

HYPERTENSION

M. Kozák, IKK, FN Brno



HT THERAPY - HISTORY

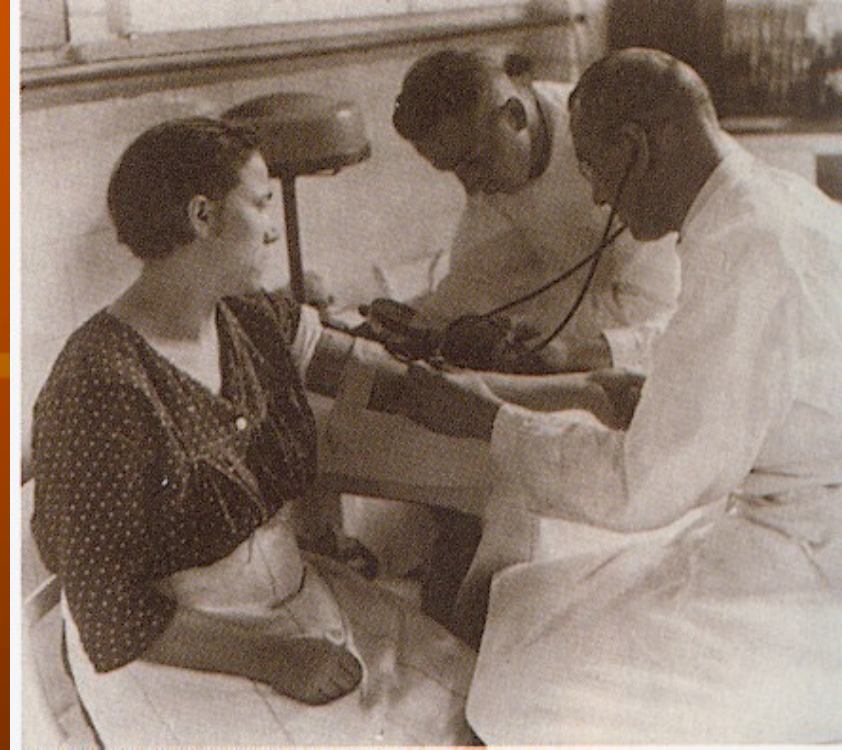
VNITŘNÍ LÉKAŘSTVÍ

MUDr. MILOŠ NETOUŠEK
profesor Karlovy university

ČTVRTÉ VYDÁNÍ

PRAHA 1954

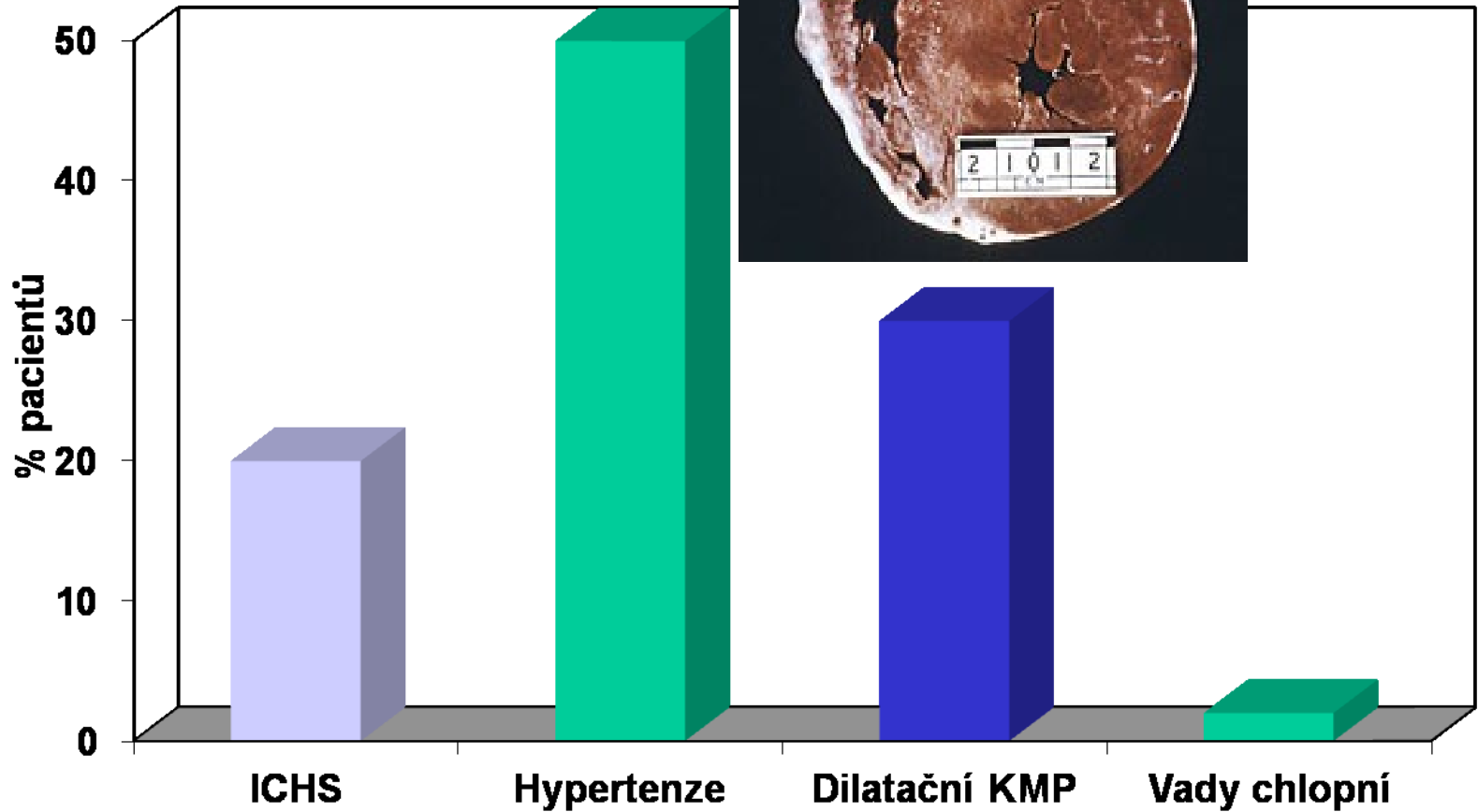
STÁTNÍ ZDRAVOTNICKÉ NAKLADATELSTVÍ



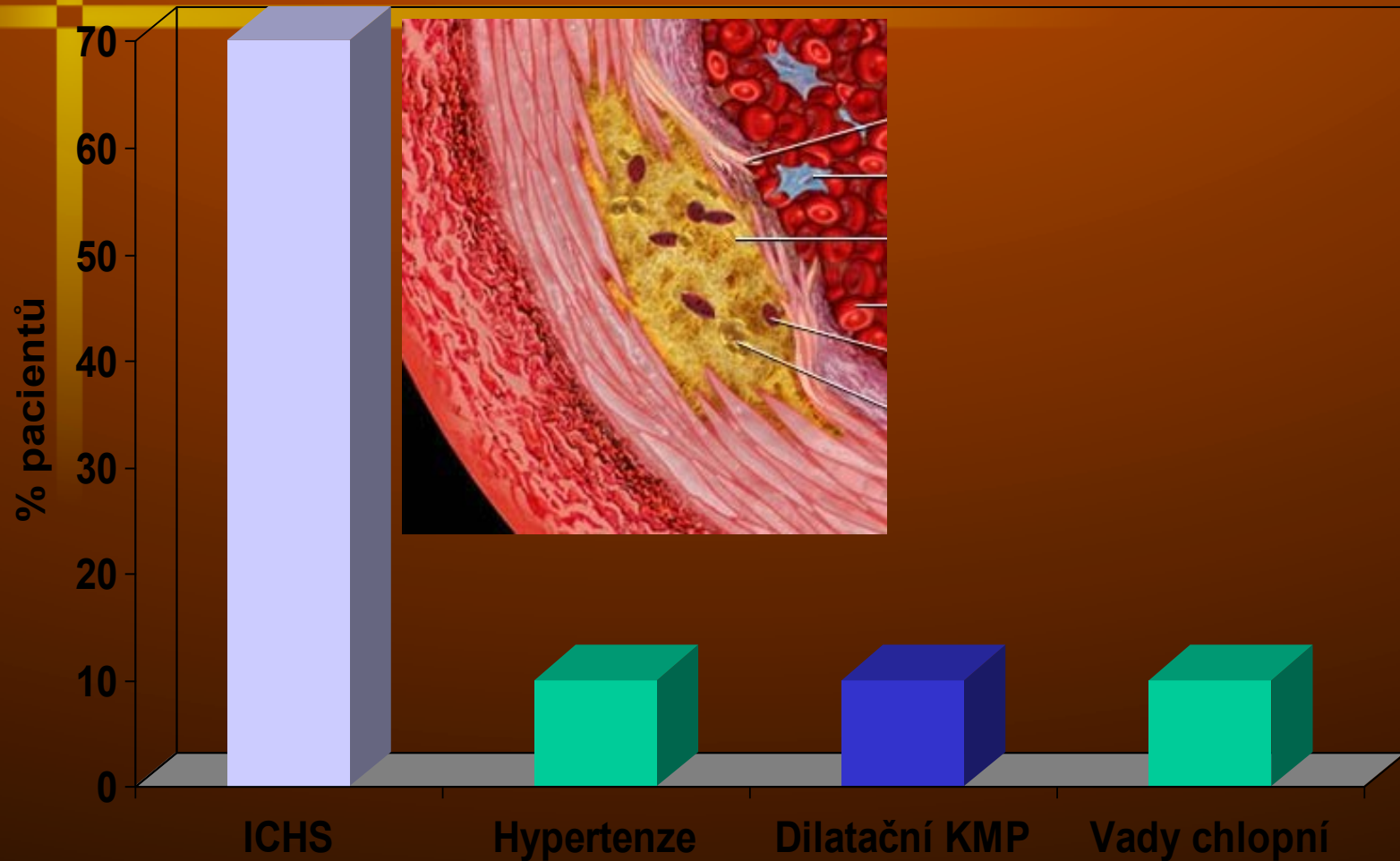
- life regime
- physical th.
- gymnastics
- liquor drenaige
- eating moderation
- iodids
- salt reducing
- rhodanid
- nonsmoking
- Ca
- analgetics
- NTG



ETIOLOGY CHF - Framingham st. 1950 -70



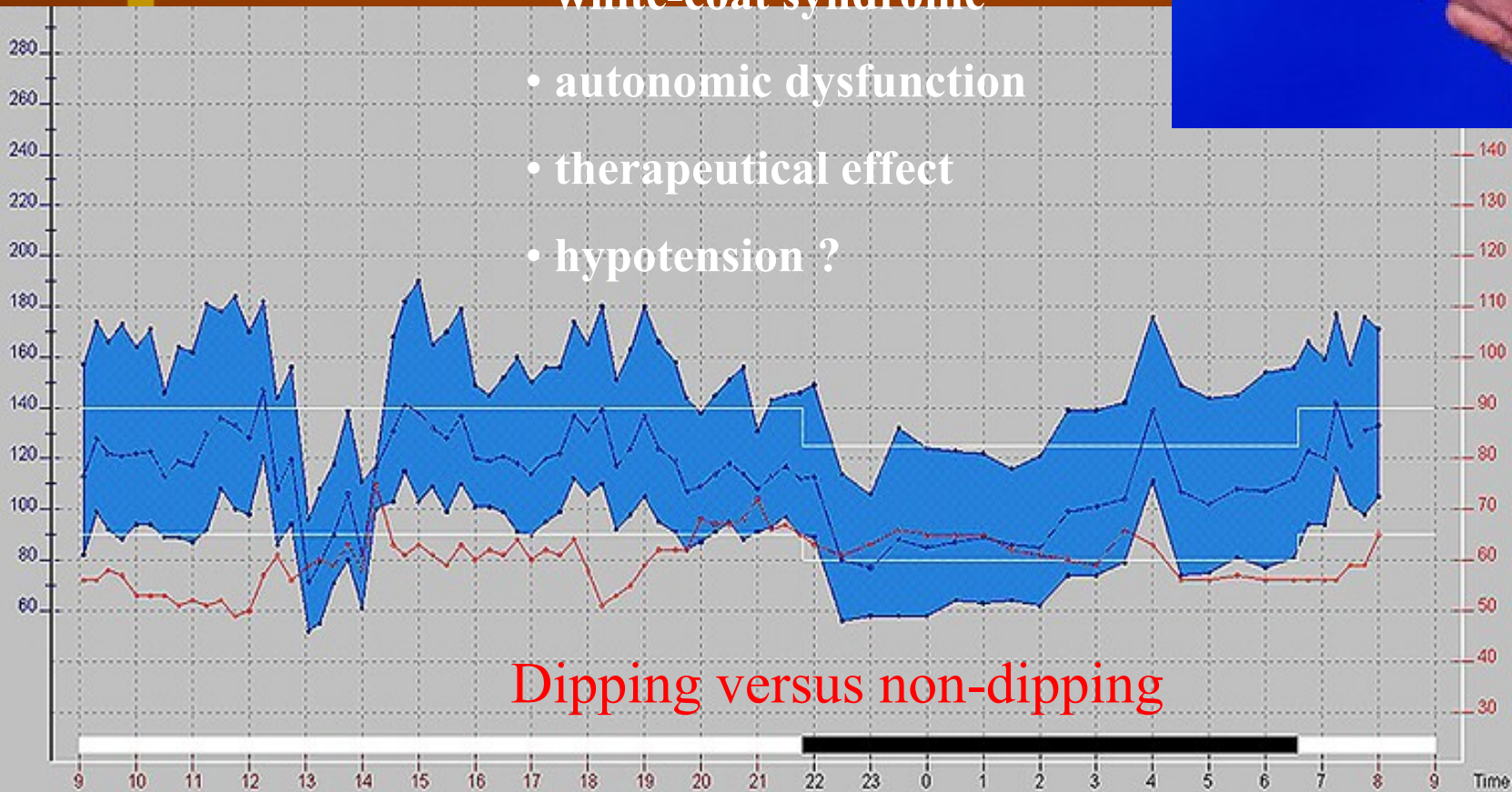
ETIOLOGY CHF - European data 1990 - 2000



BP MEASUREMENT - HOLTER

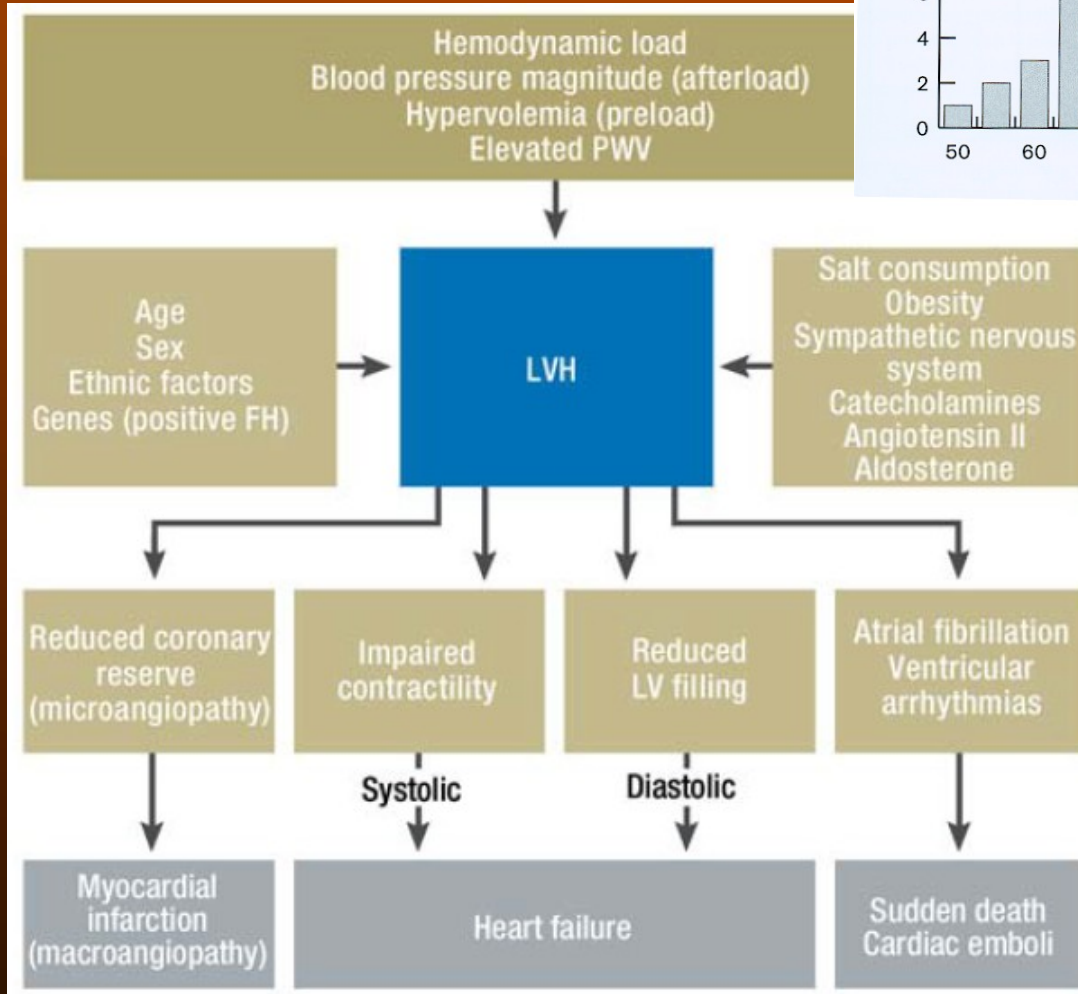
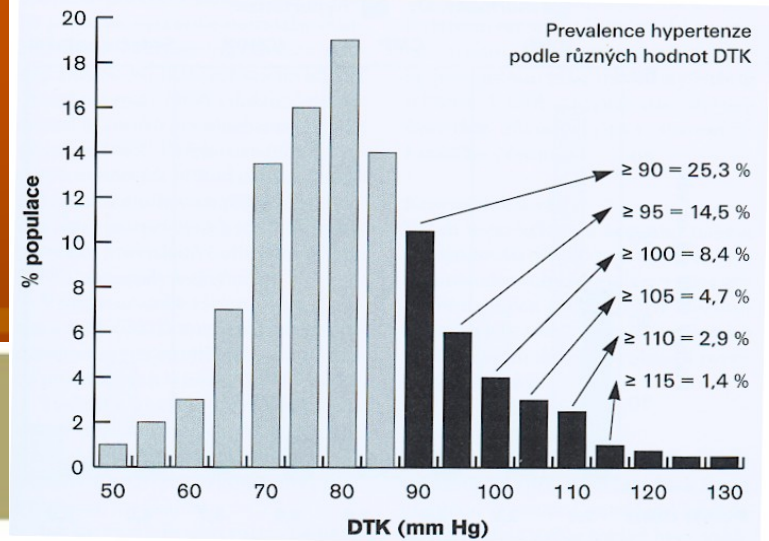
INDICATIONS

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



Dipping versus non-dipping

HT IMPACTS

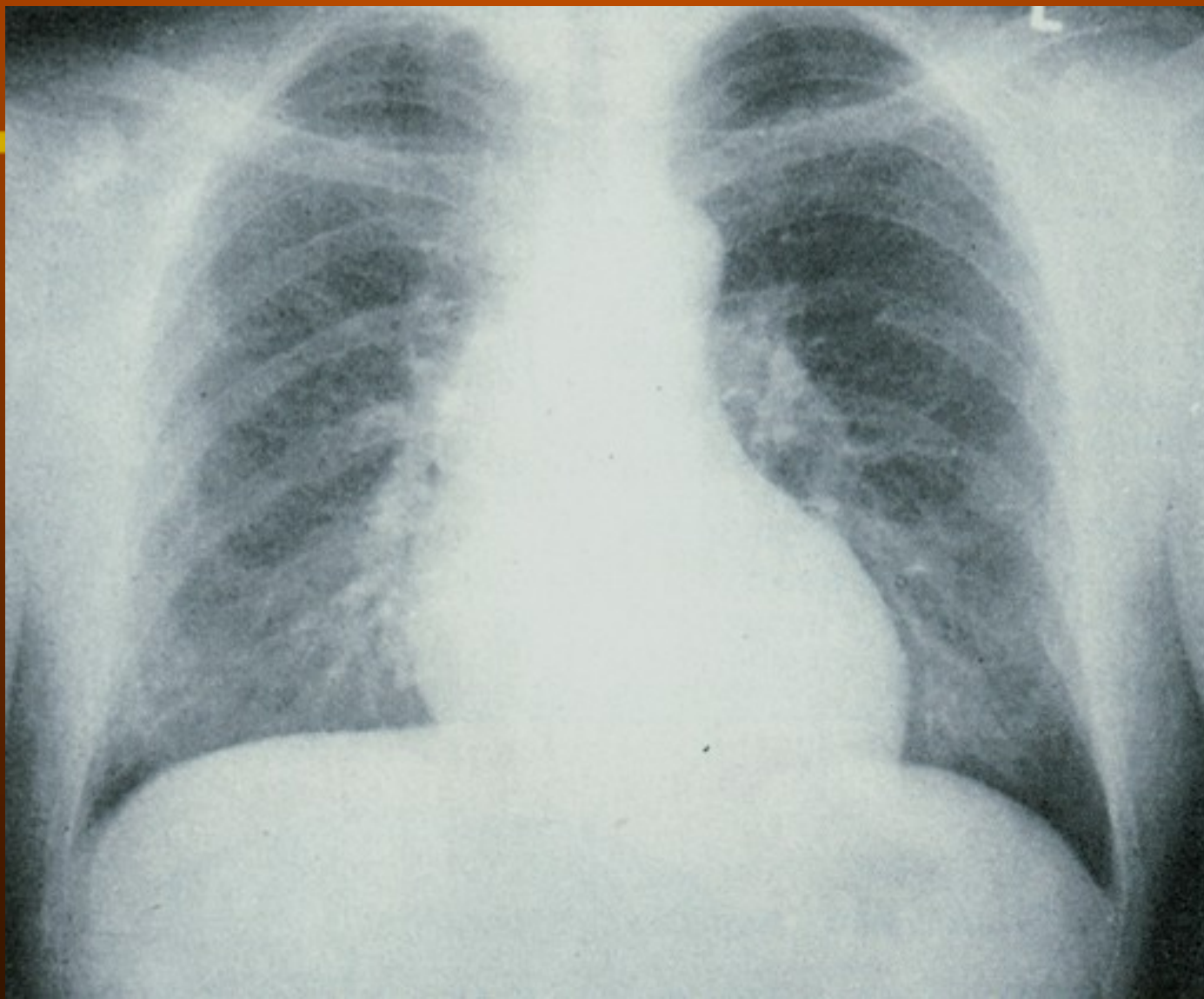


BP VALUES ACC/AHA 2018

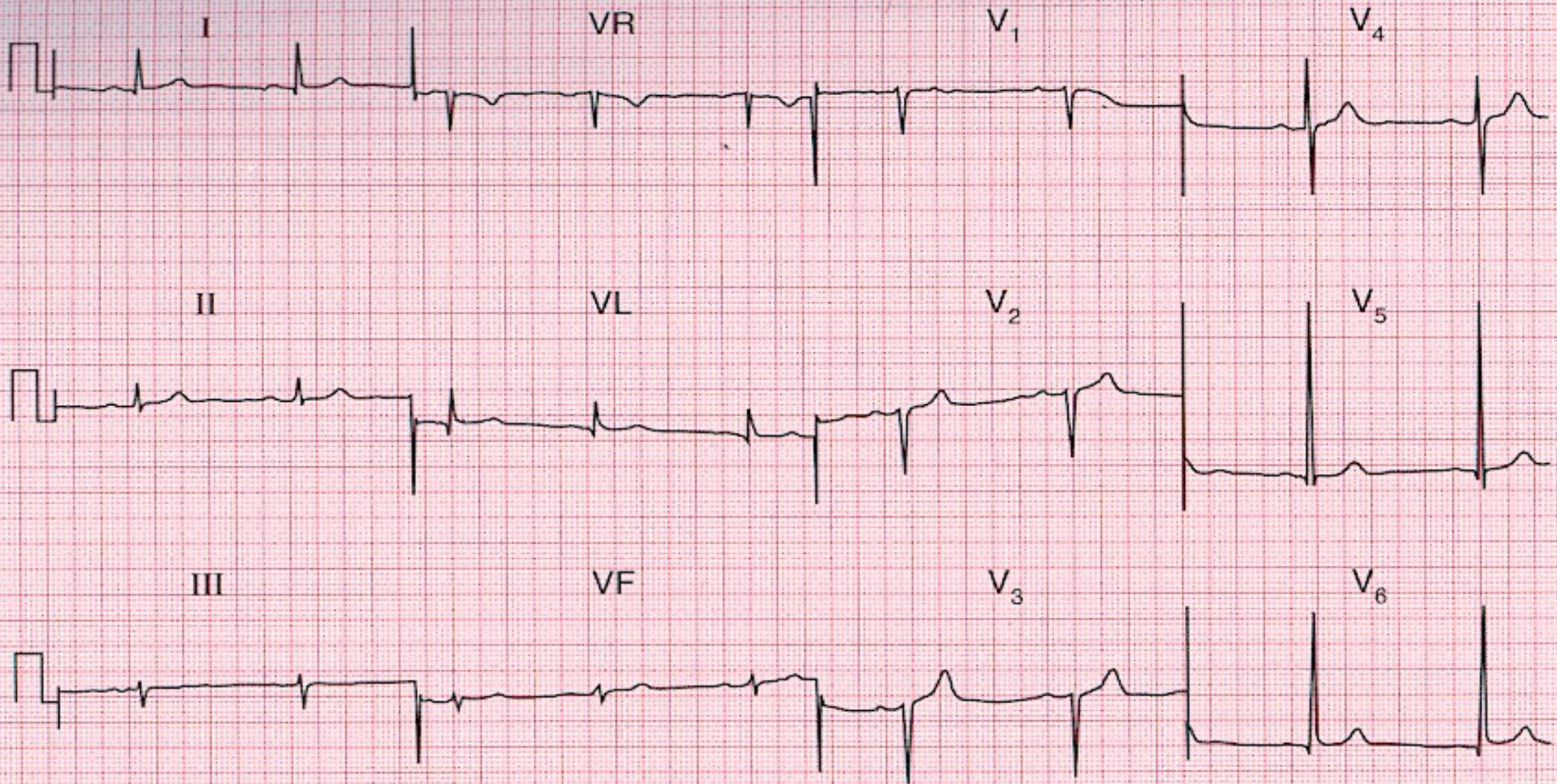
BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE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



X RAY CORRELATION



ECG CORRELATION



- McPhie - $SV_{max} + RV_{max}$ over 40 mm
- Sokolov/Lyon - $SV_1 + RV_{5,6}$ over 35 mm

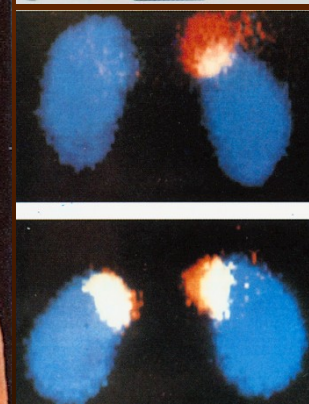
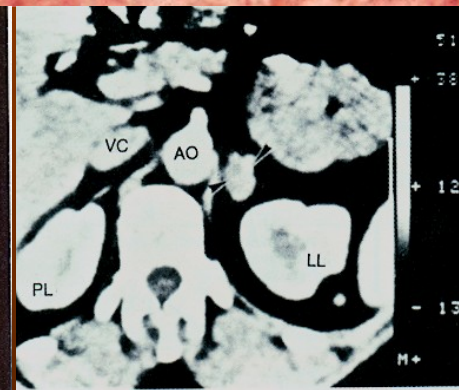


ETIOLOGY

- essential HT(primary, idiopathic)
- secondary HT (10%)
 - renal (acute, chronic disease)
 - renovascular
 - endocrine (hyperA, hyperK, feochromocytom, acromegaly, hyperparathyreozis)
 - neurogenic (Tu, injuries)
 - coarctation ao
 - sleeping apnoe
 - iatrogenic (contraceptives, steroids, cocain, liquorice)

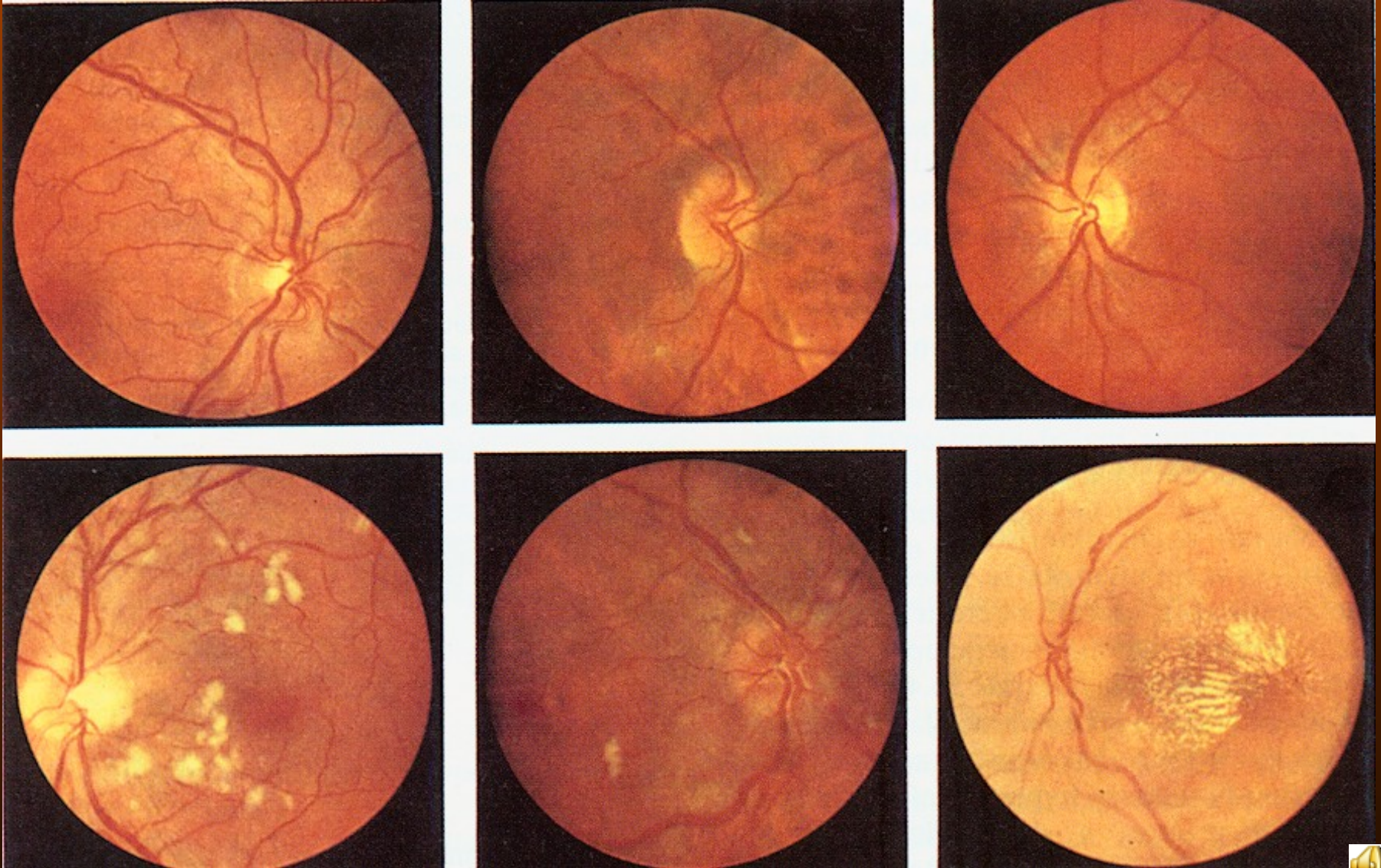


MORBUS CUSHING



FUNDUSCOPIC CORRELATION

Arteriosclerotic and
hypertensive retinopathy



HT IMPACTS

1. Hypertensive

Left ventricular hypertrophy

Heart failure

Intracerebral bleeding, ischemic stroke

Renal insufficiency (Na retention, MAU, CKD)

Hypertonic retinopathy

Hypertonic crisis with encephalopathy

Aneurysma dissecans

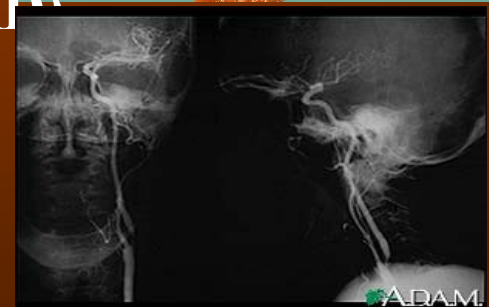
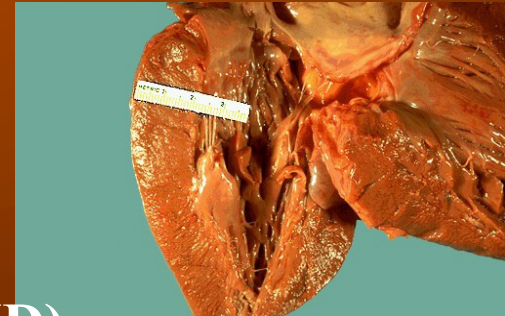
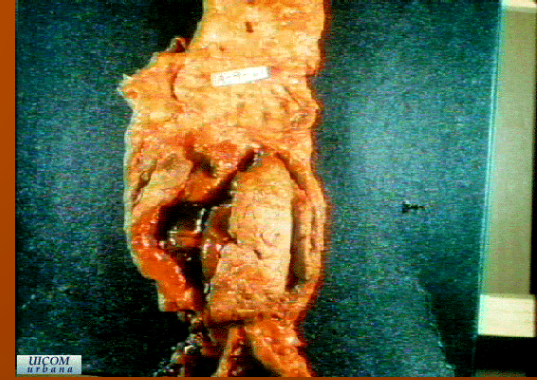
2. Atherosclerotic

CAD (AP, IM, SCD)

CVD (stroke, TIA, aneurysm, vascular malf.)

Aortic aneurysm

PAD, CLTI – chron. limb threateing, CLI – critical

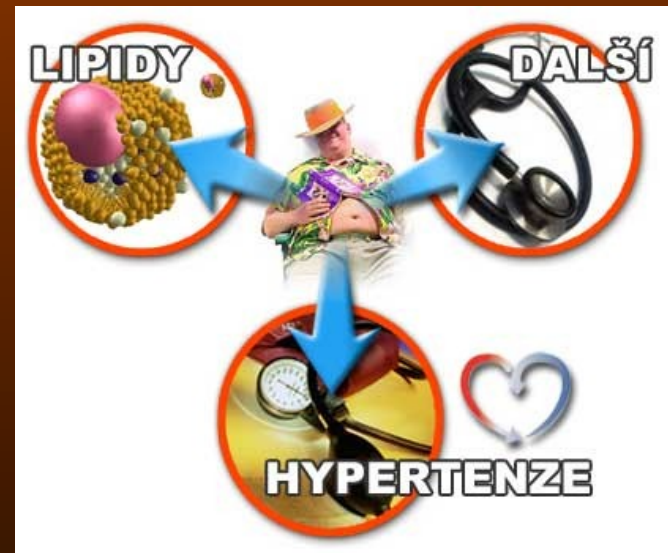


HYPERTENSION + METABOLIC SYNDROM

- **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**



PROGNOSTIC FACTORS HT

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

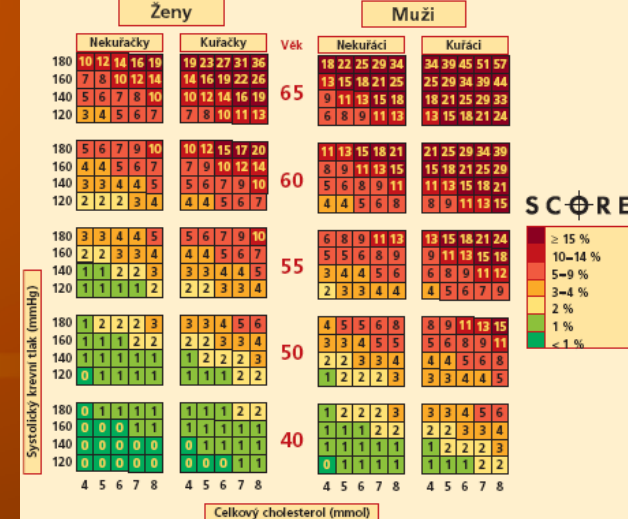


SCORE

- 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 $\geq 5\%$
- SCORECARD



SOP – SUBCLINICAL ORGAN DAMAGE

- **LV hypertrophy**

EKG: Sokolow-Lyons ≥ 38 mm

Cornell ≥ 440 mm x ms

ECHO: LVMI ≥ 25 , F ≥ 10 g/m²

- **USG thickening of the arteriol wall**

(thickening of the carotid wall $\geq 0,9$ mm or plaque)

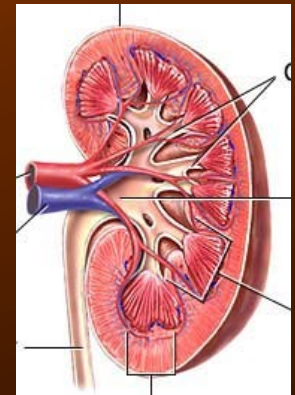
- **Moderate elevation serum creatinine level**

M 115-133, F 107-124 $\mu\text{mol/l}$

- **Lowering GF below 60ml/min**

- **Microalbuminuria 30 – 300 mg/24h**

ratio albumin/creatinine M $\geq 2,5$ F $\geq 3,5$ mg/mmol



POP – CLINICAL ORGAN DAMAGE



- **CVD:**

ischemic stroke, cerebral bleeding; TIA

- **Structural heart disease:**

CAD post MI, AP, revascularization, CHF

- **Renal disease:**

diabetic nephropathy

renal function decrease

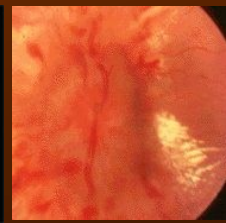
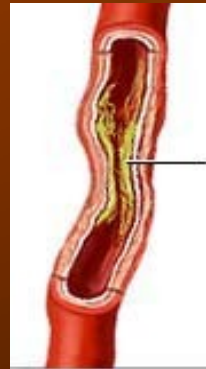
S creatinine: M █ 33, F █ 24 █ mol/l

proteinuria: █ 300 mg/24 h

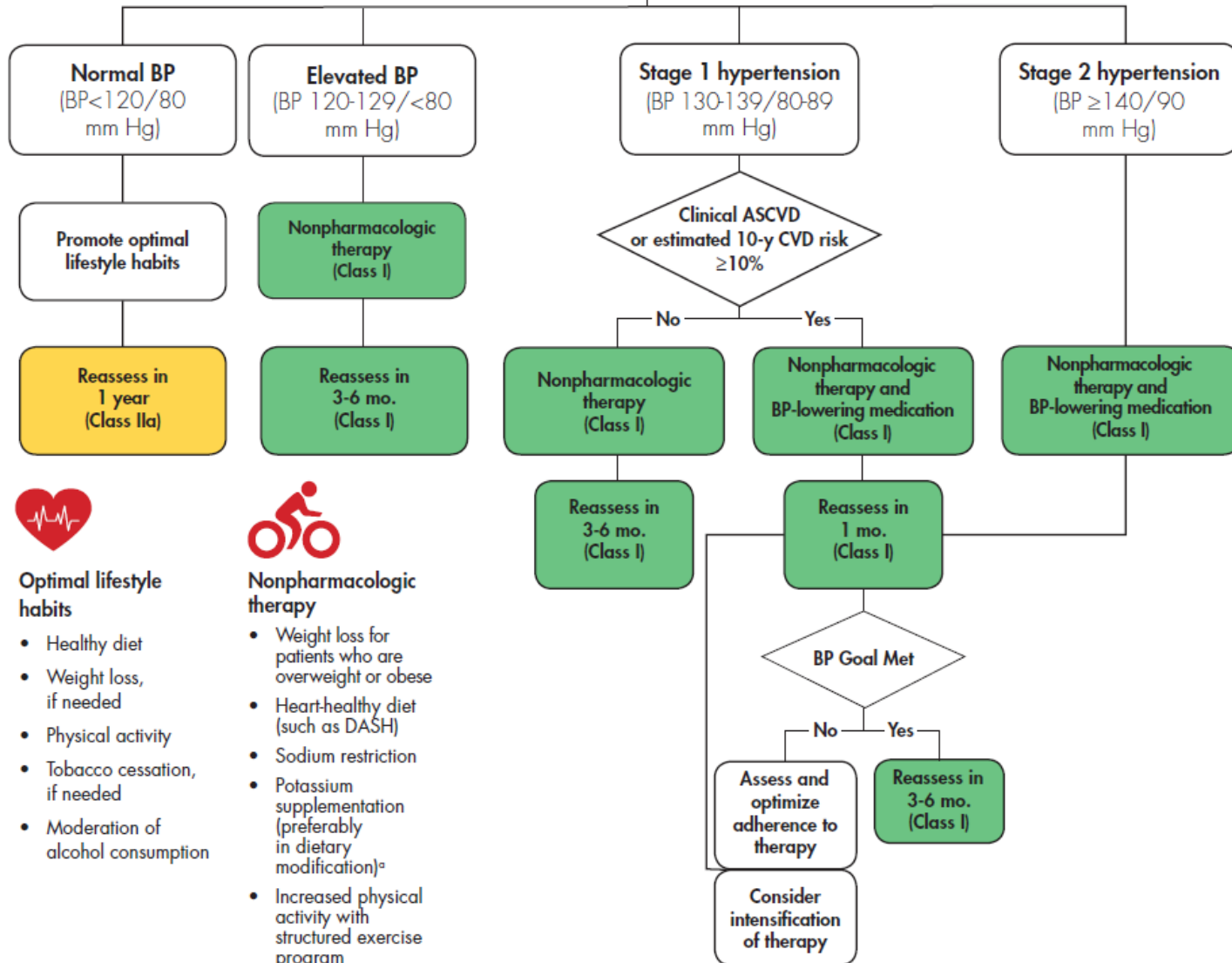
- **PAD, CLTI, CLI**

- **Advanced retinopathy:**

hemorrhage or exsudate, papilledema



BP thresholds and recommendations for treatment and follow-up



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.

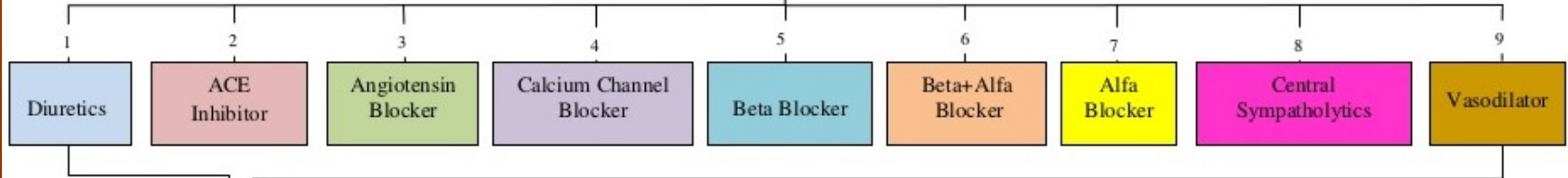
^b In the United States, one standard drink is equivalent to 12 oz of regular beer (usually about 5% alcohol), 5 oz of wine (usually about 12% alcohol), or 1.5 oz of distilled spirits (usually about 40% alcohol).



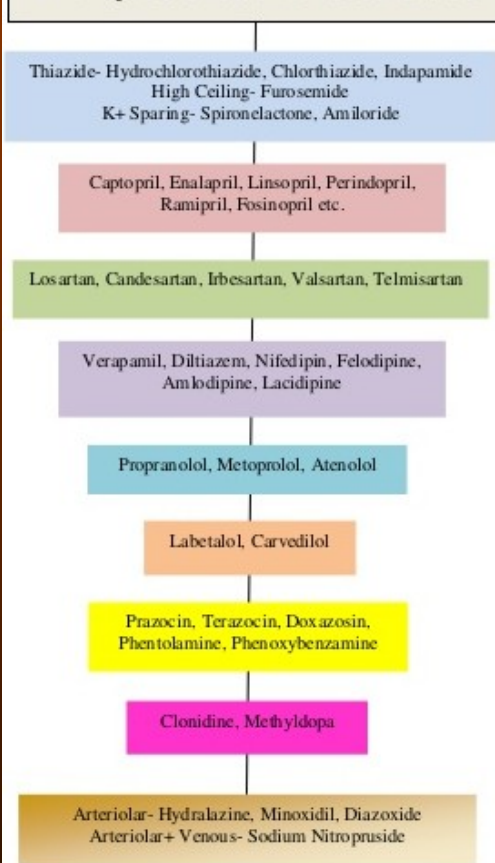
Anti-Hypertensive Drugs

Prevention is always better than cure

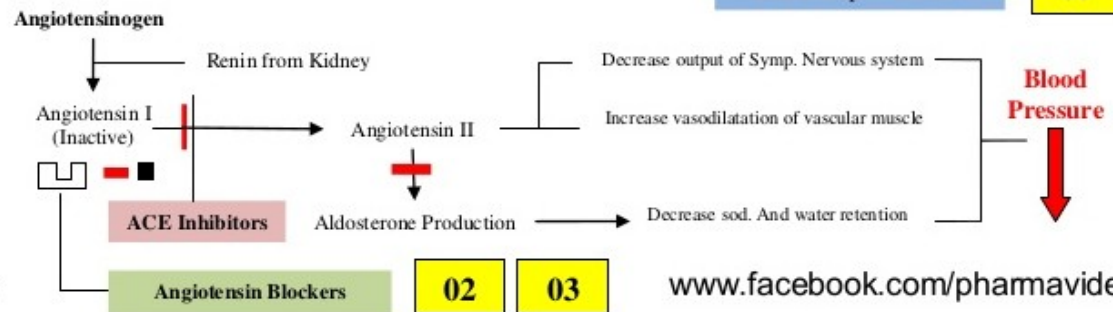
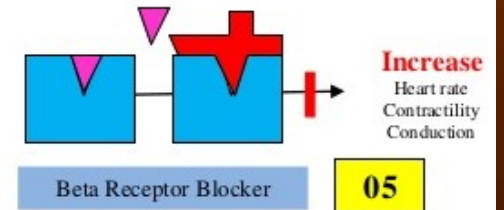
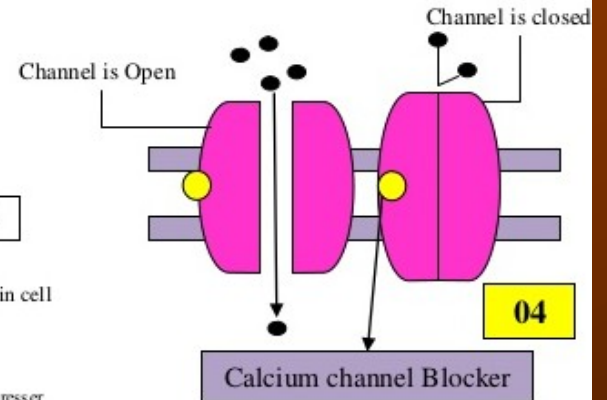
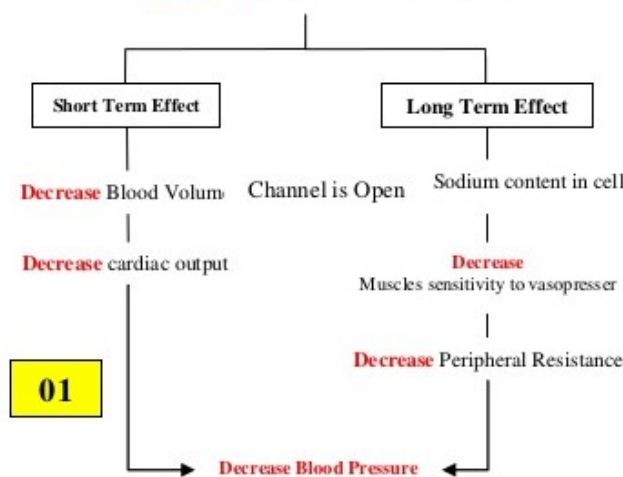
Classification- KD Tripathi



Examples of above listed Class



Increase Water & Sodium Excretion



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

Coronary Heart Disease

17%
reduced
risk

Stroke

27%
reduced
risk

Heart Failure

28%
reduced
risk

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)

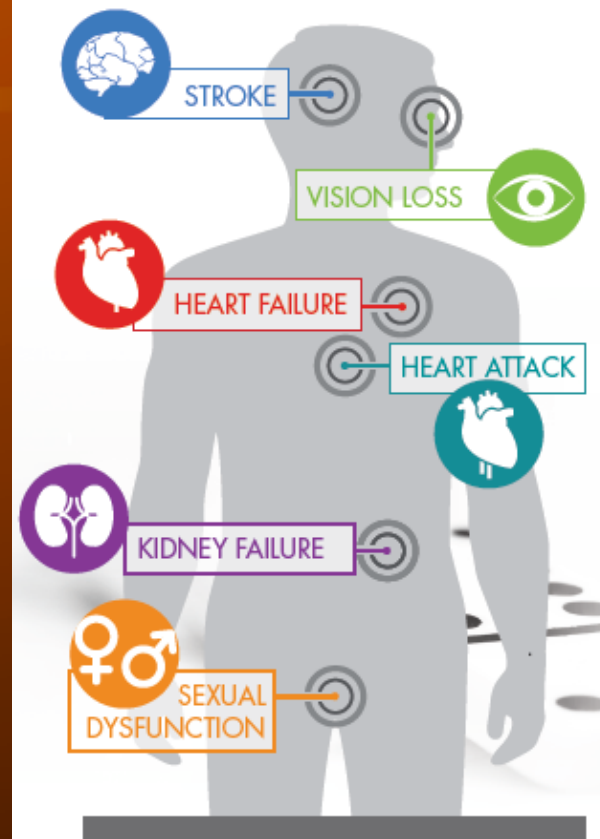
Six general classes of oral antihypertensive drugs are recommended as second-line agents

- Diuretics (loop, potassium sparing and aldosterone antagonists)
- Beta-blockers (cardioselective, and vasodilatory, noncardioselective, intrinsic sympathomimetic activity and combined alpha- and beta-receptor)
- Direct renin inhibitor
- Alpha-1 blockers
- Central alpha₂-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.



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



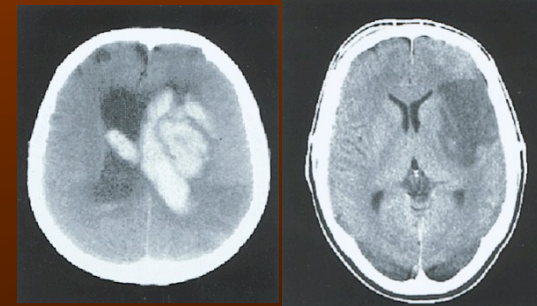
HYPERTENSION + DM

- Nonpharmacological therapy ■ Intake Na, weight
- Target BP < 130/80 mmHg
- **RAS blockade – ACEI, ARB preferred**
- Almost combined therapy
- MAU is indication for RAS blockator
- **Intervention of all risk factors**



ANTIHYPERTENSIVE DRUGS /STROKE

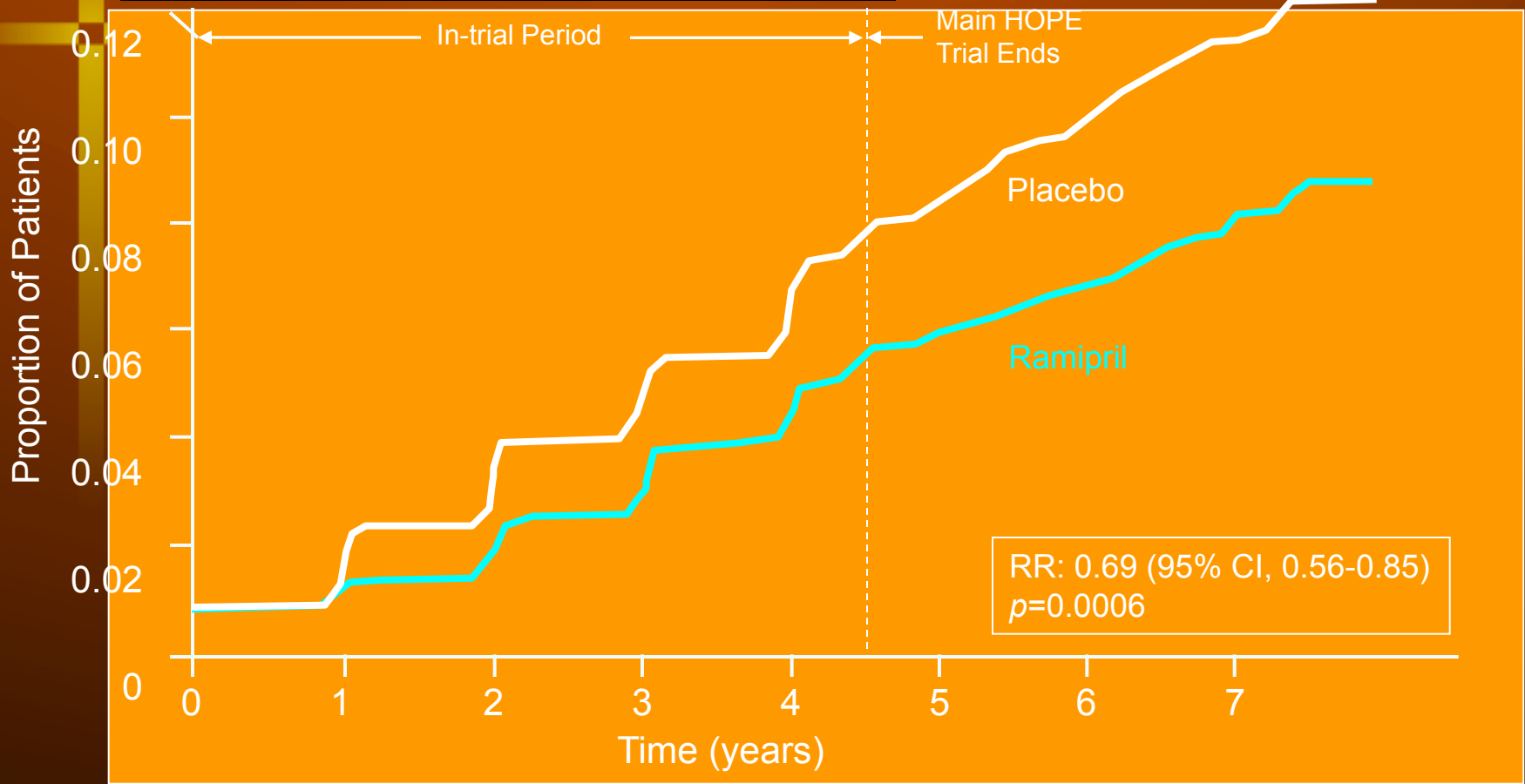
- benefit for pts with normal BP and hypertension
- profit without consideration to type of stroke
- sex and age
- time interval from stroke
- we prefer monotherapy ACEI/ARB
- CAB better in older pts



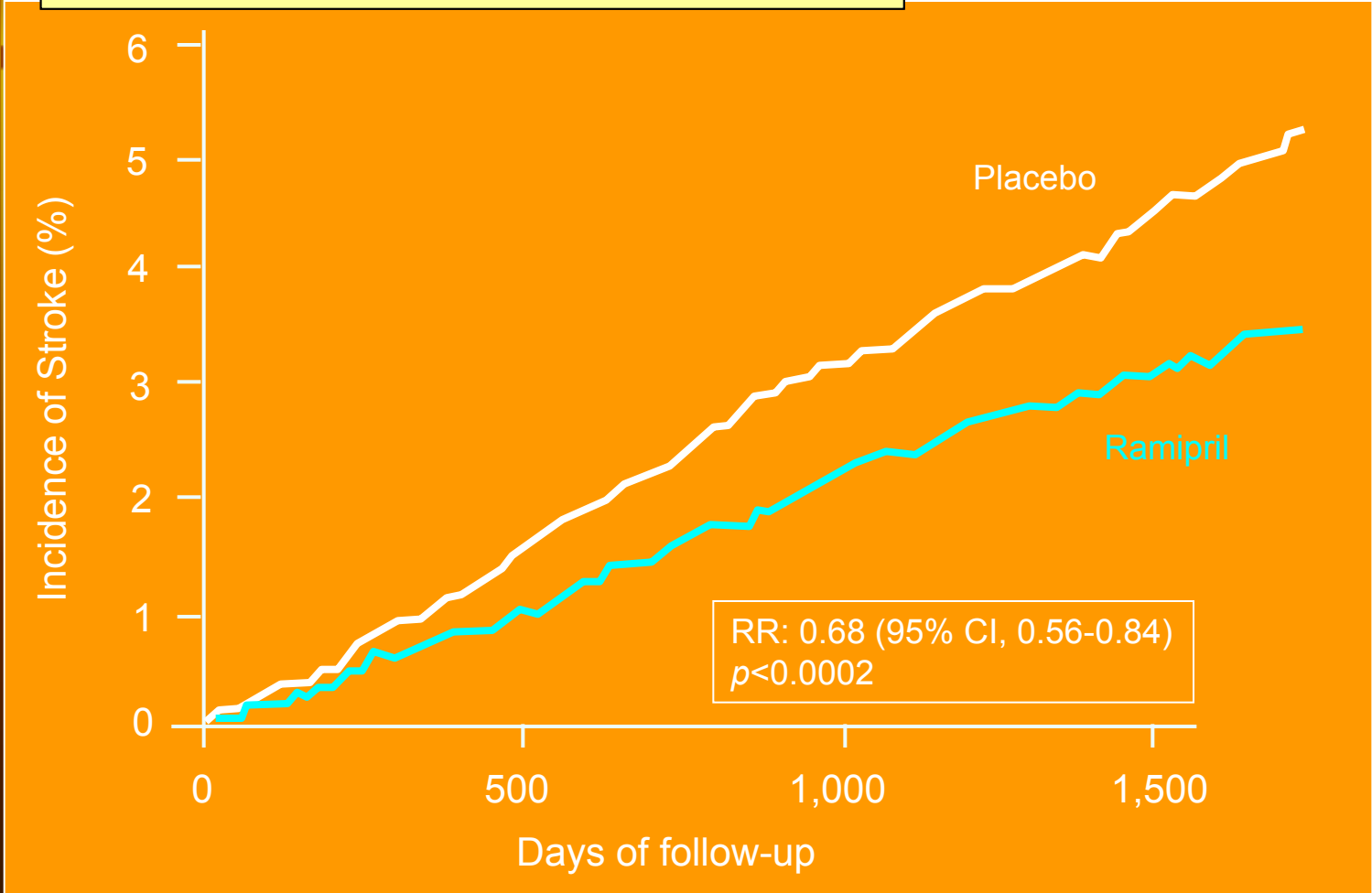
(PATS, PROGRESS, EUROPA, Syst-Eur, EWPHE, MRC, SHEP...)



DEVELOPMENT OF DM

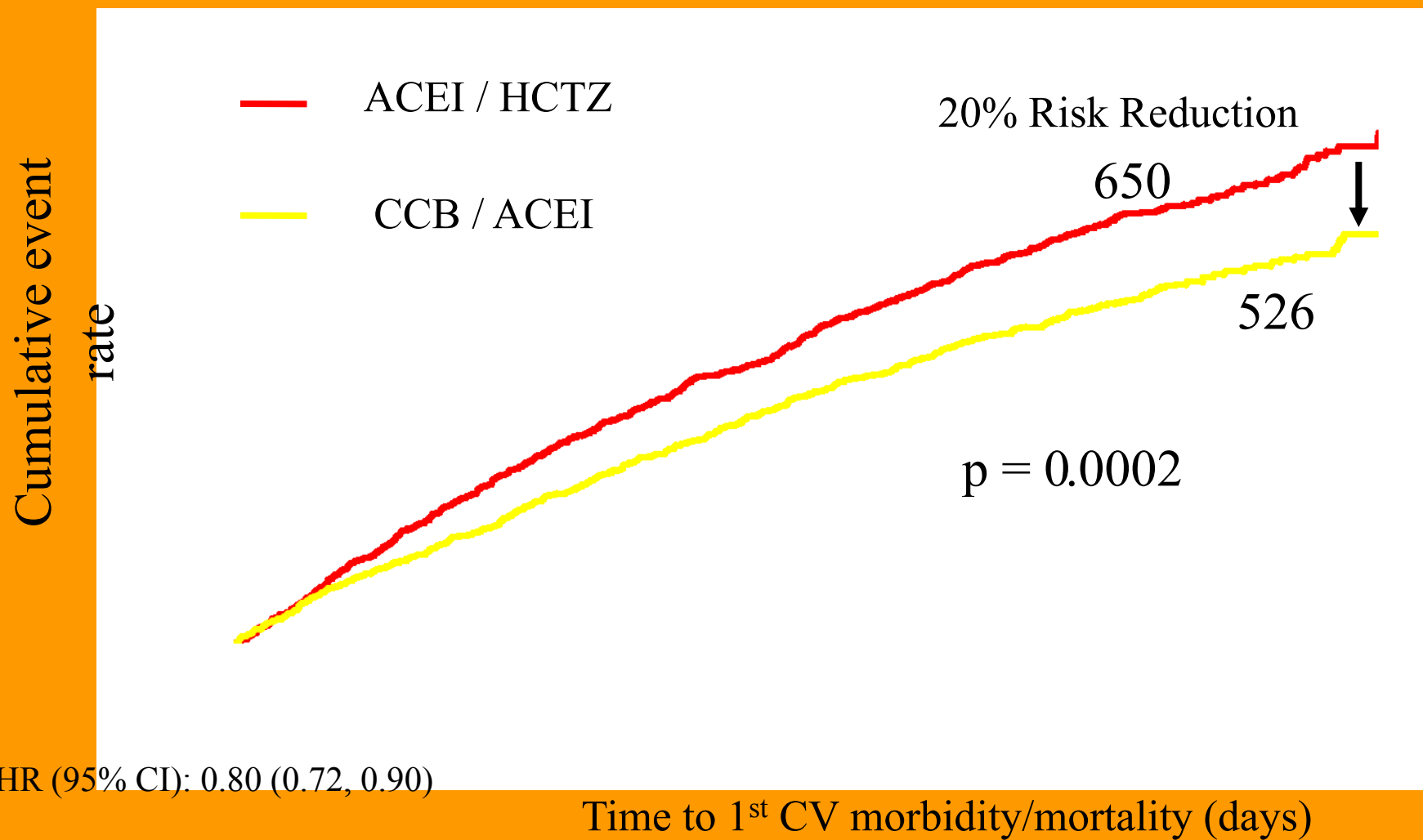


INCIDENCE OF STROKE



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



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 \times 4 mg)	Atenolol 100 mg+bendroflumethiazide 2-5 mg +potassium
Step 5	Amlodipine 10 mg+perindopril 8 mg (2 \times 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 \times 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



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 Herlitz¹, Kevin Harris², Teut Risler³, Geoffrey Boner⁴, Jacques Bernheim⁵, Jacques Chanard⁶ and Mattias Aurell¹

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



CKD

2160

The NEPHROS Study

A progression study in renal disease.

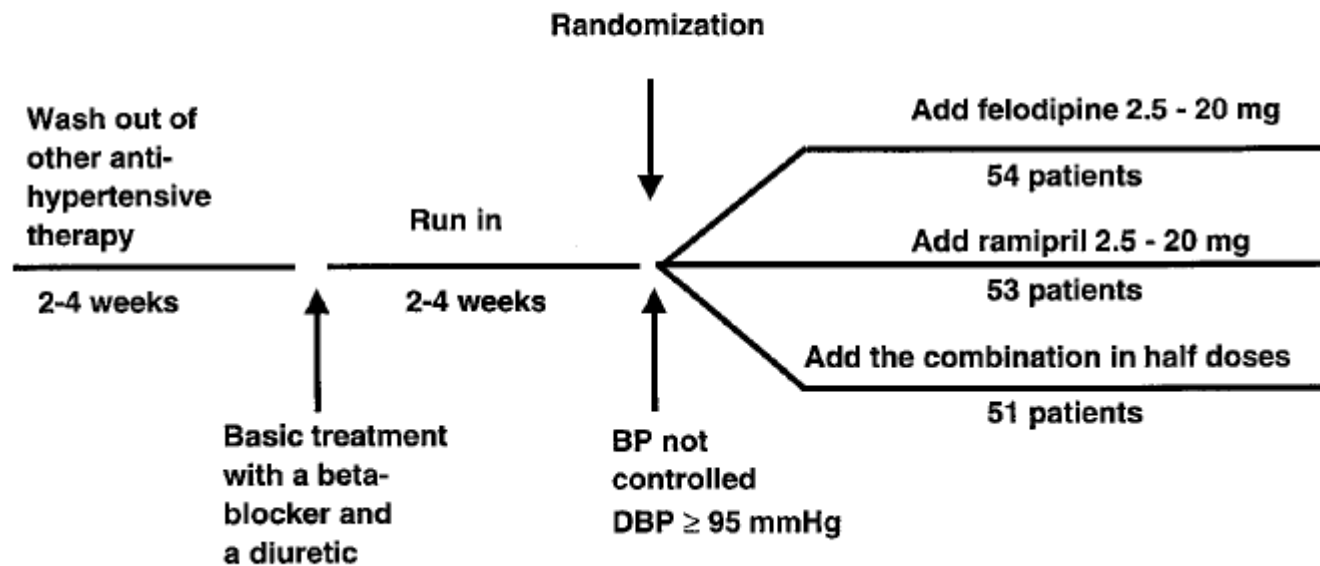


Fig. 1. Flow chart of the study.



HT - TREATMENT

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 insufficiency, 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
nausea, pain in
epigastrium, anorexia
- K depletion
- Na depletion, hypovolemia
- hyperglycemia, hyperuricemia



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, 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.

