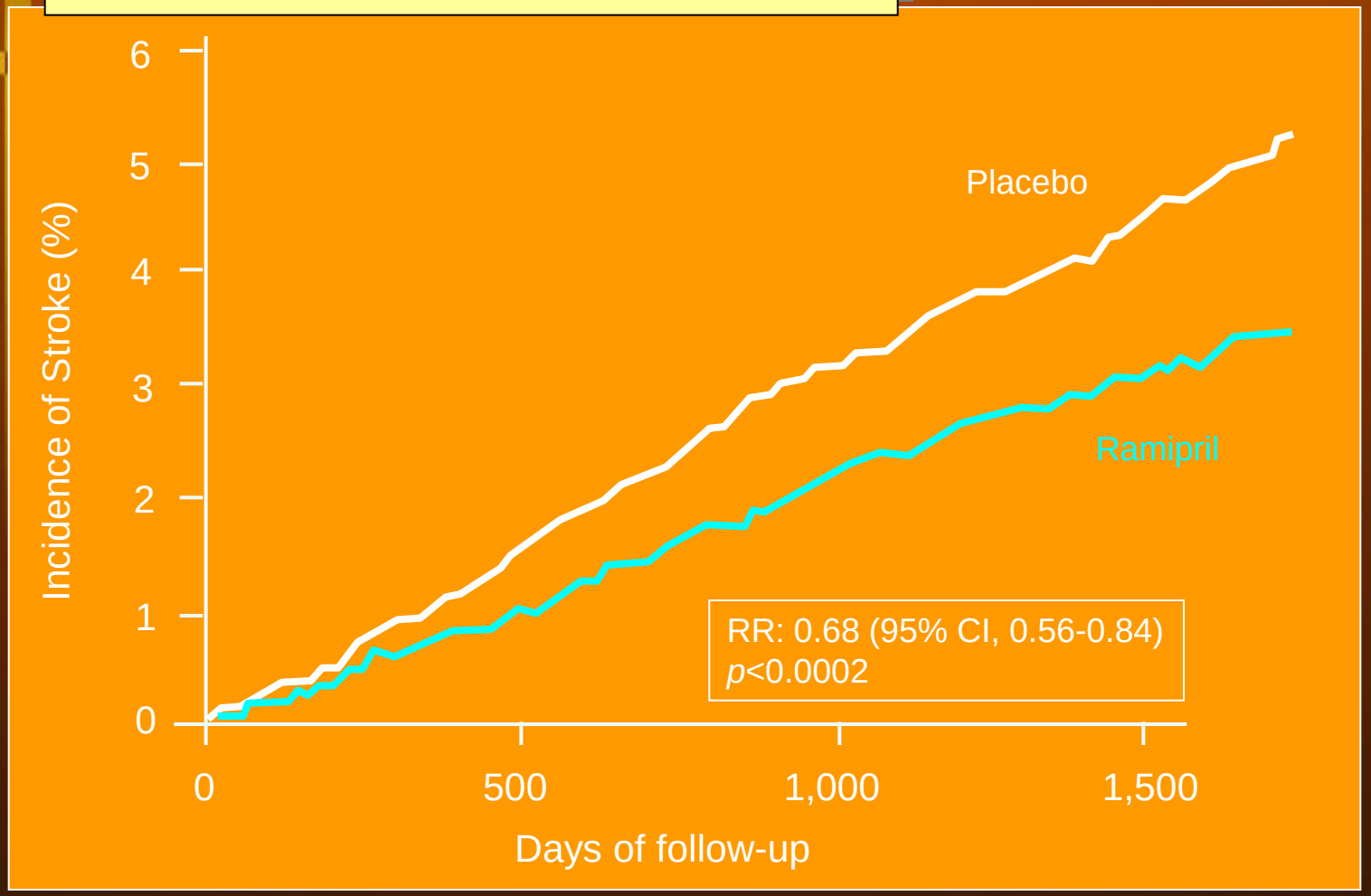
DEVELOPMENT OF DM



The HOPE and HOPE-TOO Investigators. Circulation 2005; 112:1339-46.

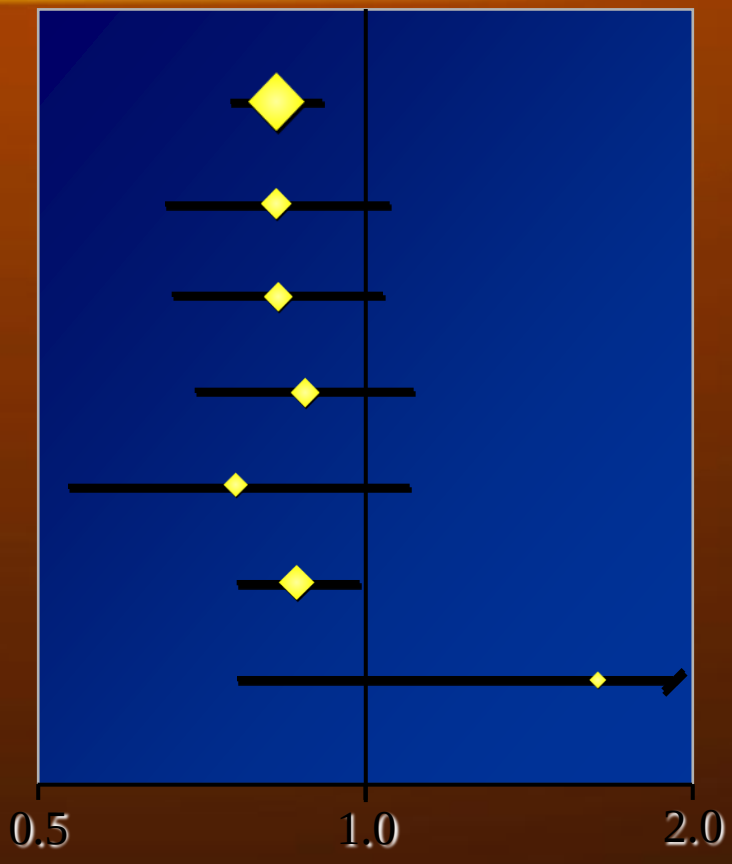
Hope

INCIDENCE OF STROKE



Bosch J, et al. BMJ 2002; 324(7339):699-702.

ACCOMPLISH - Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension

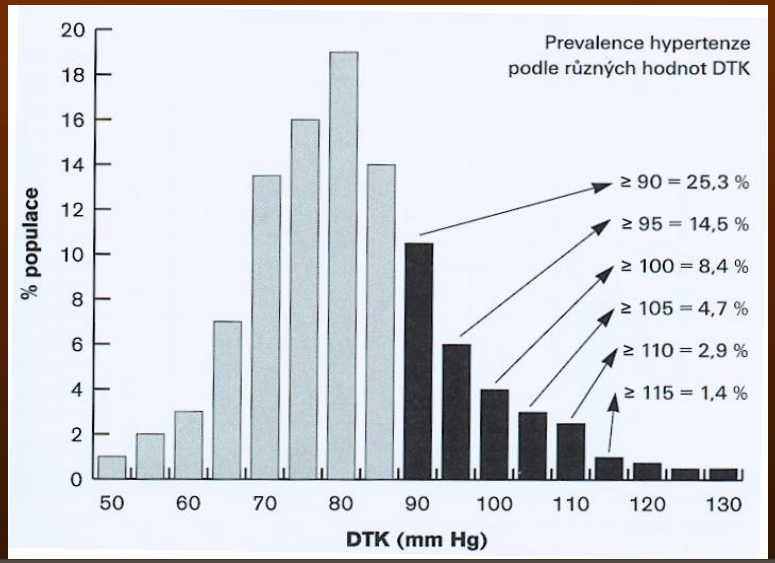


Jamerson K et al. A Engl J Med 2008;359:2417-28

PROGNOSTIC FACTORS HT

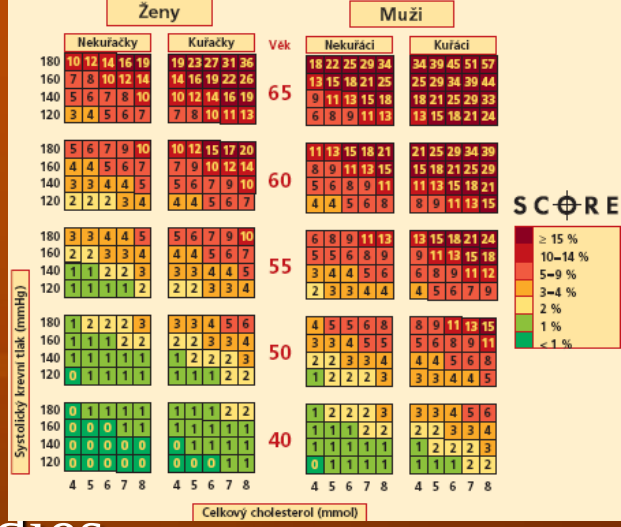
- Estimation of risk of fatal CV events (SCORE)
- Subclinical organ damage (SOP)
- Clinical organ damage (POP)

M. hypertonicus gr. I dle WHO



Hypertenze se SOP

SCORE



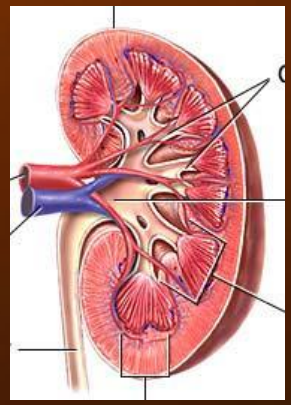
- Risk prediction of *fatal CV events*
- Based on 12 overall population studies

205 178 pts; 2,7 mil. person/years follow-up

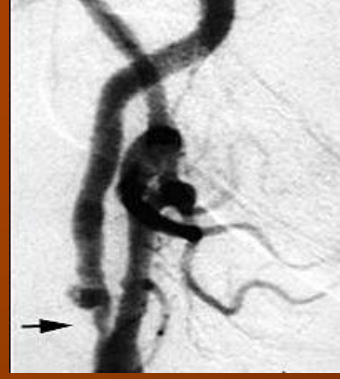
- Cholesterol level */HDL cholesterol*
- Projected *risk multiplied 2x for male DM pts, multiplied 4x for female DM pts*
- High risk ≥ 5%
- SCORECARD

SOP – SUBCLINICAL ORGAN DAMAGE

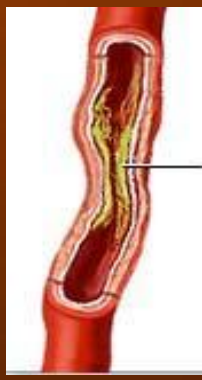
- LV hypertrophy
  - EKG: Sokolow-Lyons > 38 mm
  - Cornell > 2 440 mm x ms
  - ECHO: LVMI ≥ 125, F ≥ 110 g/m^2
- USG thickening of the arteriol wall
  (thickening of the carotid wall ≥ 0,9 mm or plaque)
- Moderate elevation serum creatinine level
  - M 115-133, F 107-124 μmol/l
- Lowering GF bellow 60ml/min
- Microalbuminuria 30 – 300 mg/24h
  - ratio albumin/creatinine M ≥ 2,5 F ≥ 3,5 mg/mmol

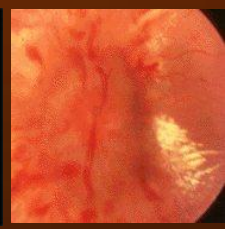


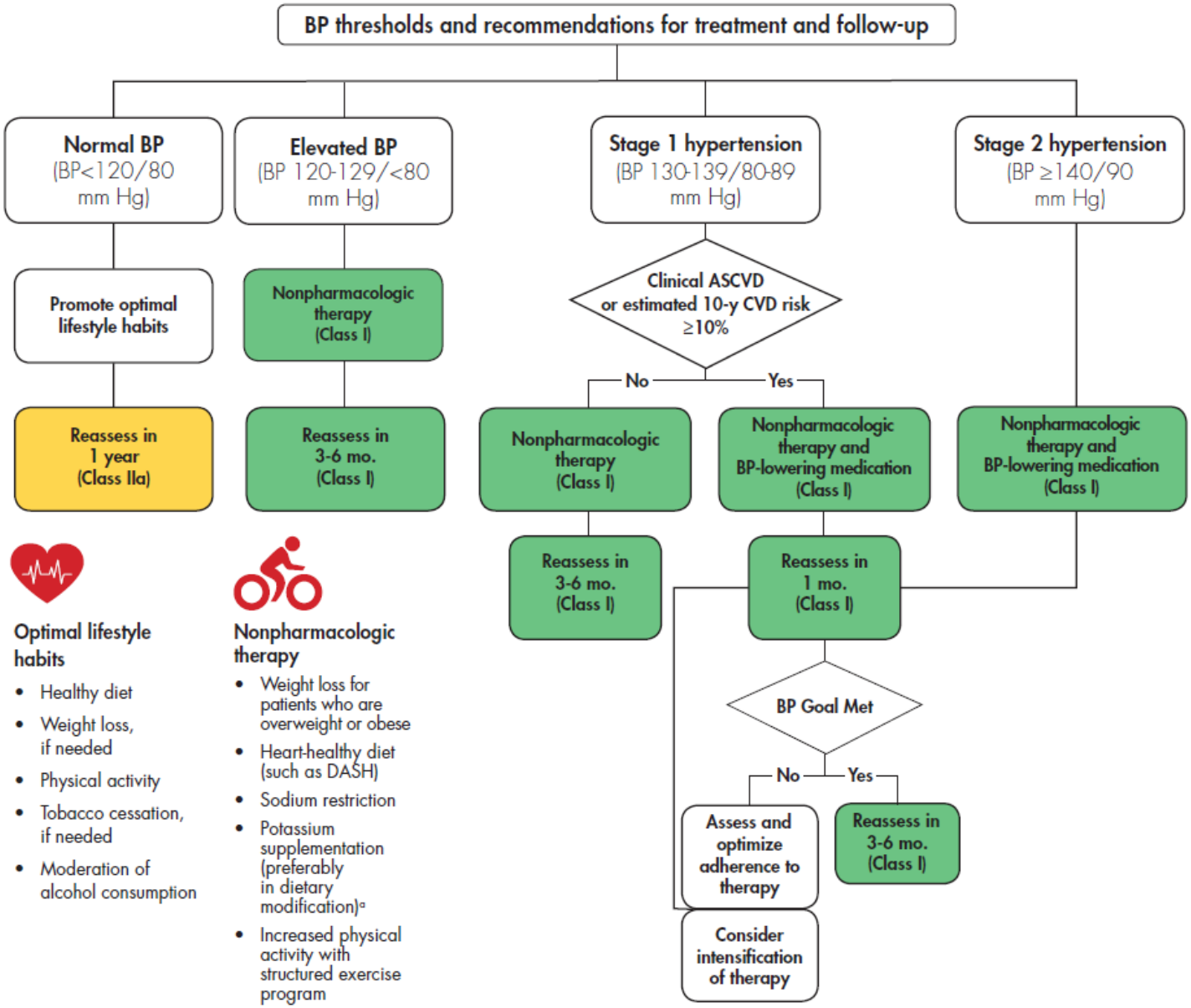
POP – CLINICAL ORGAN DAMAGE



- CVD:
  ischemic stroke, cerebral bleeding; TIA
- Structural heart disease:
  CAD post MI, AP, revascularization, CHF
- Renal disease:
  diabetic nefropathy
  renal function decrease
    S creatinine: M > 133, F > 124 μmol/l
    proteinuria: > 300 mg/24 h
- PAD, CLTI, CLI
- Advanced retinopathy:
  hemorrhage or exsudate, papilledema






BP thresholds and recommendations for treatment and follow-up
Normal BP (BP<120/80 mm Hg)
Elevated BP (BP 120-129/<80 mm Hg)
Stage 1 hypertension (BP 130-139/80-89 mm Hg)
Stage 2 hypertension (BP ≥140/90 mm Hg)
Promote optimal lifestyle habits
Nonpharmacologic therapy (Class I)
Clinical ASCVD or estimated 10-y CVD risk ≥10%
No
Yes
Reassess in 1 year (Class IIa)
Reassess in 3-6 mo. (Class I)
Nonpharmacologic therapy (Class I)
Nonpharmacologic therapy and BP-lowering medication (Class I)
Nonpharmacologic therapy and BP-lowering medication (Class I)
Reassess in 3-6 mo. (Class I)
Reassess in 1 mo. (Class I)
BP Goal Met
No
Yes
Assess and optimize adherence to therapy
Reassess in 3-6 mo. (Class I)
Consider intensification of therapy
Optimal lifestyle habits
Healthy diet
Weight loss, if needed
Physical activity
Tobacco cessation, if needed
Moderation of alcohol consumption
Nonpharmacologic therapy
Weight loss for patients who are overweight or obese
Heart-healthy diet (such as DASH)
Sodium restriction
Potassium supplementation (preferably in dietary modification)[a]
Increased physical activity with structured exercise program
Limitation of alcohol to 1 (women) or 2 (men) standard drinks per day[b]
[a] Unless contraindicated by the presence of chronic kidney disease or use of drugs that reduce potassium excretion.
[b] In the United States, one standard drink is equivalent to 12 oz of regular beer (usually about 5% alcohol), 5 oz of wine (usually about 12% alcohol), or 1.5 oz of distilled spirits (usually about 40% alcohol).

A 10 mm Hg reduction in systolic blood pressure can significantly reduce risk of several conditions:

Antihypertensive Medication

The BP threshold for antihypertensive medication should be determined on the basis of the average BP levels and CVD risk.

BP Threshold (mm Hg)	Patient Scenario
≥130/80	ASCVD risk of 10% or higher **OR** Clinical CVD
≥140/90	ASCVD risk less than 10%

Four classes of oral antihypertensive drugs are recommended as first-line agents for the treatment of hypertension.

- Thiazide or thiazide-type diuretics
- Angiotensin-converting enzyme (ACE) inhibitors
- Angiotensin receptor blockers (ARBs)
- Calcium-channel blockers (dihydropyridines and nondihydropyridines)

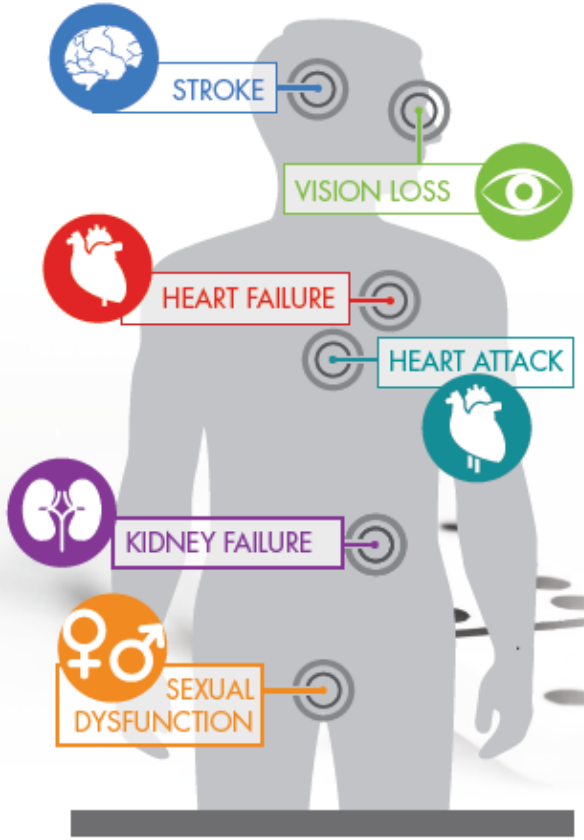
Six general classes of oral antihypertensive drugs are recommended as second-line agents

- Diuretics (loop, potassium sparing and aldosterone antagonists)
- Beta-blockers (cardioselective, and vasodilatory, noncardioselective, intrinsic sympathomimetric activity and combined alpha- and beta-receptor)
- Direct renin inhibitor
- Alpha-1 blockers
- Central alpha$_2$-agonist and other centrally acting drugs
- Direct vasodilators

Oral Antihypertensive Drugs

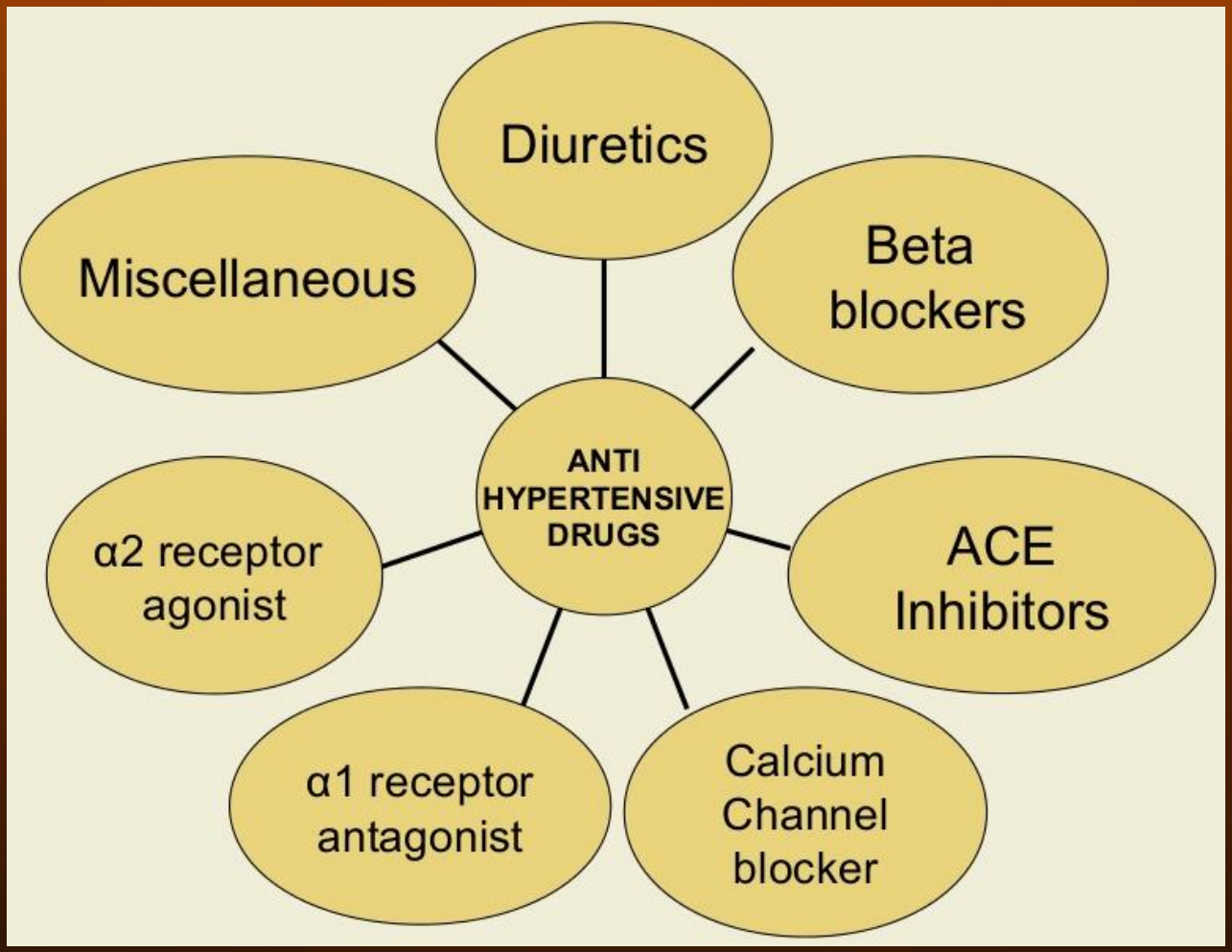
Simultaneous use of an ACE inhibitor, ARB and/or renin inhibitor is potentially harmful and is not recommended for the treatment of adults with hypertension.

High blood pressure is often the first domino in a chain or "domino effect" leading to devastating consequences, like:



Hypertension, the "silent killer," is associated with a variety of life-threatening diseases or conditions.

ANTIHYPERTENSIVE DRUGS



THIAZIDE DIURETICS

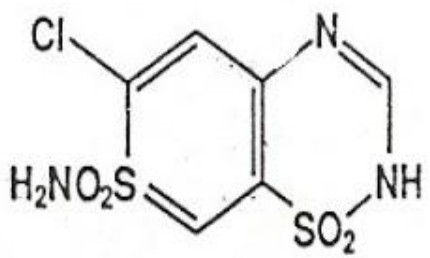
Sodium, water retention

Blood volume

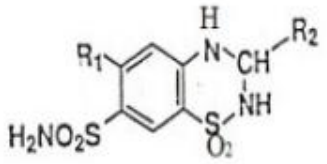
Cardiac output

Peripheral resistance

Decrease in blood pressure



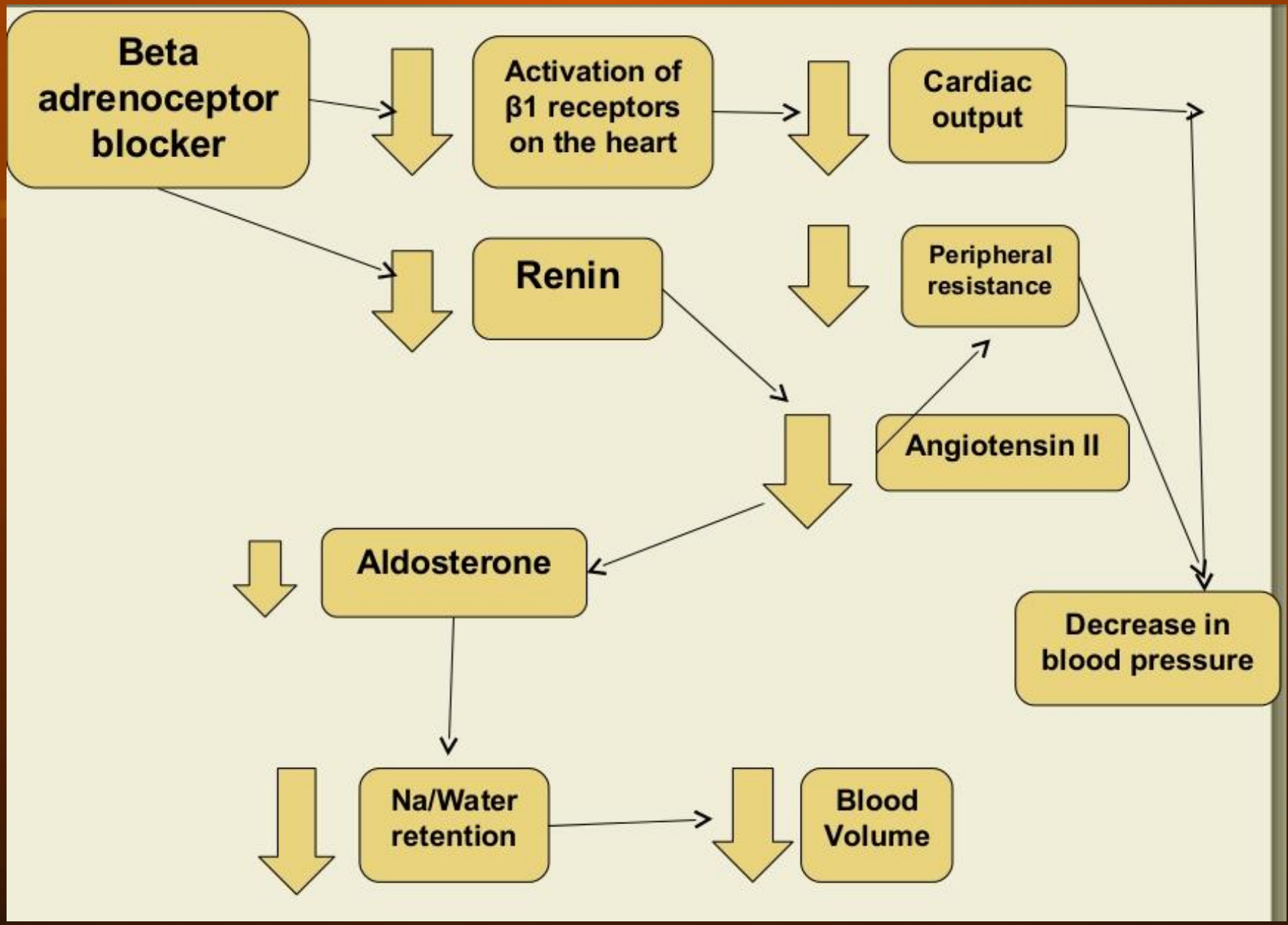
Chlorothiazide



hydrochlorothiazide (R_1 :Cl;R2=H)

bendroflumethiazide (R_1=CF_3;R_2=CH_2-C$_6$H$_5$)

trichlormethazide (R1=Cl;R2=$CHCl_2$)


Beta adrenoceptor blocker
Activation of β1 receptors on the heart
Cardiac output
Renin
Peripheral resistance
Angiotensin II
Aldosterone
Decrease in blood pressure
Na/Water retention
Blood Volume

Anti-Hypertensive Drugs

Prevention is always better than cure

Classification- KD Tripathi

1. Diuretics
2. ACE Inhibitor
3. Angiotensin Blocker
4. Calcium Channel Blocker
5. Beta Blocker
6. Beta+Alfa Blocker
7. Alfa Blocker
8. Central Sympatholytics
9. Vasodilator

Examples of above listed Class

- Thiazide- Hydrochlorothiazide, Chlorthiazide, Indapamide
  High Ceiling- Furosemide
  K+ Sparing- Spironelactone, Amiloride
- Captopril, Enalapril, Linsopril, Perindopril, Ramipril, Fosinopril etc.
- Losartan, Candesartan, Irbesartan, Valsartan, Telmisartan
- Verapamil, Diltiazem, Nifedipin, Felodipine, Amlodipine, Lacidipine
- Propranolol, Metoprolol, Atenolol
- Labetalol, Carvedilol
- Prazocin, Terazocin, Doxazosin, Phentolamine, Phenoxybenzamine
- Clonidine, Methyldopa
- Arteriolar- Hydralazine, Minoxidil, Diazoxide
  Arteriolar+ Venous- Sodium Nitropruside

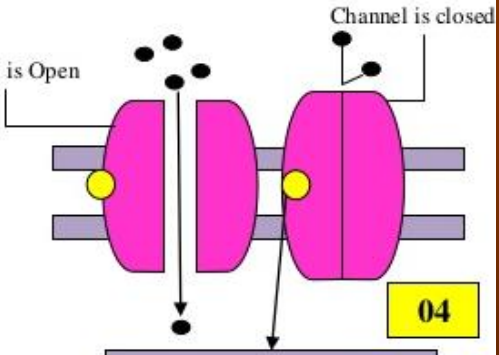
Thiazide Diuretics

Increase Water & Sodium Excretion

- **Short Term Effect**
  - **Decrease** Blood Volum
  - **Decrease** cardiac output
- **Long Term Effect**
  - Channel is Open
  - Sodium content in cell
  - **Decrease** Muscles sensitivity to vasopresser
  - **Decrease** Peripheral Resistance

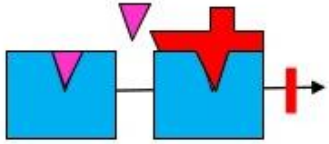
Decrease Blood Pressure

01



04

Calcium channel Blocker



Increase
Heart rate
Contractility
Conduction

Beta Receptor Blocker

05

Angiotensinogen

Renin from Kidney

Angiotensin I (Inactive)

ACE Inhibitors

Angiotensin II

- Decrease output of Symp. Nervous system
- Increase vasodilatation of vascular muscle
- Aldosterone Production → Decrease sod. And water retention

Blood Pressure

Angiotensin Blockers

02 **03**

ll diagrams and design- Solution-Pharmacy

www.facebook.com/pharmavideo/

HYPERTENSION + DM

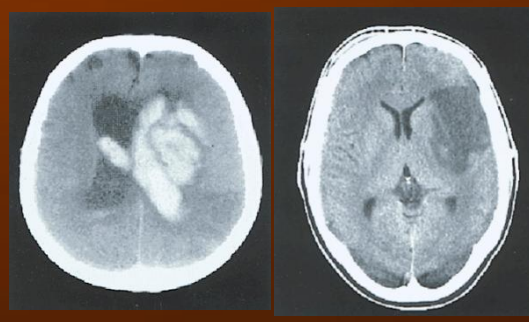
- 2-3x higher prevalence of HT in DM population
- comparable total risk of HT + DM and HT +MI populations
- CV risk estimation male 2x, female 4x higher with DM
- treated HT - positive effect to macroangiopathy

HYPERTENSION + DM

- Nonpharmacological therapy ↓ intake Na, weight
- Target BP < 130/80 mmHg
- RAS blockade – ACEI, ARB prefered
- Almoust combined therapy
- MAU is indication for RAS blockator
- Intervention of all risk factors

ANTIHYPERTENSIVE DRUGS /STROKE

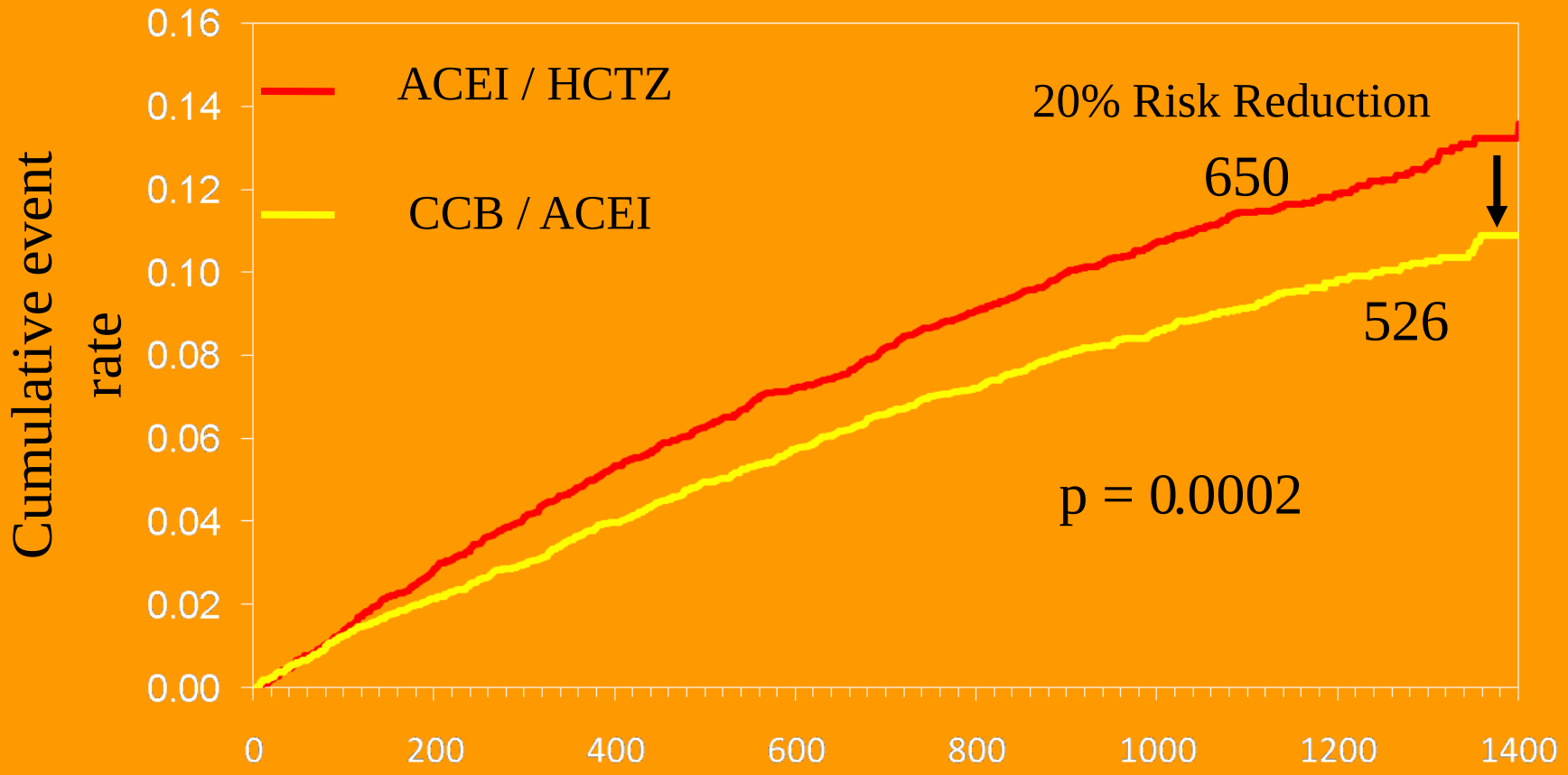
- benefit for pts with normal BP and hypertension
- profit without consideration to type of stroke
- sex and age
- time interval from stroke
- we prefer monotherapy ACEI/ARB
- CAB better in older pts



(PATS, PROGRESS, EUROPA, Syst-Eur, EWPHE, MRC, SHEP…)

ACCOMPLISH - Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension

11.000 hypertonics with CV risk or CKD. - amlodipin 10, benazepril 40 mg



HR (95% CI): 0.80 (0.72, 0.90)

Jamerson K et al. A Engl J Med 2008;359:2417-28

ASCOT

Anglo-Scandinavian Cardiac Outcomes Trial

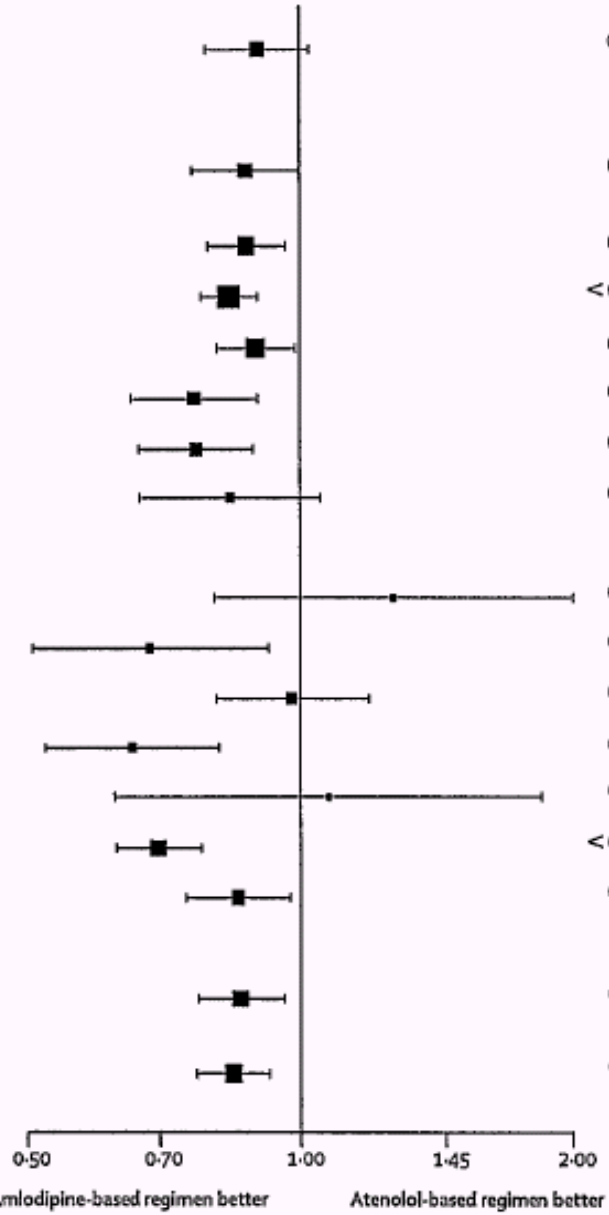
- 19.257 pts. hypertension + 3 risk factors
- 5year follow-up

	Calcium-channel blocker-based regimen	β blocker-based regimen
Step 1	Amlodipine 5 mg	Atenolol 50 mg
Step 2	Amlodipine 10 mg	Atenolol 100 mg
Step 3	Amlodipine 10 mg+perindopril 4 mg	Atenolol 100 mg+bendroflumethiazide 1·25 mg +potassium
Step 4	Amlodipine 10 mg+perindopril 8 mg (2×4 mg)	Atenolol 100 mg+bendroflumethiazide 2·5 mg +potassium
Step 5	Amlodipine 10 mg+perindopril 8 mg (2×4 mg) +doxazosin gastrointestinal transport system 4 mg	Atenolol 100 mg+bendroflumethiazide 2·5 mg +potassium+doxazosin gastrointestinal transport system 4 mg
Step 6	Amlodipine 10 mg+perindopril 8 mg (2×4 mg) +doxazosin gastrointestinal transport system 8 mg	Atenolol 100 mg+bendroflumethiazide 2·5 mg +potassium+doxazosin gastrointestinal transport system 8 mg

Further treatment to achieve blood-pressure goal outlined at http://www.ascotstudy.org. All drugs given orally.

Table 1: Treatment algorithm

	Amlodipine-based regimen (n=9639)		Atenolol-based regimen (n=9618)			
	Number (%)	Rate per 1000	Number (%)	Rate per 1000	Unadjusted HR (95% CI)	p
Primary endpoints						
Non-fatal myocardial infarction (including silent)+fatal CHD	429 (5%)	8·2	474 (5%)	9·1	0·90 (0·79–1·02)	0·1052
Secondary endpoints						
Non-fatal myocardial infarction (excluding silent)+fatal CHD	390 (4%)	7·4	444 (5%)	8·5	0·87 (0·76–1·00)	0·0458
Total coronary endpoint	753 (8%)	14·6	852 (9%)	16·8	0·87 (0·79–0·96)	0·0070
Total cardiovascular events and procedures	1362 (14%)	27·4	1602 (17%)	32·8	0·84 (0·78–0·90)	<0·0001
All-cause mortality	738 (8%)	13·9	820 (9%)	15·5	0·89 (0·81–0·99)	0·0247
Cardiovascular mortality	263 (3%)	4·9	342 (4%)	6·5	0·76 (0·65–0·90)	0·0010
Fatal and non-fatal stroke	327 (3%)	6·2	422 (4%)	8·1	0·77 (0·66–0·89)	0·0003
Fatal and non-fatal heart failure	134 (1%)	2·5	159 (2%)	3·0	0·84 (0·66–1·05)	0·1257
Tertiary endpoints						
Silent myocardial infarction	42 (0·4%)	0·8	33 (0·3%)	0·6	1·27 (0·80–2·00)	0·3089
Unstable angina	73 (1%)	1·4	106 (1%)	2·0	0·68 (0·51–0·92)	0·0115
Chronic stable angina	205 (2%)	3·9	208 (2%)	4·0	0·98 (0·81–1·19)	0·8323
Peripheral arterial disease	133 (1%)	2·5	202 (2%)	3·9	0·65 (0·52–0·81)	0·0001
Life-threatening arrhythmias	27 (0·3%)	0·5	25 (0·3%)	0·5	1·07 (0·62–1·85)	0·8009
Development of diabetes mellitus	567 (6%)	11·0	799 (8%)	15·9	0·70 (0·63–0·78)	<0·0001
Development of renal impairment	403 (4%)	7·7	469 (5%)	9·1	0·85 (0·75–0·97)	0·0187
Post-hoc endpoints						
Primary endpoint+coronary revascularisation procedures	596 (6%)	11·5	688 (7%)	13·4	0·86 (0·77–0·96)	0·0058
Cardiovasular death+myocardial infarction+stroke	796 (8%)	15·4	937 (10%)	18·4	0·84 (0·76–0·92)	0·0003



CKD

Nephrol Dial Transplant (2001) 16: 2158–2165

Nephrology Dialysis Transplantation

Original Article

The effects of an ACE inhibitor and a calcium antagonist on the progression of renal disease: the Nephros Study

Hans Herlitz[1], Kevin Harris[2], Teut Risler[3], Geoffrey Boner[4], Jacques Bernheim[5], Jacques Chanard[6] and Mattias Aurell[1]

[1]Mattias Aurell and Hans Herlitz, Department of Nephrology, Sahlgrenska Hospital, Göteborg University, Sweden, [2]Kevin Harris, Department of Nephrology, Leicester General Hospital, University of Leicester, UK, [3]Teut Risler, Sektion Nieren- und Hochdruckkrankheiten, Universitätsklinikum Tübingen, Germany, [4]Geoffrey Boner, Institute of Hypertension and Kidney Diseases, Rabin Medical Center, Tel-Aviv University, Israel, [5]Jacques Bernheim, Department of Nephrology and Hypertension, Meir General Hospital, Sapir Medical Center, Israel and [6]Jacques Chanard, Service de Nephrologie, Dialyse, Hypertension et Transplantation Rénale, Reims, France

CKD

2160

The NEPHROS Study

A progression study in renal disease.

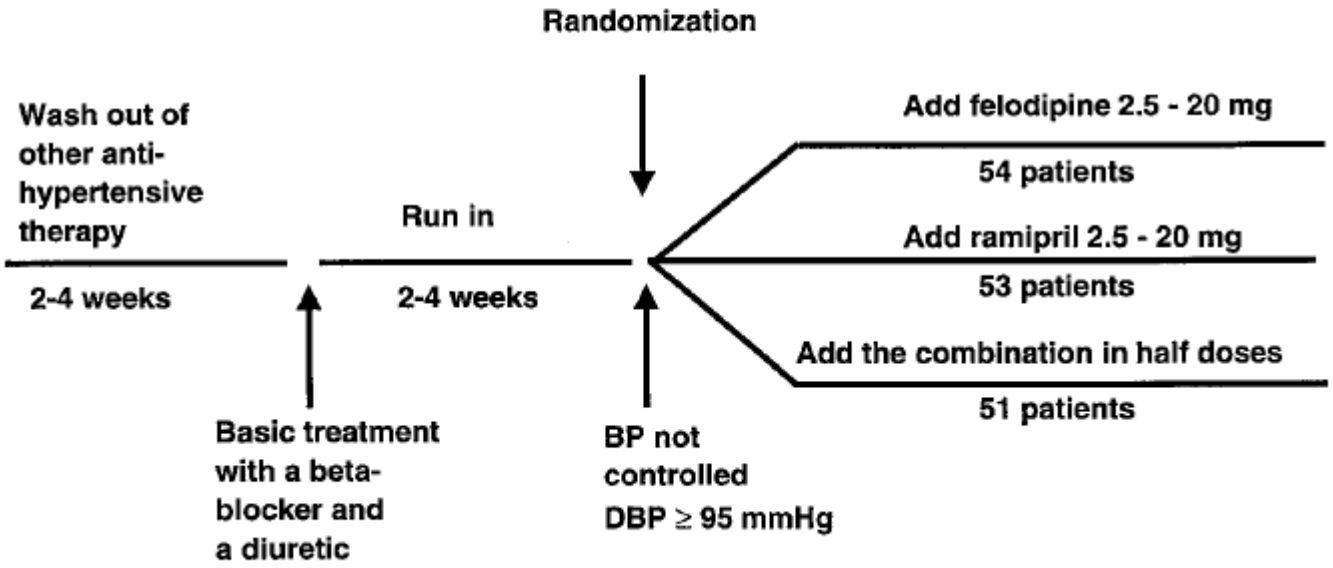


Fig. 1. Flow chart of the study.

CKD

Table 4. The effect of the combination of ramipril and felodipine ER and each drug alone on SBP and DBP

	Ramipril + felodipine $n = 51$	Ramipril $n = 53$	Felodipine $n = 54$
Change in SBP (mmHg)	−19.0 (−34.7 to 10.8)***	−14.3 (−24.2 to 4.8)***	−13.5 (−29 to −7.5)***
Change in DBP (mmHg)	−14.5 (−21.7 to 9.7)***	−15.0 (−20.7 to 9.7)***	−13.3 (−19.3 to −10.9)***
Attained SBP (mmHg)	134 (127 to 144)#	139 (130 to 153)	139 (129 to 152)
Attained DBP (mmHg)	85.2 (79.9 to 88.3)	87.7 (79.3 to 94.3)	85.7 (82.3 to 88.3)

Both reductions (baseline−mean of the three last values) and absolute values (mean of the three last values) are given. Values are median and 25th and 75th percentiles. Adjustment for multiple comparisons has been performed. ***$P < 0.001$ compared with 0; #$P < 0.05$ R + F *vs* R.

Table 5. Regression coefficient (change per year) for GFR and 1/serum creatinine in patients treated with the combination of ramipril-felodipine ER or each drug alone

	Ramipril + felodipine $n = 45$	Ramipril $n = 41$	Felodipine $n = 50$
Overall effect calculated from baseline GFR (ml/min/year)	−3.2 (−6.8 to −0.4)***	−4.7 (−8.8 to −1.5)***	−4.8 (−8.1 to 0.8)***
1/creatinine (l/μmol/year) × 10^{-3}	0 (−1 to 0)*	0 (−1 to 0)***	0 (−1 to 0)***
	−2.4 ± 7.3	−3.8 ± 6.9	−7.4 ± 13
Long-term effect calculated from 3 months GFR (ml/min/year)	−3.8 (−6.8 to 0.9)**#	−5.8 (−8.7 to 0.3)**	−6.0 (−11.0 to 2.3)***
1/creatinine (l/μmol/year) × 10^{-3}	0 (−1 to 0)	0 (−1 to 0)	0 (−1 to 0)***
	−2.8 ± 9.6	−2.1 ± 10.0	−9.0 ± 22

HT - TREATMENT

Schmieder RE: End organ damage in hypertension.
Dtsch Arztebl Int 2010; 107(49): 866–73.
DOI: 10.3238/arztebl.2010.0866

Differential treatment considerations for the selection of antihypertensive agents (2, 3)

Subclinical end organ damage	
Left-ventricular hypertrophy	ACEI, ARB, CA
Elevated albuminuria	ACEI, ARB
Renal dysfunction	ACEI, ARB
Irreversible hypertensive end organ damage	
Prior stroke	Any antihypertensive
Prior myocardial infarction	BB, ACEI, ARB
Angina pectoris, CHD	BB, CA
Heart failure	Diuretics, BB, ACEI, ARB, MR antagonists
Left-ventricular dysfunction	ACEI, ARB
Atrial Fibrillation	
– Prevention, recurrence	ARB, ACEI
– Permanent	BB, non-dihydropyridine calcium antagonists
Tachyarrhythmia	BB
Chronic renal insufficieny, proteinuria	ACEI, ARB, loop diuretics
Peripheral arterial occlusive disease	CA

SIDE EFFECTS

ACEI + CAB

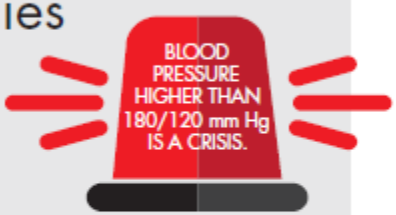
- **cough**
- **peripheral edema, palpitations**
- **flush**

ACEI + diuretic

- **cough**
- **obstipation, dryness in mouth nauzea, pain in epigastrium, anorexie**
- **K depletion**
- **Na depletion, hypovolemia**
- **hyperglycemia, hyeruricemia**

CCB—dihydropyridines	Nicardipine	Initial 5 mg/h, increasing every 5 min by 2.5 mg/h to maximum 15 mg/h.
	Clevidipine	Initial 1–2 mg/h, doubling every 90 s until BP approaches target, then increasing by less than double every 5–10 min; maximum dose 32 mg/h; maximum duration 72 h.
Vasodilators—Nitric-oxide dependent	Sodium nitroprusside	Initial 0.3–0.5 mcg/kg/min; increase in increments of 0.5 mcg/kg/min to achieve BP target; maximum dose 10 mcg/kg/min; duration of treatment as short as possible. For infusion rates ≥4–10 mcg/kg/min or duration >30 min, thiosulfate can be coadministered to prevent cyanide toxicity.
	Nitroglycerin	Initial 5 mcg/min; increase in increments of 5 mcg/min every 3–5 min to a maximum of 20 mcg/min.
Vasodilators—direct	Hydralazine	Initial 10 mg via slow IV infusion (maximum initial dose 20 mg); repeat every 4–6 h as needed.
Adrenergic blockers—$beta_1$ receptor selective antagonist	Esmolol	Loading dose 500–1000 mcg/kg/min over 1 min followed by a 50-mcg/kg/min infusion. For additional dosing, the bolus dose is repeated and the infusion increased in 50-mcg/kg/min increments as needed to a maximum of 200 mcg/kg/min.
Adrenergic blockers—combined $alpha_1$ and nonselective beta receptor antagonist	Labetalol	Initial 0.3–1.0-mg/kg dose (maximum 20 mg) slow IV injection every 10 min or 0.4–1.0-mg/kg/h IV infusion up to 3 mg/kg/h. Adjust rate up to total cumulative dose of 300 mg. This dose can be repeated every 4–6 h.
Adrenergic blockers—nonselective alpha receptor antagonist	Phentolamine	IV bolus dose 5 mg. Additional bolus doses every 10 min as needed to lower BP to target.
$Dopamine_1$-receptor selective agonist	Fenoldopam	Initial 0.1–0.3 mcg/kg/min; may be increased in increments of 0.05–0.1 mcg/kg/min every 15 min until target BP is reached. Maximum infusion rate 1.6 mcg/kg/min.
ACE inhibitor	Enalaprilat	Initial 1.25 mg over a 5-min period. Doses can be increased up to 5 mg every 6 h as needed to achieve BP target.

Hypertensive Crises: Emergencies and Urgencies



Hypertensive emergencies are defined as severe elevation of BP (greater than 180/120 mm Hg) associated with evidence of new or worsening target organ damage. In such cases, BP must be immediately reduced to prevent or limit further damage.