Αρτηριακή Υπέρταση

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ΕΚΠΑ

“The greatest danger to a man with high blood pressure lies in its discovery, because then some fool is certain to try and reduce it !!!”.

Hay, BMJ 1931;2:43-47

Επιδημιολογία

- Η ΑΥ είναι συχνή
- Η συχνότητα επηρεάζεται από ηλικία και τρόπο ζωής
- 25% ενηλίκων
- 50% ενηλίκων >60 ετών

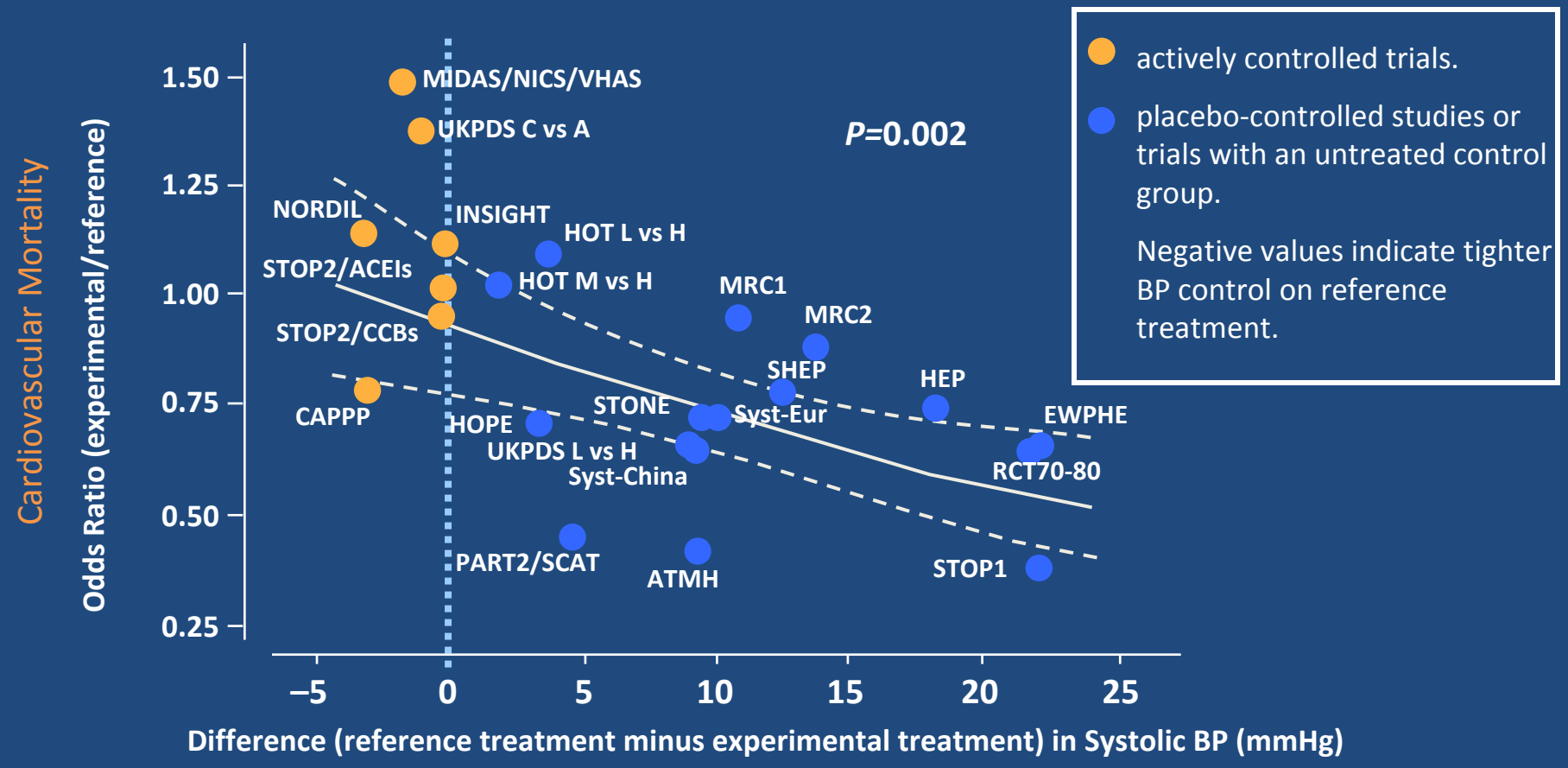
Νόσοι και παθολογικές καταστάσεις αποδιδόμενες στην Υπέρταση

Προσαρμογή από Dustan HP et al. Arch Intern Med. 1996;156;1926-1935

Υπέρταση και καρδιαγγειακός κίνδυνος

- Ισχυρός και ανεξάρτητος παράγοντας κινδύνου για ΣΝ, ΚΑ, ΑΕΕ, περιφερική αρτηριοπάθεια, νεφρική ανεπάρκεια, διαταραχή νοητικών λειτουργιών, πρόωρο θάνατο
- Η συσχέτιση με τον κίνδυνο είναι συνεχής και βαθμιαία
- Αύξηση 2 mmHg ΣΑΠ οδηγείσε αυξημένη θνητότητα:
  - 7% από καρδιοπάθεια
  - 10% από ΑΕΕ

Lowering BP and CV mortality



Greater differences in SBP reduction = greater reductions in CV mortality

Staessen JA et al. *Hypertension Research.* 2005;28:385-407.

Συνύπαρξη νόσων σε Υπερτασικούς Ασθενείς

- Ισχαιμική καρδιοπάθεια (IHD) 20-30%
- Συμφορητική καρδ. ανεπάρκεια (CHF) 10-20%
- Δυσλιπιδαιμία 25-35%
- Σ. Διαβήτης 10-15%
- Αρρυθμίες 10-15%
- Υπερτροφία της Αρ. Κοιλίας 10-40%
- Νεφρική βλάβη 3 - 5%
- Άσθμα 5 -10%
- Περιφερική αρτηριοπάθεια

Am J Med 1996; 101: 50S - 55S

Definitions and Classification of BP Levels (mmHg)

Category	Systolic		Diastolic
Optimal	<120	and	<80
Normal	120-129	and/or	80-84
High Normal	130-139	and/or	85-89
Grade 1 Hypertension	140-159	and/or	90-99
Grade 2 Hypertension	160-179	and/or	100-109
Grade 3 Hypertension	≥ 180	and/or	≥ 110
Isolated Systolic Hypertension	≥ 140	and	< 90

Stratification of CV risk in four categories

Blood pressure (mmHg)

Other risk factors, TOD or disease	Normal SBP 120-129 or DBP 80-84	High normal SBP 130-139 or DBP 85-89	Grade 1 HT SBP 140-159 or DBP 90-99	Grade 2 HT SBP 160-179 or DBP 100-109	Grade 3 HT SBP ≥180 or DBP ≥110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1-2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors, TOD, DM or MS	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Established CV or renal disease	Very high added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

Risk factors

- Systolic and diastolic BP levels

- Levels of pulse pressure (in the elderly)
- Age (M > 55 years; W > 65 years)
- Smoking
- Dyslipidaemia
  - TC > 5.0 mmol/l (190 mg/dl) or:
  - LDL-C > 3.0 mmol/l (115 mg/dl) or:
  - HDL-C: M < 1.0 mmol/l (40 mg/dl), W <1.2 mmol/l (46 mg/dl) or:
  - TG > 1.7 mmol/l (150 mg/dl)

- Fasting plasma glucose 5.6–6.9 mmol/L (102–125 mg/dl)

- Abnormal glucose tolerance test
- Abdominal obesity (Waist circumference >102 cm (M), >88 cm (W))
- Family history of premature CV disease (M at age <55 years; W at age <65 years)

Established CV or renal disease

- Cerebrovascular disease: ischaemic stroke; cerebral haemorrhage; transient ischaemic attack
- Heart disease: myocardial infarction; angina; coronary revascularization; heart failure
- Renal disease: diabetic nephropathy; renal impairment (serum creatinine M >133, W >1 24 mmol/l); proteinuria (> 300 mg/24 h)
- Peripheral artery disease
- Advanced retinopathy: haemorrhages or exudates, papilloedema

Subclinical organ damage

- Electrocardiographic LVH (Sokolow-Lyon >38 mm; Cornell >2440 mm*ms) or:
- Echocardiographic LVH° (LVMI M ≥ 125 g/m^2, W ≥ 110 g/m^2)
- Carotid wall thickening (IMT > 0.9 mm) or plaque
- Carotid-femoral pulse wave velocity >12 m/s
- Ankle/brachial BP index <0.9
- Slight increase in plasma creatinine:
  M: 115–133 μmol/l (1.3–1.5 mg/dl);
  W: 107–124 μmol/l (1.2–1.4 mg/dl)

- Low estimated glomerular filtration rate† (<60 ml/min/1.73 m^2) or creatinine clearance◇ (<60 ml/min)
- Microalbuminuria 30–300 mg/24 h or albumin-creatinine ratio: ≥22 (M); or ≥31 (W) mg/g creatinine

High/Very High Risk Subjects

- SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg
- High SBP > 160 mmHg with low DBP (< 70 mmHg)
- ≥ 3 cardiovascular risk factors
- Diabetes mellitus or Metabolic syndrome
- Target Organ Damage
- Established CV or renal disease

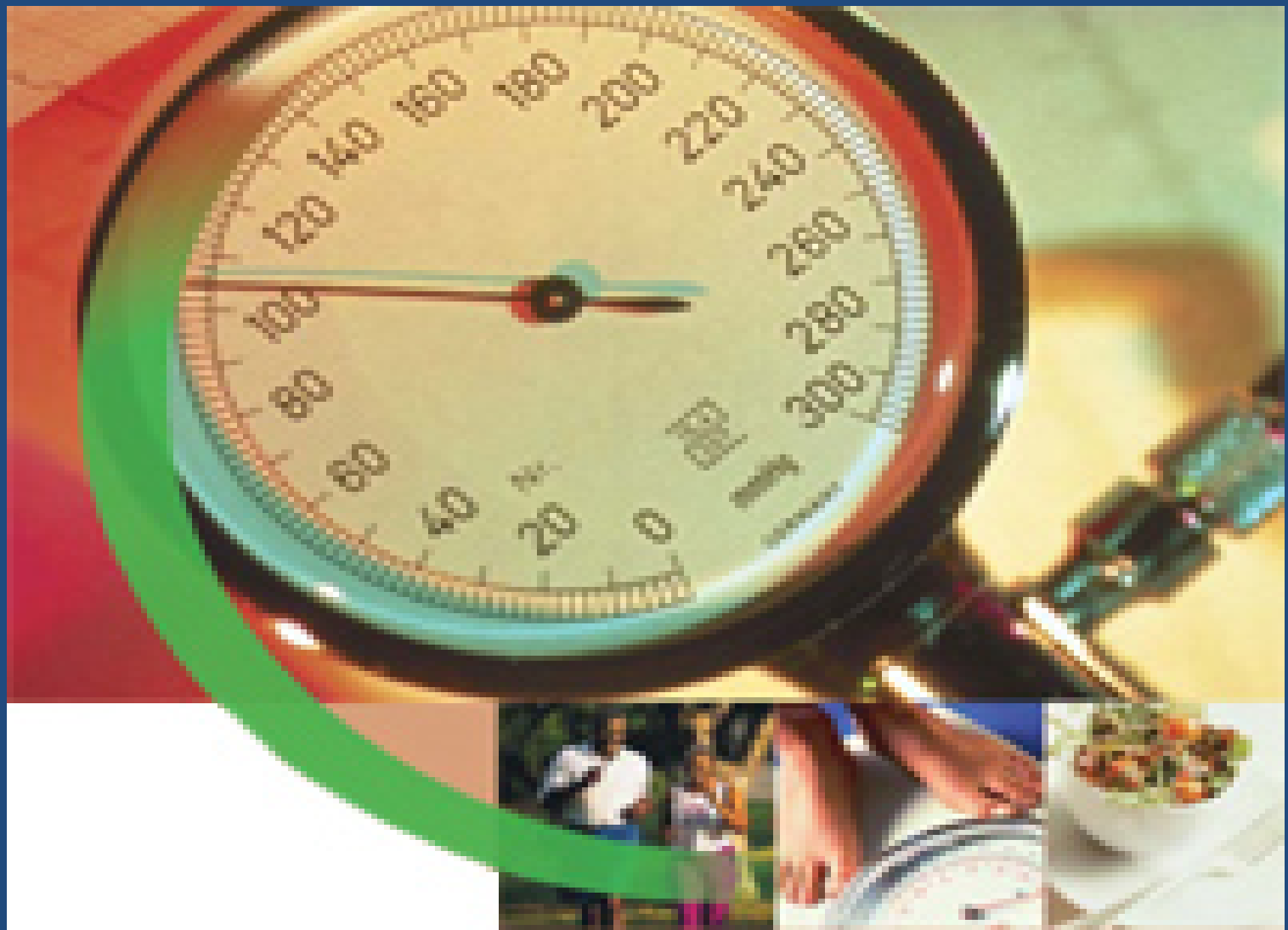
High/Very High Risk Subjects

- subclinical organ damage:
  - Heart: LVH, EKG (particularly with strain) or Echo (particularly concentric)
  - CNS: Carotid artery wall thickening or plaque (U/S)
  - Vessels: Increased arterial stiffness
  - Kidneys: Slight increase in serum creatinine
  - Kidneys: Reduced estimated GFR or creat. clearance
  - Kidneys: Microalbuminuria or proteinuria

High/Very High Risk Subjects

- Established CV disease
  - Heart
  - Cerebrovascular
  - Renal
  - Peripheral artery
  - Ophthalmic disease

Μετρούμε σωστά την αρτηριακή πίεση?



ΙΔΑΝΙΚΗ ΜΕΤΡΗΣΗ ΑΠ

- ΠΕΡΙΒΑΛΛΟΝ-ΚΑΤΑΣΤΑΣΕΙΣ

1. Καφείνη (1h), Κάπνισμα (30min)
2. Αδρενεργικοί παράγοντες (Ρινικά αποσυμφορητικά, οφθαλμικά διαστολτικά κόρης)

Ι Δ Α Ν Ι Κ Η Μ Ε Τ Ρ Η Σ Η Α Π

- Θ Ε Σ Η

1. Κ Α Θ Ι Σ Τ Η: Σ τ ή ρ ι ξ η κ ο ρ μ ο ύ, σ τ ή ρ ι ξ η β ρ α χ ί ο ν α σ τ ο ε π ί π ε δ ο τ η ς κ α ρ δ ι ά ς
2. Ο Ρ Θ Ι Α: (2-3 min)

   Η λ ι κ ι ω μ έ ν ο ι , Σ Δ ,

   Φ ά ρ μ α κ α

Ι Δ Α Ν Ι Κ Η Μ Ε Τ Ρ Η Σ Η Α Π Τ Ρ Ο Π Ο Σ

1. Φ ο ύ σ κ ω μ α π ε ρ ι χ ε ι ρ ί δ α ς γ ρ ή γ ο ρ α 20-30 mmHg >SBP (ε ξ α φ ά ν ι σ η σ φ υ γ μ ο ύ κ ε ρ κ ι δ ι κ ή ς α ρ τ η ρ ί α ς)
2. Ξ ε φ ο ύ σ κ ω μ α 3mmHg/sec.
3. Η χ ο ι KOROTKOFF α σ θ ε ν ε ί ς : Σ ή κ ω μ α β ρ α χ ί ο ν α ,

Ι Δ Α Ν Ι Κ Η Μ Ε Τ Ρ Η Σ Η Α Π

Ε Ξ Ο Π Λ Ι Σ Μ Ο Σ

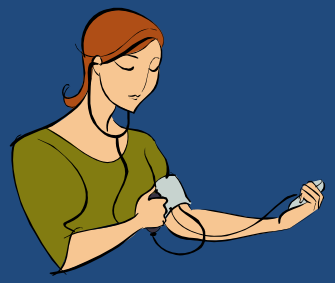
- Μ Ε Γ Ε Θ Ο Σ Π Ε Ρ Ι Χ Ε Ι Ρ Ι Δ Ο Σ : 2/3
  μ ή κ ο υ ς β ρ α χ ί ο ν α , ε ά ν ό χ ι π ά ν ω α π ό τ η ν β ρ α χ ι ό ν ι α α ρ τ η ρ ί α , μ ι κ ρ ή π ε ρ ι χ ε ι ρ ί δ α >> ΒΡ
- ΜΑΝΟΜΕΤΡΟ : Ρ ύ θ μ ι σ η α ν ά 6 *μ ή ν ε ς σ ε σ ύ γ κ ρ ι σ η μ ε υ δ ρ α ρ γ υ ρ ι κ ό*

ΙΔΑΝΙΚΗ ΜΕΤΡΗΣΗ ΑΠ

ΤΕΧΝΙΚΗ ΑΡΙΘΜΟΣ ΜΕΤΡΗΣΕΩΝ

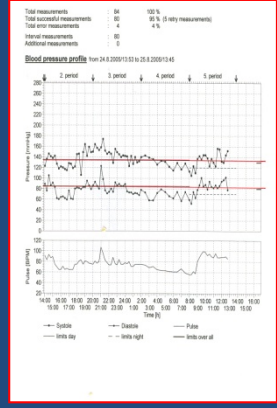
- 2 μετρήσεις απέχουσες μερικά min
- Διαφορά ΑΠ > 5 mmHg - επιπρόσθετες μετρήσεις μέχρι που δυο να είναι παραπλήσιες
- Για διάγνωση: 3 εκτιμήσεις με εβδομαδιαίο διάστημα

Home BP measurements



- Self-measurement of BP at home should be encouraged in order to:
  - provide information on effect of treatment, therapeutic coverage throughout the dose-to-dose time interval
  - improve patient's adherence to treatment regimens
- On the contrary, Self-measurement of BP should be discouraged when:
  - it causes anxiety to the patient
  - it induces self-modification of the treatment regimen

Ambulatory BP measurements



- Indications:
  - Marked variability of office BP
  - Marked discrepancy between office and home BP values
  - treament resistance
  - possible hypotensive episodes are suspected (elderly and DM)
  - when pre-eclampsia is suspected

BP thresholds (mmHg) for definition of Hypertension with different types of measurement

	SBP	DBP
Office or clinic	140	90
Home	130-135	85
24-hour	125-130	80
Day	130-135	85
Night	120	70

Particular conditions

Isolated office hypertension (White coat hypertension)

- Office BP persistently ≥ 140/90 mmHg
- Normal daytime ambulatory or home BP < 130-135/85

Due to stress and SNS stimulation. CV risk is less than by raised office and ambulatory or home BP but may be slightly greater than by normotension

Isolated ambulatory hypertension (Masked hypertension)

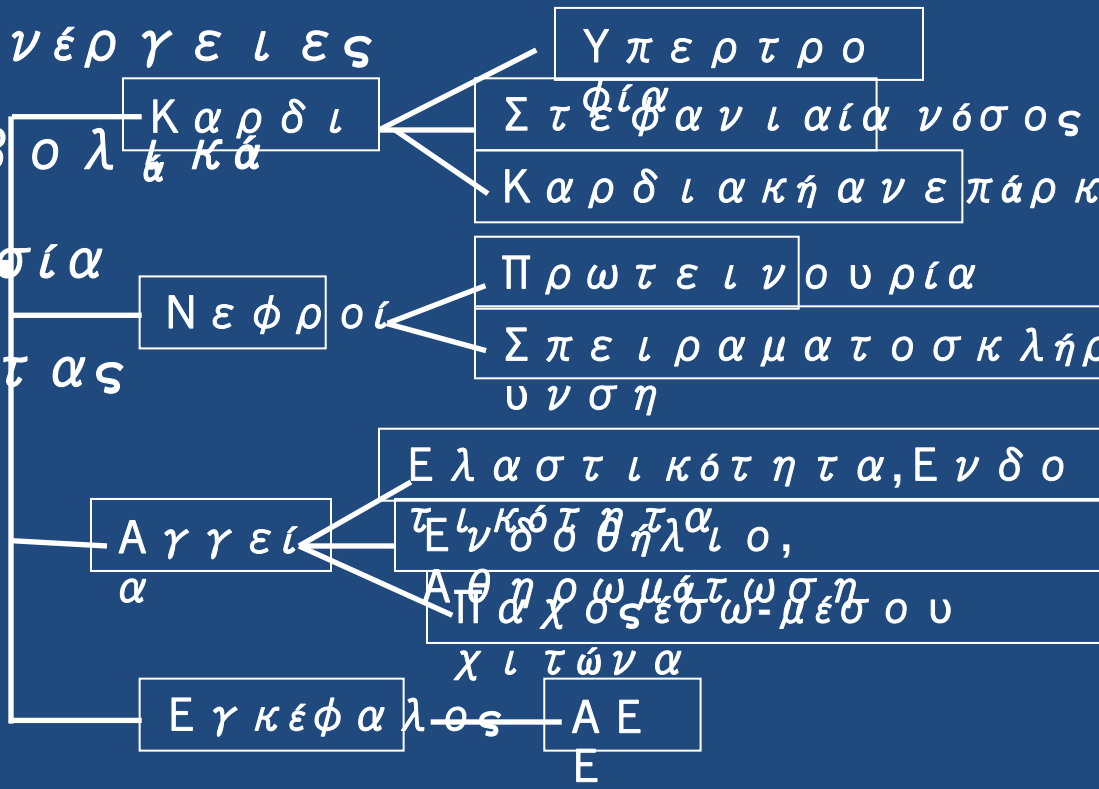
- Office BP persistently normal (< 140/90 mmHg)
- Elevated ambulatory (≥ 125-130/80 mmHg) or home BP (≥ 130-135/85 mmHg)

CV risk is close to that of hypertension.
Due to «normal» variation of circadian rhythm, autonomic nervous system dysfunction, physical or psychological stress, night consumption of alcohol, smoking and sleep apnea.

Θ ε ρ α π ε ί α
Α ρ τ η ρ ι α κ ή ς
Υ π έ ρ τ α σ η ς

Απαιτήσεις Αντιυπερτασικής Θεραπείας

- Αποτελεσματική μείωση ΑΠ
- 24-ωρη δράση
- Ελάχιστες παρενέργειες
- Ουδέτερη μεταβολική
- Οργανοπροστασία
- Μείωση θνητότητας



Goals of treatment

- Primary goal: maximum reduction in the long-term total risk of CV disease
- This requires not only the treatment of raised BP per se, but also of all associated reversible CV risk factors

Goals of treatment

- <140/90 mmHg

Treatment of hypertension

1. Non pharmacological

2. Pharmacological

Lifestyle changes

- smoking cessation
- weight reduction (and stabilization)
- physical exercise
- reduction of salt intake
- reduction of excessive alcohol intake
- increase in fruit and vegetable intake and decrease in saturated and total fat intake (Mediterranean diet)

Lifestyle changes

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Adoption of lifestyle changes

Recommendations	Class[a]	Level[b,d]	Level[b,e]	Ref.[c]
Salt restriction to 5–6 g per day is recommended.	I	A	B	339, 344–346, 351
Moderation of alcohol consumption to no more than 20–30 g of ethanol per day in men and to no more than 10–20 g of ethanol per day in women is recommended.	I	A	B	339, 354, 355
Increased consumption of vegetables, fruits, and low-fat dairy products is recommended.	I	A	B	339, 356–358
Reduction of weight to BMI of 25 kg/m^2 and of waist circumference to <102 cm in men and <88 cm in women is recommended, unless contraindicated.	I	A	B	339, 363–365
Regular exercise, i.e. at least 30 min of moderate dynamic exercise on 5 to 7 days per week is recommended.	I	A	B	339, 369, 373, 376
It is recommended to give all smokers advice to quit smoking and to offer assistance.	I	A	B	384–386

Initiation of antihypertensive treatment

Other risk factors, Target Organ Damage or disease	Normal SBP 120-129 or DBP 80-84	High normal SBP 130-139 or DBP 85-89	Grade 1 HT SBP 140-159 or DBP 90-99	Grade 2 HT SBP 160-179 or DBP 100-109	Grade 3 HT SBP ≥180 or DBP ≥110
No other risk factors	No BP intervention	No BP intervention	Lifestyle changes for several months then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + immediate drug treatment
1-2 risk factors	Lifestyle changes	Lifestyle changes	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + immediate drug treatment
≥3 risk factors, MS or TOD	Lifestyle changes	Lifestyle changes and consider drug treatment	Lifestyle changes + drug treatment	Lifestyle changes + drug treatment	Lifestyle changes + immediate drug treatment
Diabetes	Lifestyle changes	Lifestyle changes + drug treatment			
Established CV or renal disease	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment

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Established CV or renal disease	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment

Drug therapy

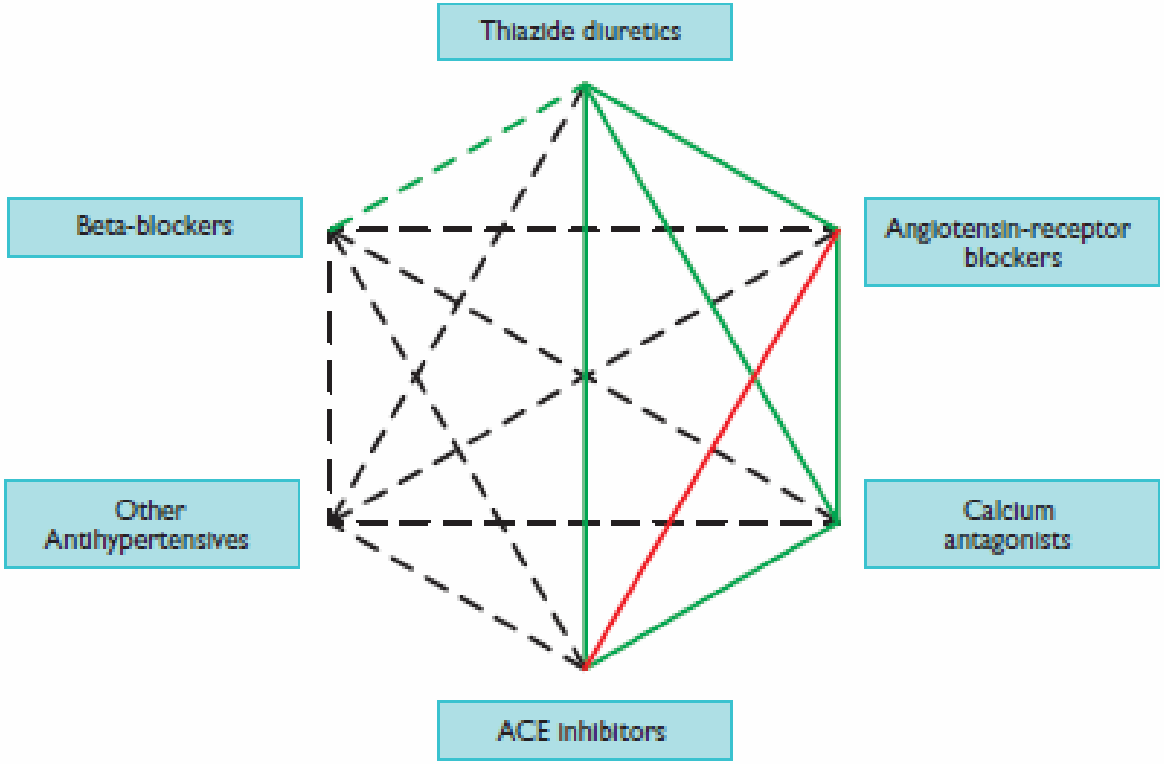

Figure 4 Possible combinations of classes of antihypertensive drugs. Green continuous lines: preferred combinations; green dashed line: useful combination (with some limitations); black dashed lines: possible but less well-tested combinations; red continuous line: not recommended combination. Although verapamil and diltiazem are sometimes used with a beta-blocker to improve ventricular rate control in permanent atrial fibrillation, only dihydropyridine calcium antagonists should normally be combined with beta-blockers.

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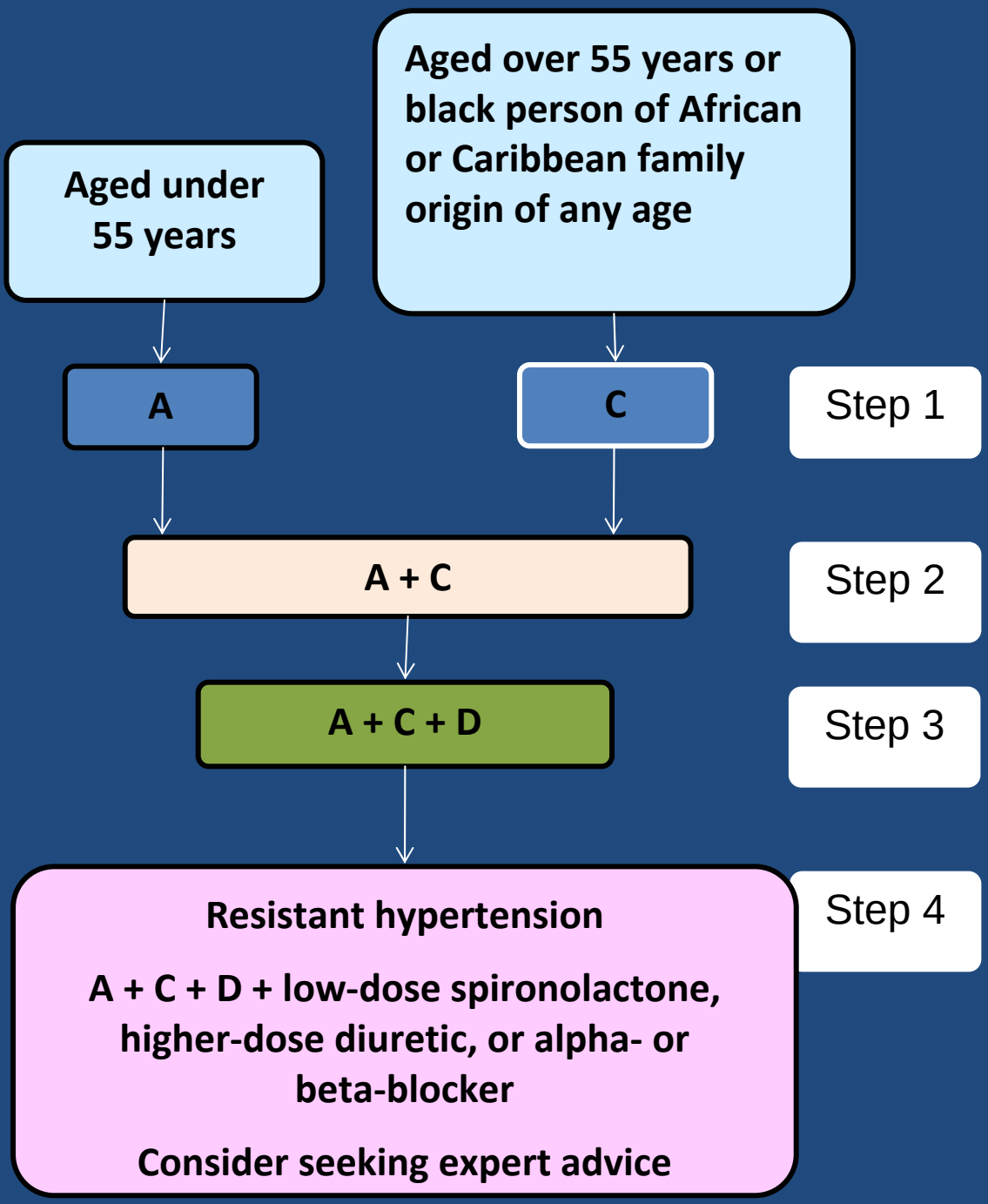
Summary of antihypertensive drug treatment



Key

A – ACE inhibitor or low-cost angiotensin II receptor blocker (ARB)[1]

C – Calcium-channel blocker (CCB)

D – Thiazide-like diuretic

Basic algorithm (NICE Guidelines 2011)

Step 1

- <55 years, ACEi (or ARB)
- >55 years, CCB (or thiazide, if CCD not tolerated or HF)

Step 2

- ACEi (or ARB) + CCB (or thiazide)

Step 3

- ACEi (or ARB) + CCB + thiazide

**Evaluation every 3-4 weeks*

Basic algorithm (NICE Guidelines 2011)

Step 4 (Resistant):

- Low-dose spironolactone (25 mg) if K<4.5 mmol/L
- Higher dose thiazide-like diuretic if K>4.5 mmol/L.
- β blocker
- α blocker

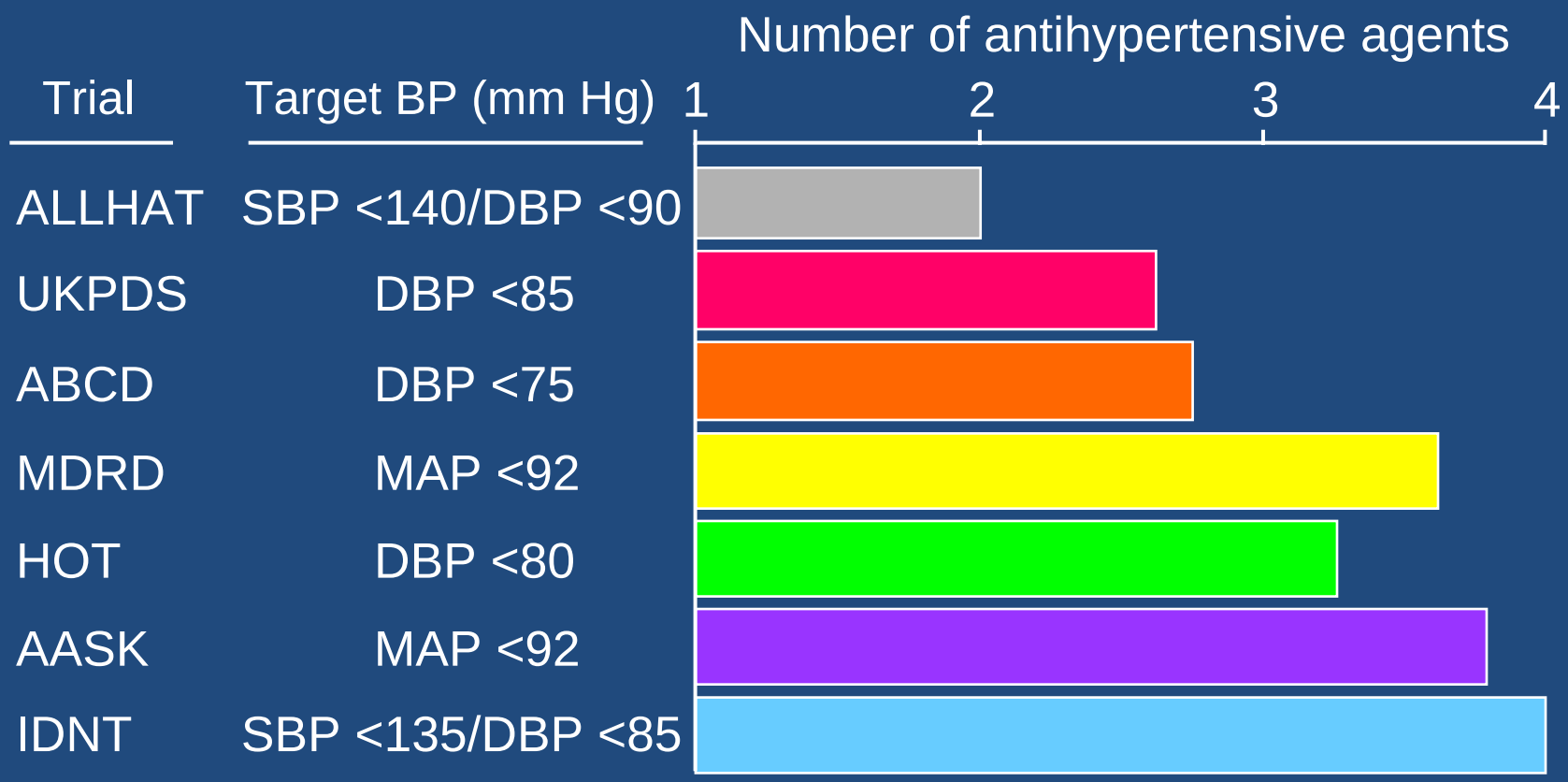
**Evaluation every 3-4 weeks*

JNC 7 Treatment Guidelines

- Consider initiating therapy with two drugs in patients whose BP is >20/10mmHg above goal (Stage 2 and Stage 1 patients at high risk)
- More than 2/3 of patients will require two or more agents

Chobanian et al., JAMA 2003; 289:2560–72,

Multiple Agents to Achieve Target BP



Trial	Target BP (mm Hg)
ALLHAT	SBP <140/DBP <90
UKPDS	DBP <85
ABCD	DBP <75
MDRD	MAP <92
HOT	DBP <80
AASK	MAP <92
IDNT	SBP <135/DBP <85

Bakris GL et al. *Am J Kidney Dis.* 2000;36:646-661.
Lewis EJ et al. *N Engl J Med.* 2001;345:851-860.
Cushman WC et al. *J Clin Hypertens*. 2002;4:393-405.

Combination therapy

<u>If BP>20 mmHg above target</u>

1.ACEi (or ARB) + CCB (or thiazide)

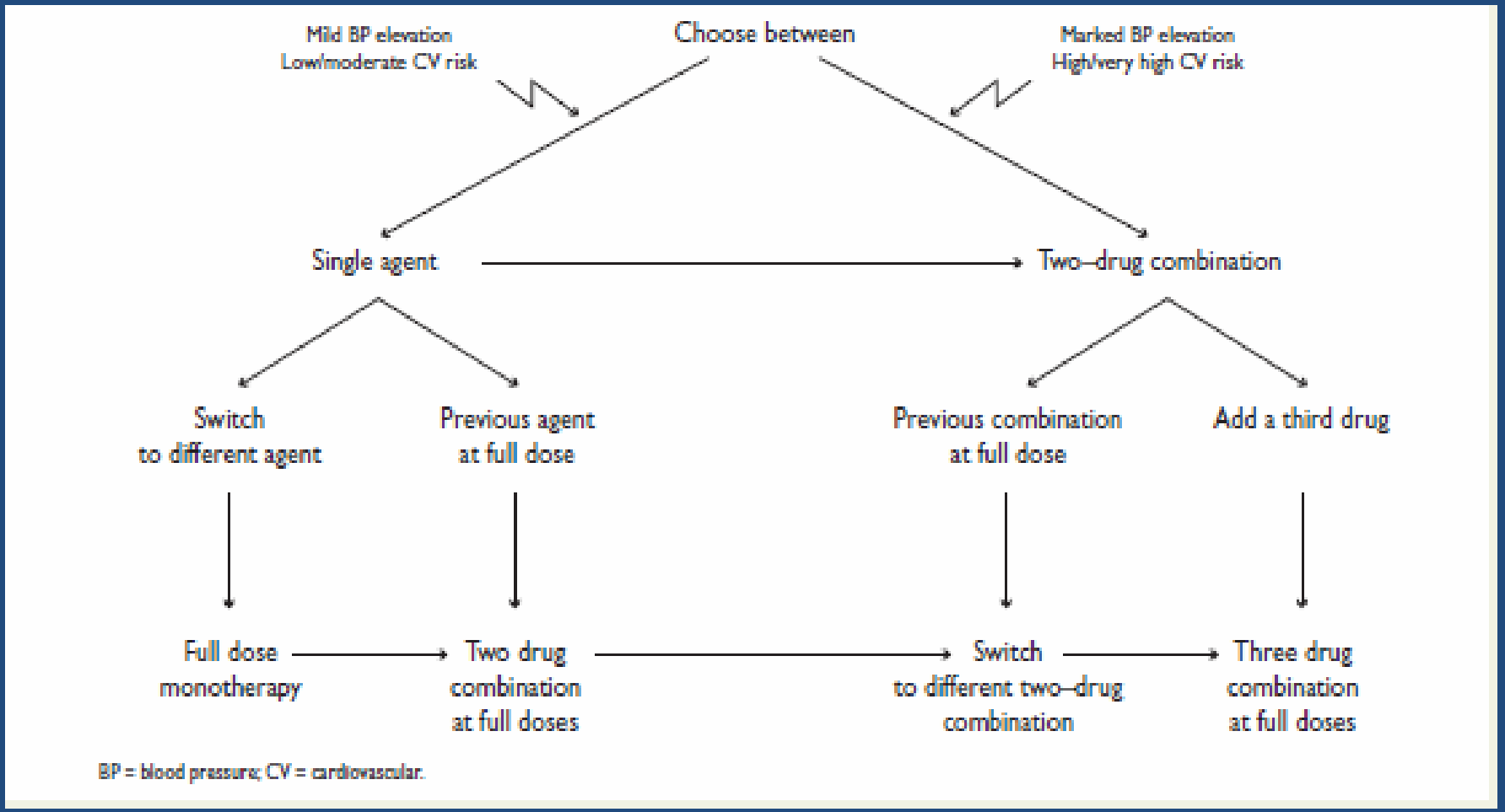
2.ACEi (or ARB) + CCB + thiazide

3.+ spironolactone or β blocker

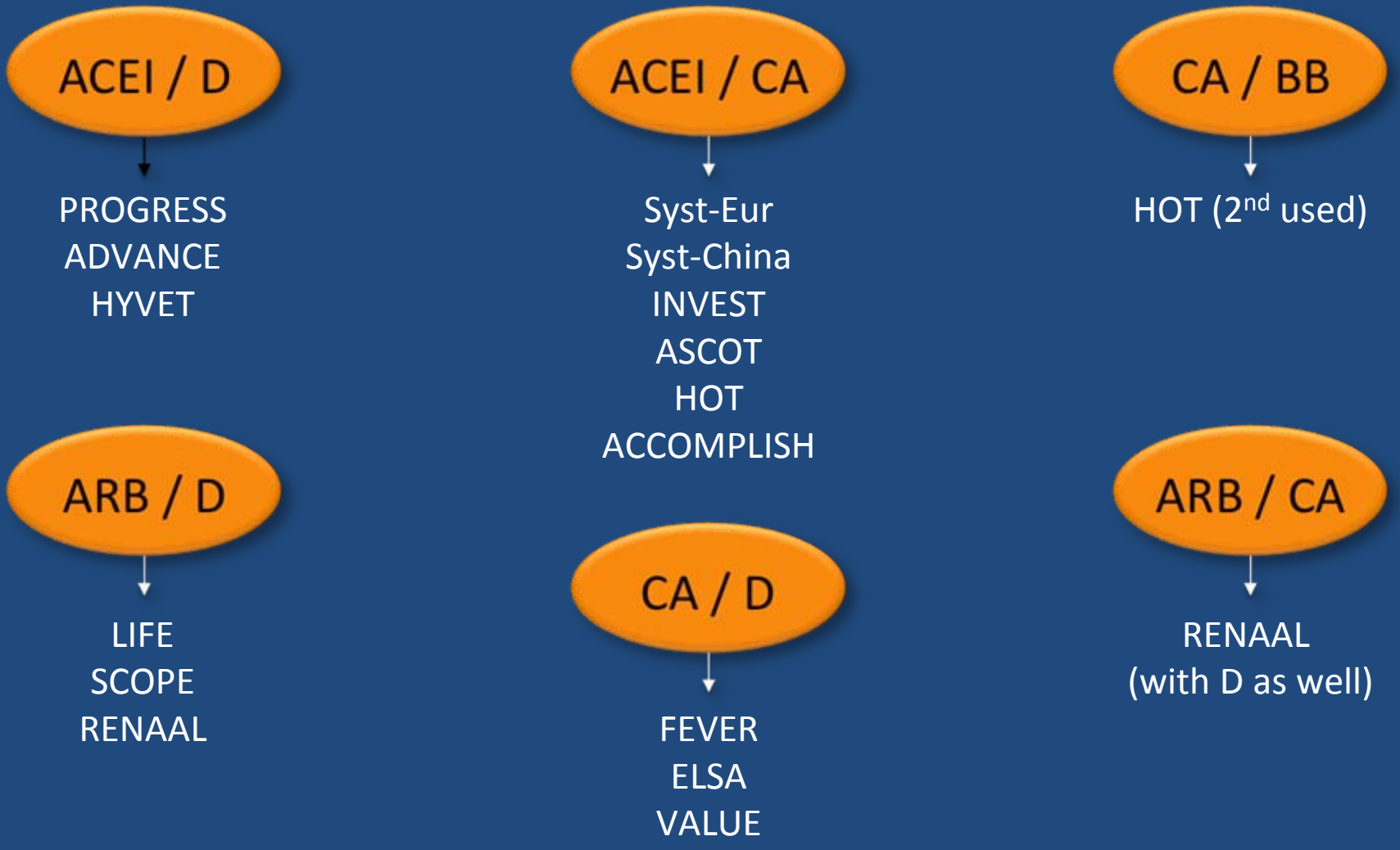
- **Evaluation every 3-4 weeks*

Sarafidis & Bakris, J Am Coll Cardiol 2008

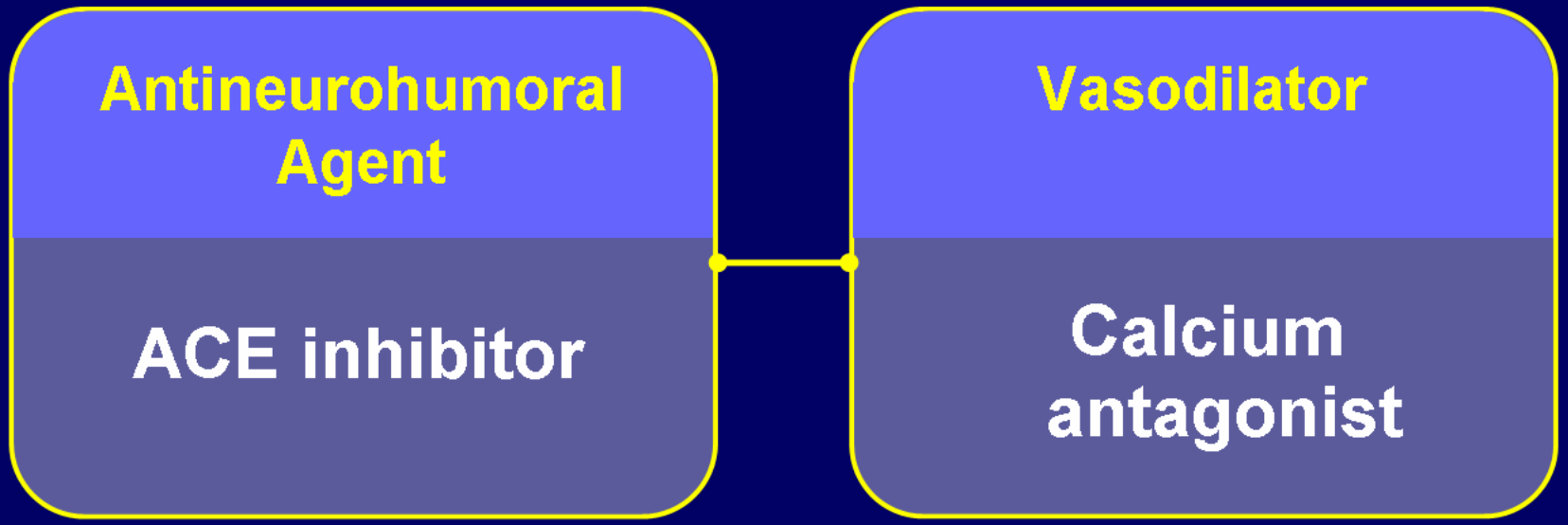
Combination therapy



Combinations Tested or Widely Used in Outcome (CV-renal events) Trials



Potential 2-Drug Strategies



CCB + ACE Inhibitor: Multiple Benefits

CCBs

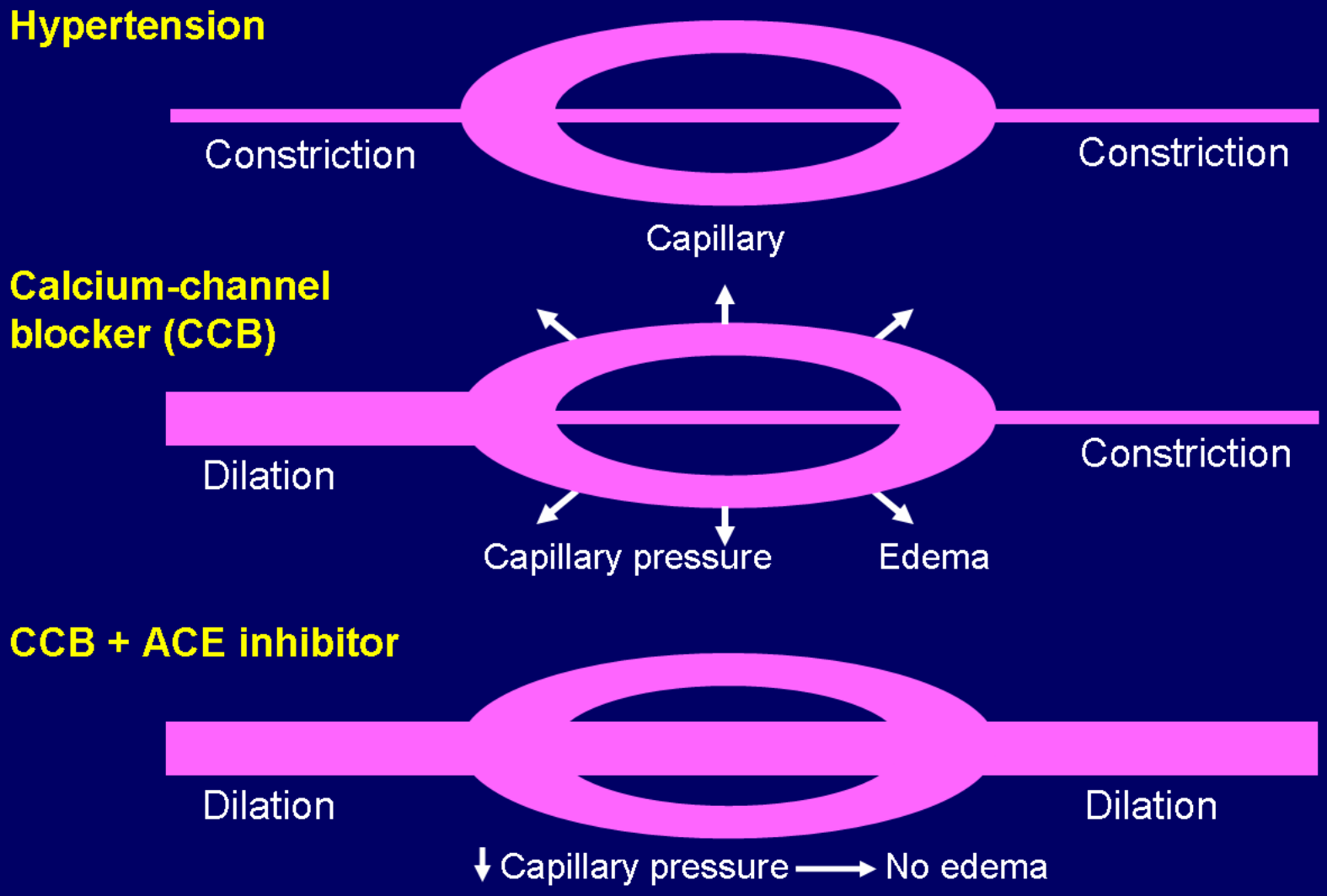
- Provide excellent efficacy
- Produce arterial vasodilation
- Show efficacy in low-renin hypertension or isolated systolic hypertension
- Work in all populations

ACE inhibitors

- Produce arterial and venous vasodilation
- Show efficacy in low-renin hypertension
- Work in many populations

Opie LH et al. In: *Drugs for the Heart*. 3rd ed. 1991:100-129.
Neutel JM, Smith DHG. *Hospital Med*. Oct. 1998.
Kloner RA et al. *Am J Cardiol*. 1996;77:713-722.
Fogari R et al. *Clin Drug Invest*. 1997;13(suppl 1):50-55.

Effect of CCB/ACE Inhibitor Combination Therapy on Capillary Pressure



Fixed-dose (or Single Tablet) Combinations

- Guidelines have long favoured the use of two-drug combinations in a single tablet (improvement in compliance which is low in hypertension)
- Single tablet combination can be the first treatment step when high CV risk makes early BP control desirable

Drug choice in certain conditions

Table 15 **Drugs to be preferred in specific conditions**

Condition	Drug
Asymptomatic organ damage	
LVH	ACE inhibitor, calcium antagonist, ARB
Asymptomatic atherosclerosis	Calcium antagonist, ACE inhibitor
Microalbuminuria	ACE inhibitor, ARB
Renal dysfunction	ACE inhibitor, ARB
Clinical CV event	
Previous stroke	Any agent effectively lowering BP
Previous myocardial infarction	BB, ACE inhibitor, ARB
Angina pectoris	BB, calcium antagonist
Heart failure	Diuretic, BB, ACE inhibitor, ARB, mineralocorticoid receptor antagonists
Aortic aneurysm	BB
Atrial fibrillation, prevention	Consider ARB, ACE inhibitor, BB or mineralocorticoid receptor antagonist
Atrial fibrillation, ventricular rate control	BB, non-dihydropyridine calcium antagonist
ESRD/proteinuria	ACE inhibitor, ARB
Peripheral artery disease	ACE inhibitor, calcium antagonist
Other	
ISH (elderly)	Diuretic, calcium antagonist
Metabolic syndrome	ACE inhibitor, ARB, calcium antagonist
Diabetes mellitus	ACE inhibitor, ARB
Pregnancy	Methyldopa, BB, calcium antagonist
Blacks	Diuretic, calcium antagonist

Main contraindications

Table 14 Compelling and possible contra-indications to the use of antihypertensive drugs

Drug	Compelling	Possible
Diuretics (thiazides)	Gout	Metabolic syndrome Glucose intolerance Pregnancy Hypercalcaemia Hypokalaemia
Beta-blockers	Asthma A–V block (grade 2 or 3)	Metabolic syndrome Glucose intolerance Athletes and physically active patients Chronic obstructive pulmonary disease (except for vasodilator beta-blockers)
Calcium antagonists (dihydropyridines)		Tachyarrhythmia Heart failure
Calcium antagonists (verapamil, diltiazem)	A–V block (grade 2 or 3, trifascicular block) Severe LV dysfunction Heart failure	
ACE inhibitors	Pregnancy Angioneurotic oedema Hyperkalaemia Bilateral renal artery stenosis	Women with child bearing potential
Angiotensin receptor blockers	Pregnancy Hyperkalaemia Bilateral renal artery stenosis	Women with child bearing potential
Mineralocorticoid receptor antagonists	Acute or severe renal failure (eGFR <30 mL/min) Hyperkalaemia	

BP therapy in the elderly

Antihypertensive treatment strategies in the elderly

Recommendations	Class [a]	Level [b]	Ref. [c]
In elderly hypertensives with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A	141, 265

Resistant hypertension

- failure to achieve goal BP* when a patient *adheres* to *adequate doses* of 3 antihypertensive drugs including a *diuretic*

* <140/90 mmHg or 130/80 mmHg in DM or CKD

Chobanian, Bakris, Black, et al. Hypertension 2003

Resistant hypertension

- failure to achieve goal BP* when a patient *adheres* to *adequate doses* of 3 antihypertensive drugs including a *diuretic*

≠ Uncontrolled hypertension

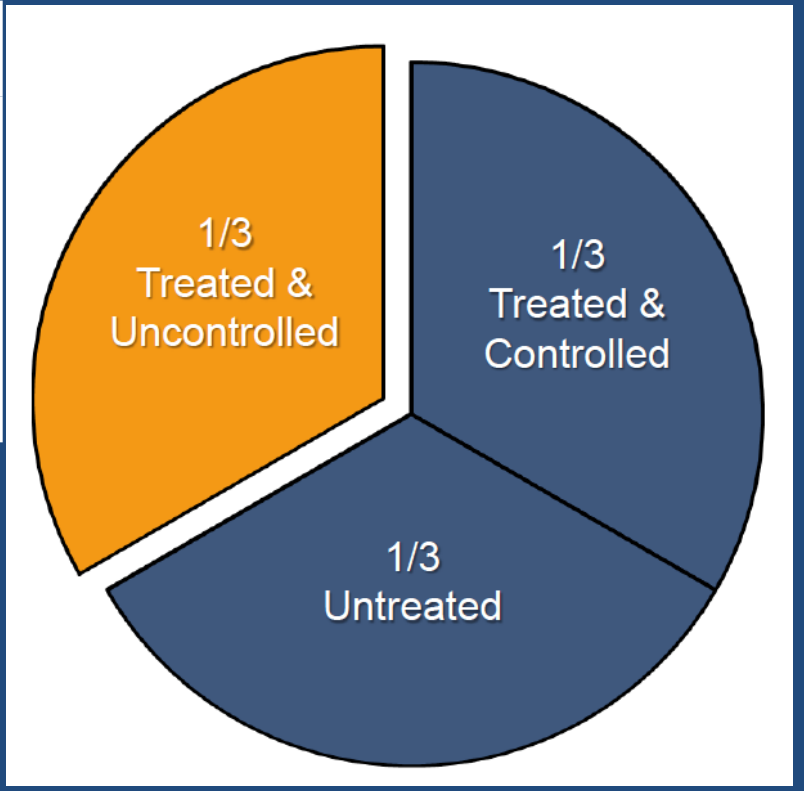
- failure to achieve goal BP while on treatment

* <140/90 mmHg or 130/80 mmHg in DM or CKD

Chobanian, Bakris, Black, et al. Hypertension 2003

Data on 13375 pts with hypertension between 1988-2008

Untreated	36%
Treated & controlled	33%
Treated & uncontrolled • 1-2 drugs • 3 or more drugs (Resistant)	31% • 24% • 7%



Egan et al, Circulation 2011

Causes of resistant hypertension

- Poor adherence to therapeutic plan
- Failure to modify lifestyle including:
  - weight gain
  - heavy alcohol intake (NB: binge drinking)
- Continued intake of drugs that raise blood pressure (liquorice, cocaine, glucocorticoids, non-steroid anti-inflammatory drugs, etc.)
- Obstructive sleep apnoea
- Unsuspected secondary cause
- Irreversible or scarcely reversible organ damage
- Volume overload due to:
  - inadequate diuretic therapy
  - progressive renal insufficiency
  - high sodium intake
  - hyperaldosteronism

Causes of spurious resistant hypertension:

- Isolated office (white-coat) hypertension
- Failure to use large cuff on large arm
- Pseudohypertension

Secondary hypertension

- Renal: reno-parechymal, reno-vascular
- Endocrine: aldosteronism, phoecromocytoma Cushing hyperthyroidism
- Sleep apnea
- Aortic coarctation
- Intracranial tumors

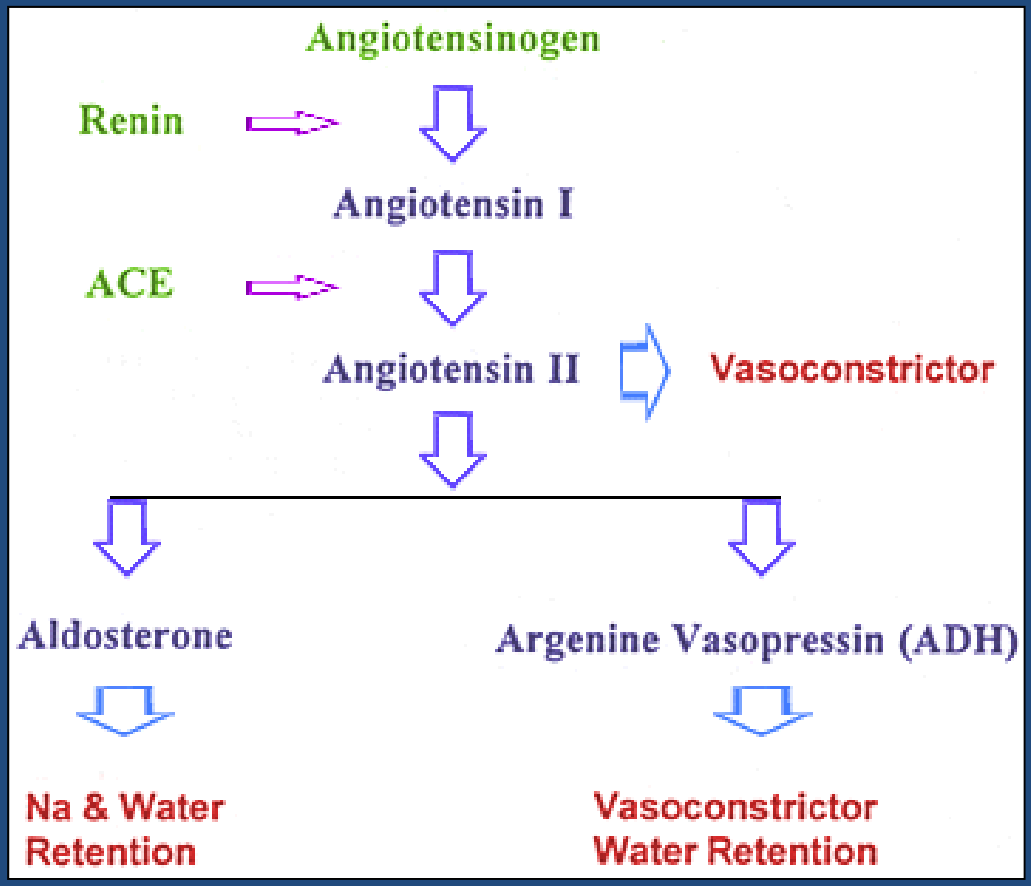
- *Check for secondary HT in young!*

Novel approaches to hypertension treatment

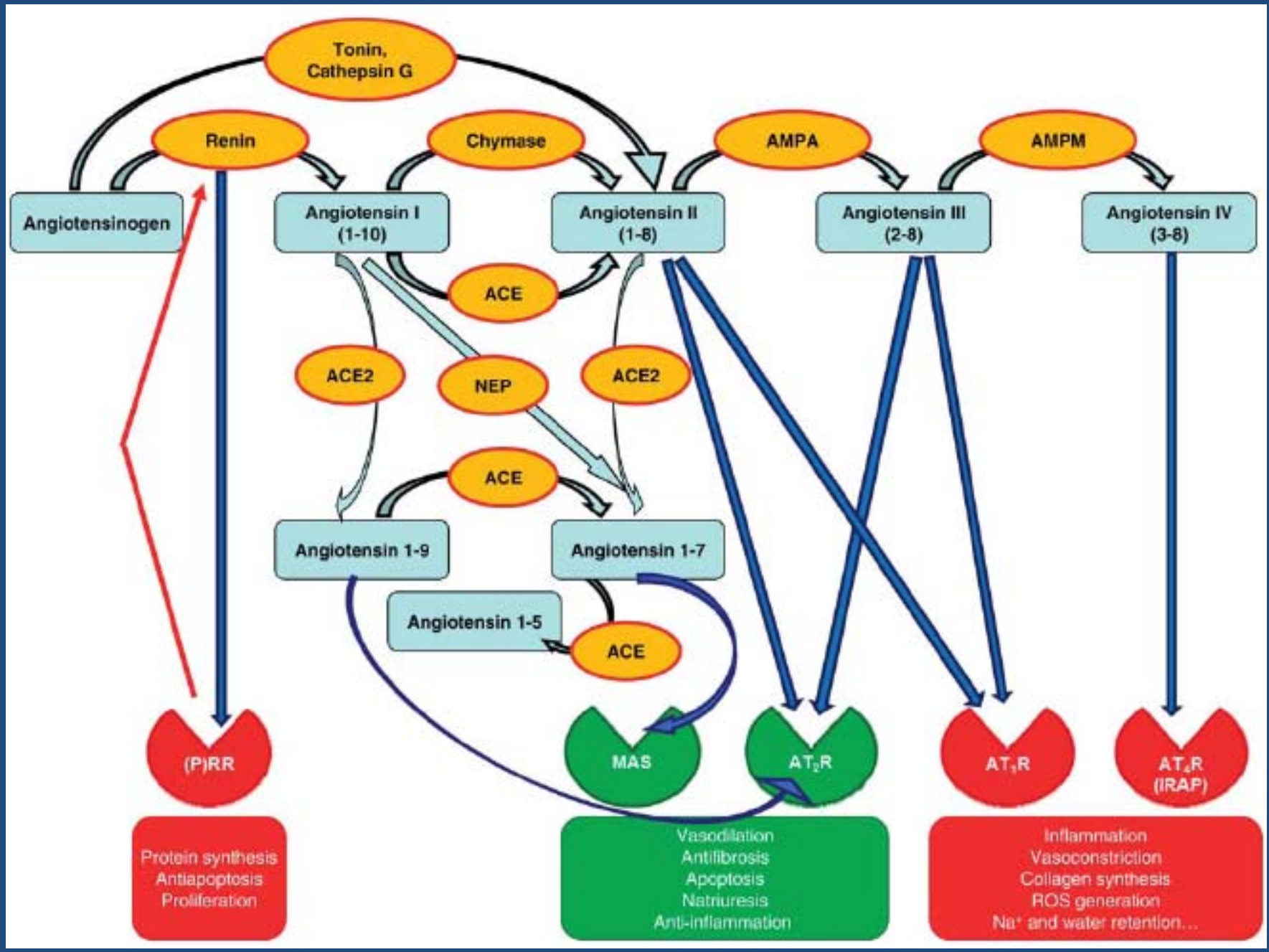
1. New drugs
   - targeting traditional pathways (e.g. RAAS)
   - targeting less-well studied pathways (e.g. endothelin)
   - fixed combinations
2. Gene and vaccine therapies
3. Device-based therapies:
   - renal sympathetic denervation
   - baroreflex activation

Unger et al. Eur Heart J 2011

The RAAS



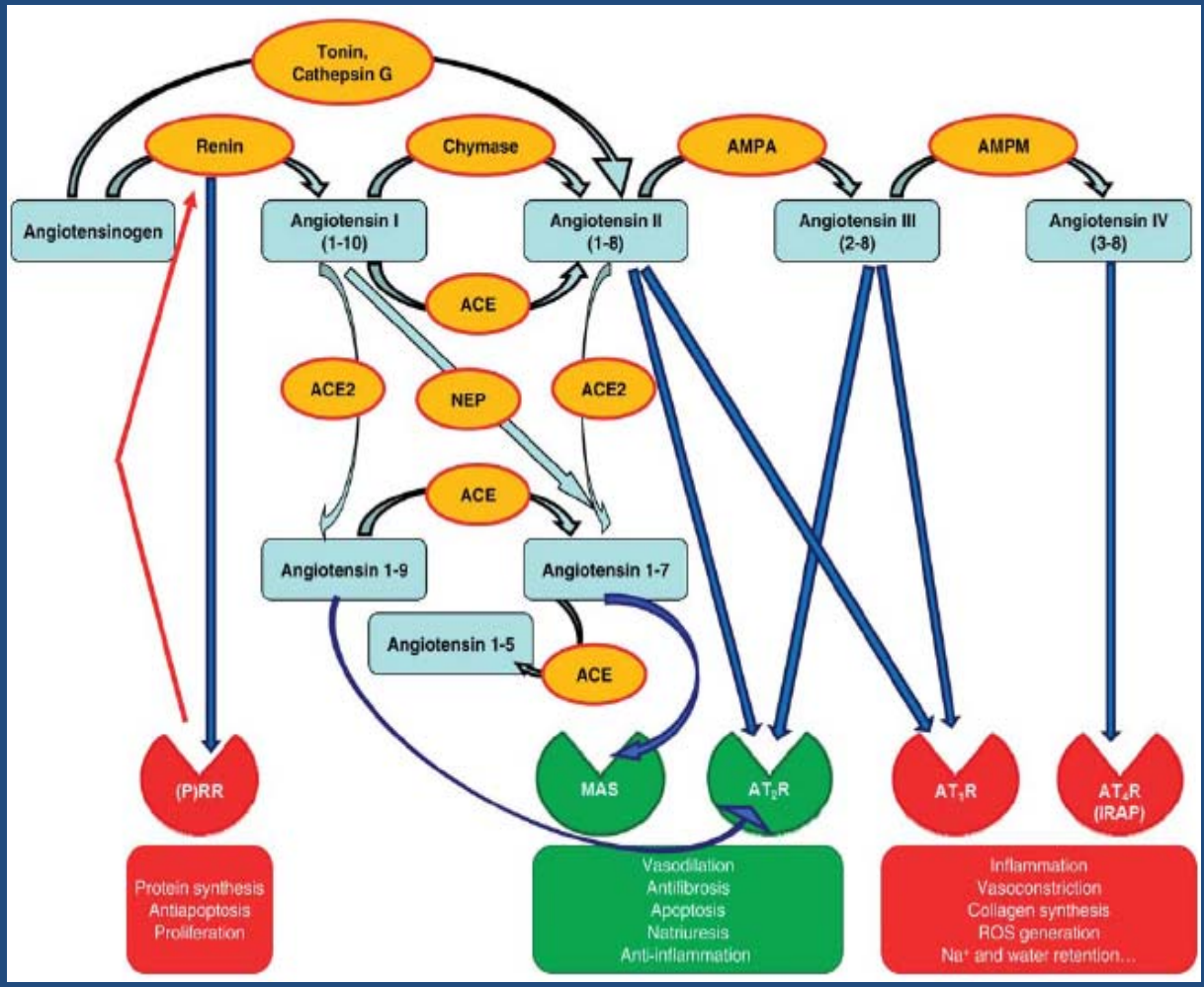
… once upon a time



Unger et al. Eur Heart J 2011

New drugs: RAAS I

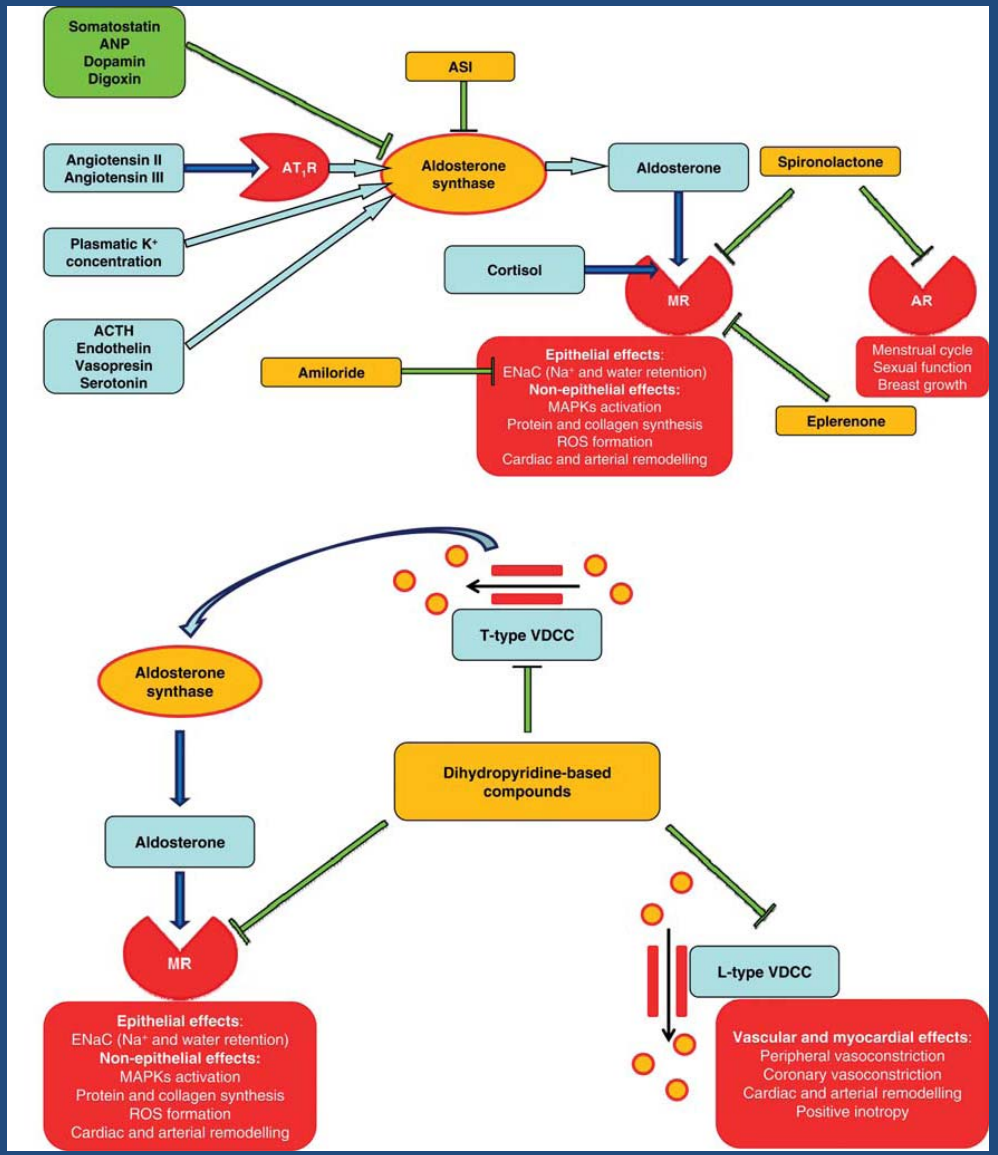
- Renin inhibitors (aliskiren)
- Prorenin receptor antagonists (controversial data)
- Vasopeptidase inhibitors (AT1R/NEP antagonists)



Unger et al. Eur Heart J 2011

New drugs: RAAS II

- Aldosterone receptor antagonists (CCB with dual action)
- Aldosterone synthase inhibitors



Unger et al. Eur Heart J 2011

Vaccines & gene therapy

- Vaccines
  - against Angiotensin I & II

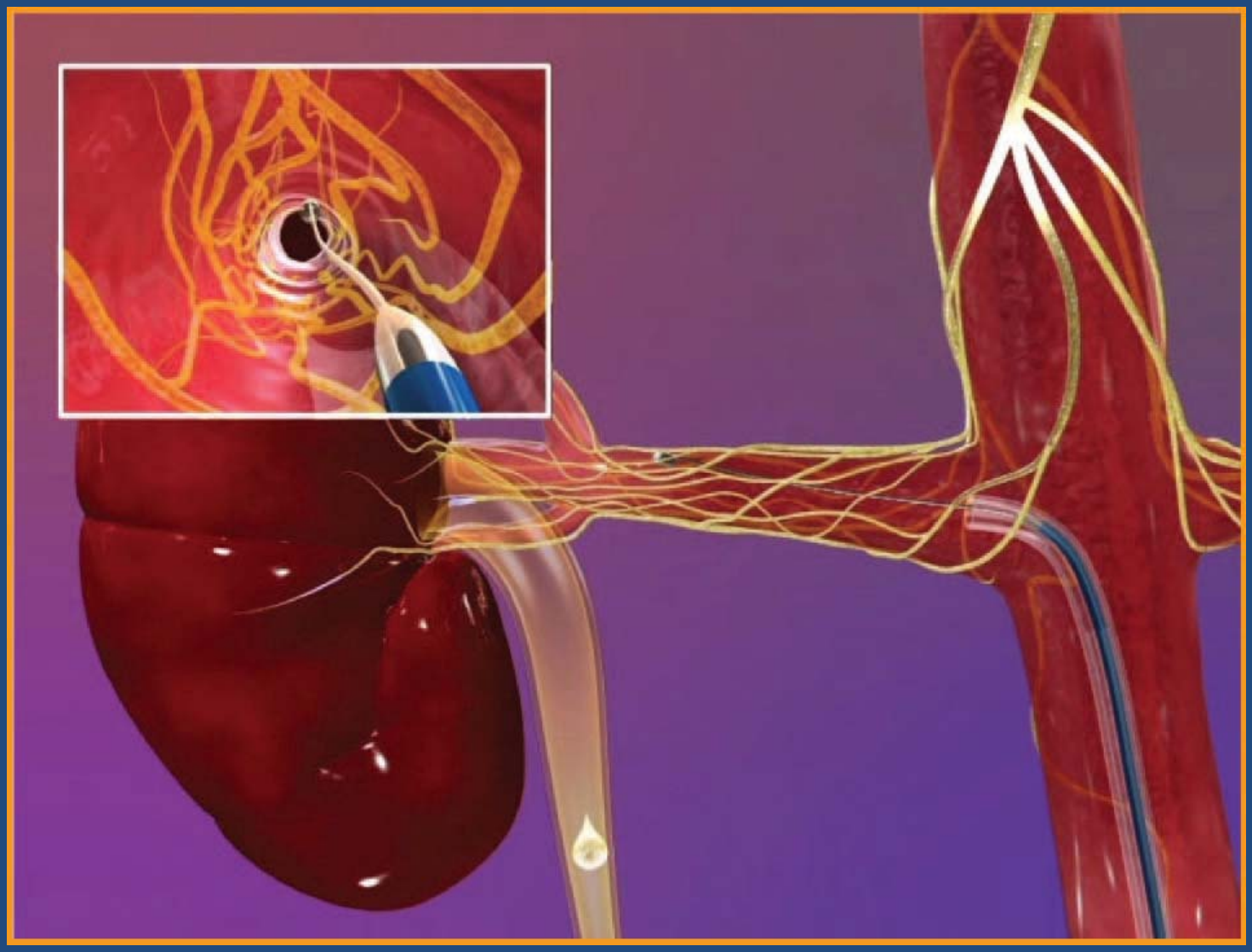
- Gene therapy
  - Gene transfer (AT_2R, ACE2 etc)
  - Antisense cDNA (AT_1R, ACE etc)

Unger et al. Eur Heart J 2011

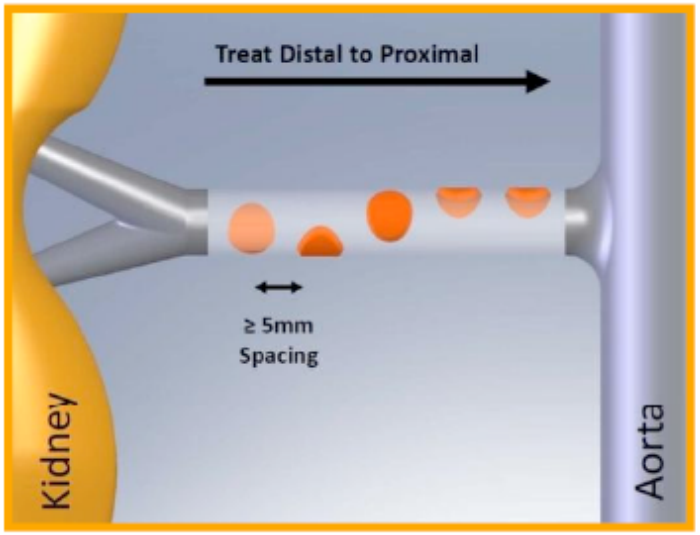
Device-based therapies

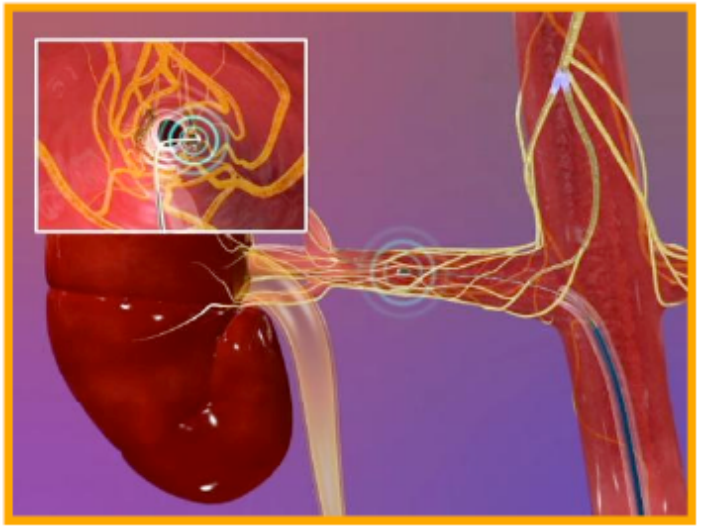
- Renal sympathetic denervation
- Baroreflex activation

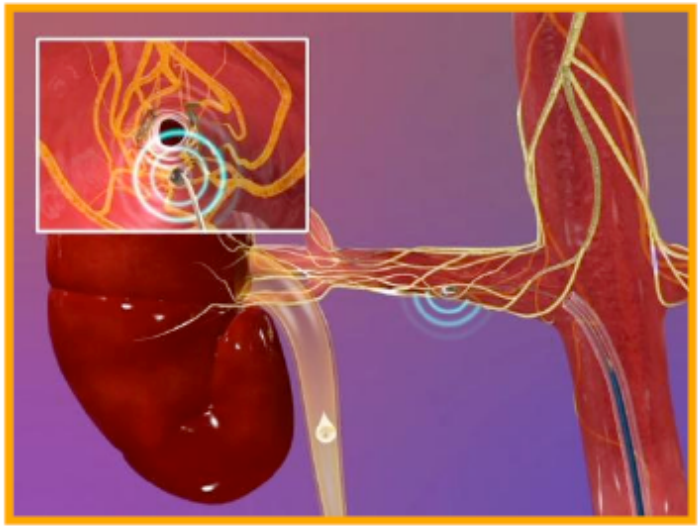
Renal sympathetic ablation

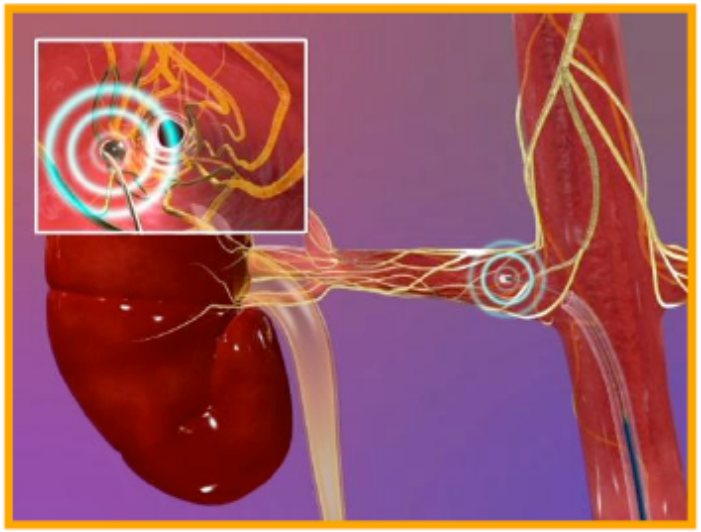


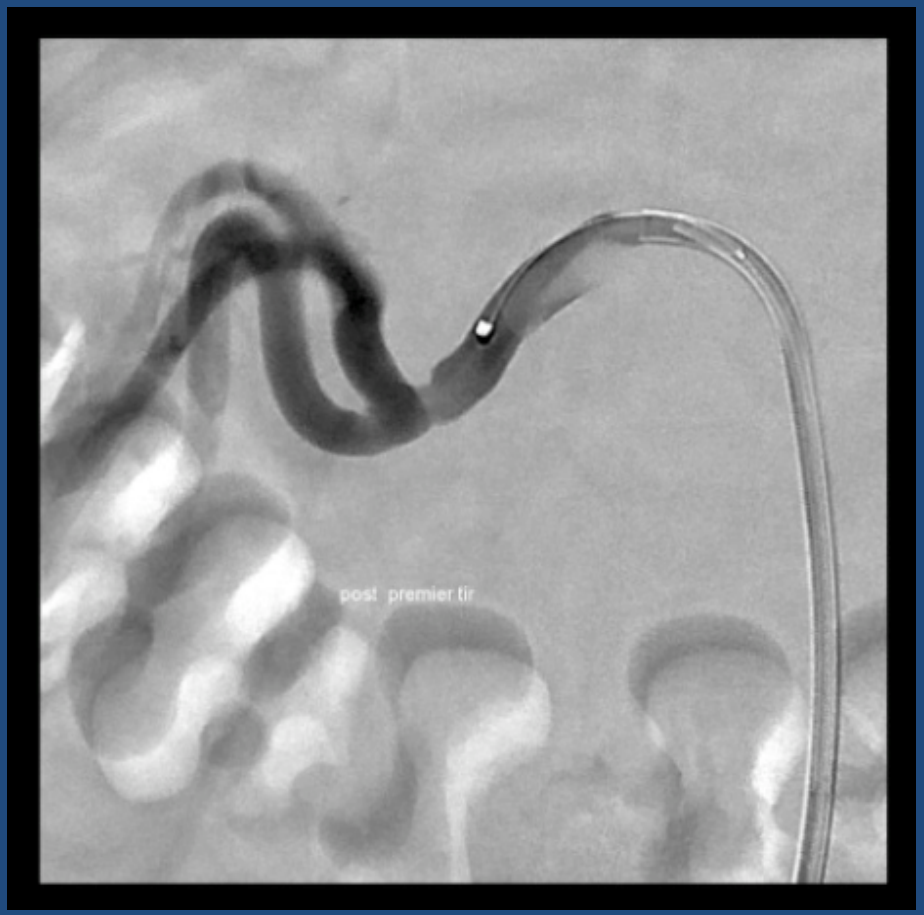
MULTIPLE DISCRETE TREATMENTS MAXIMIZE NERVE COVERAGE WITHOUT APPLYING CIRCUMFERENTIAL ENERGY IN A SINGLE SEGMENT.







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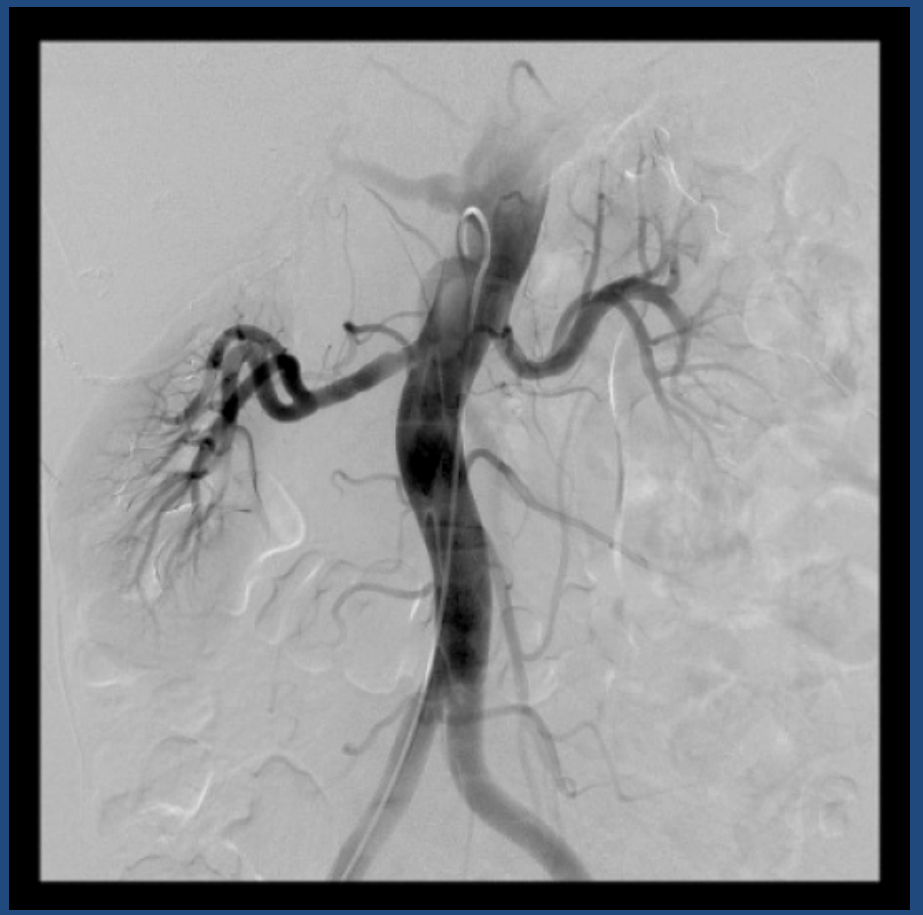
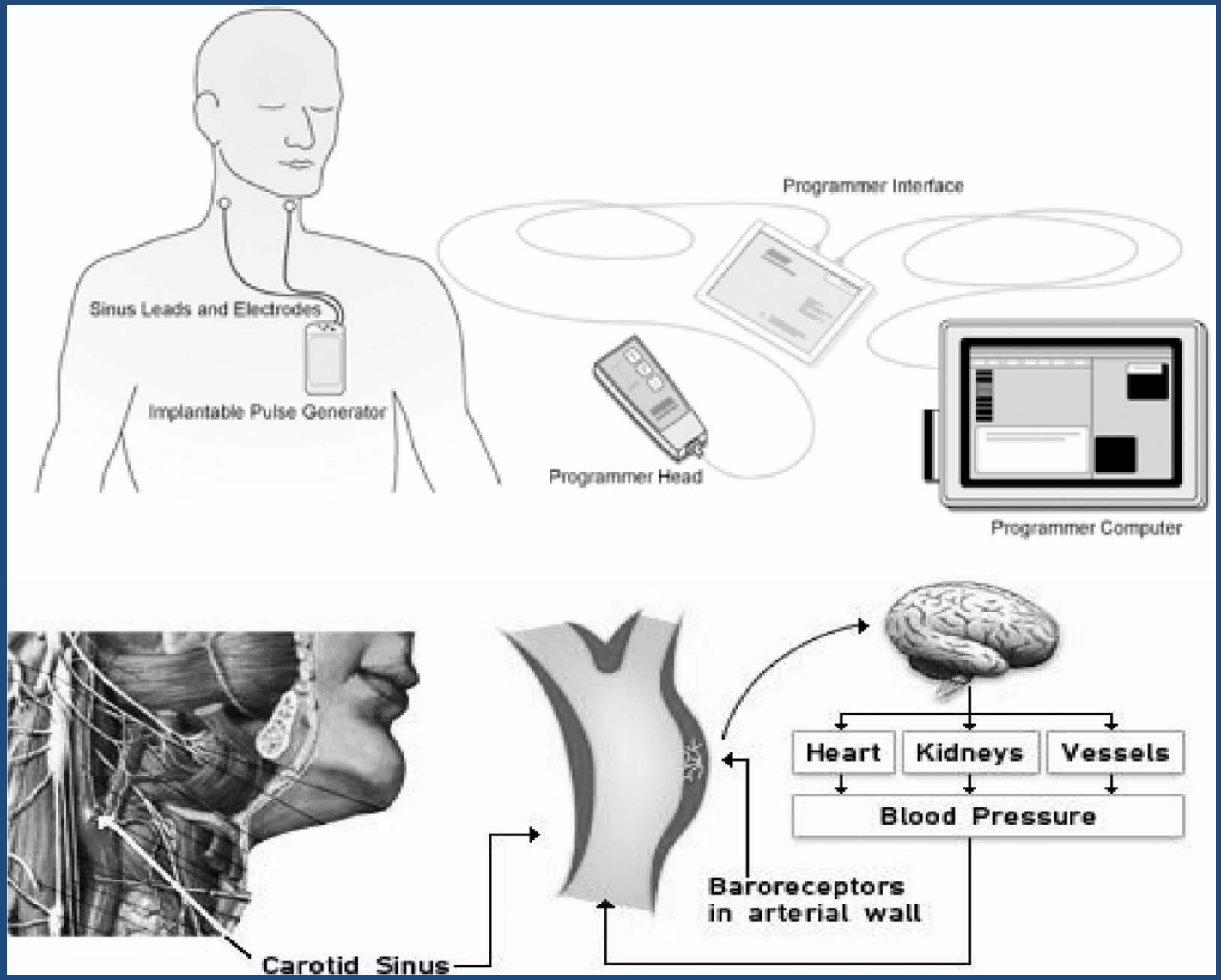
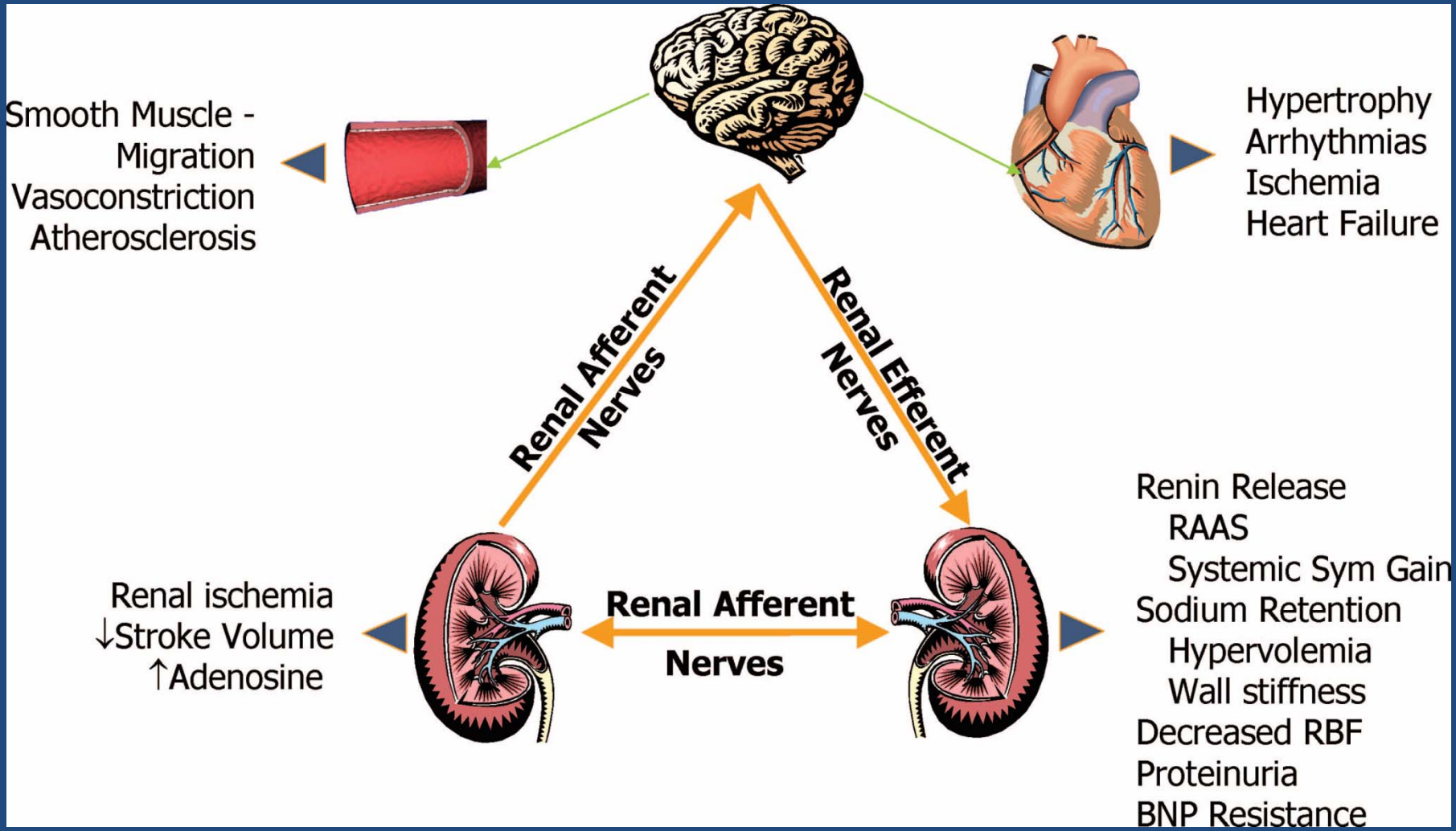


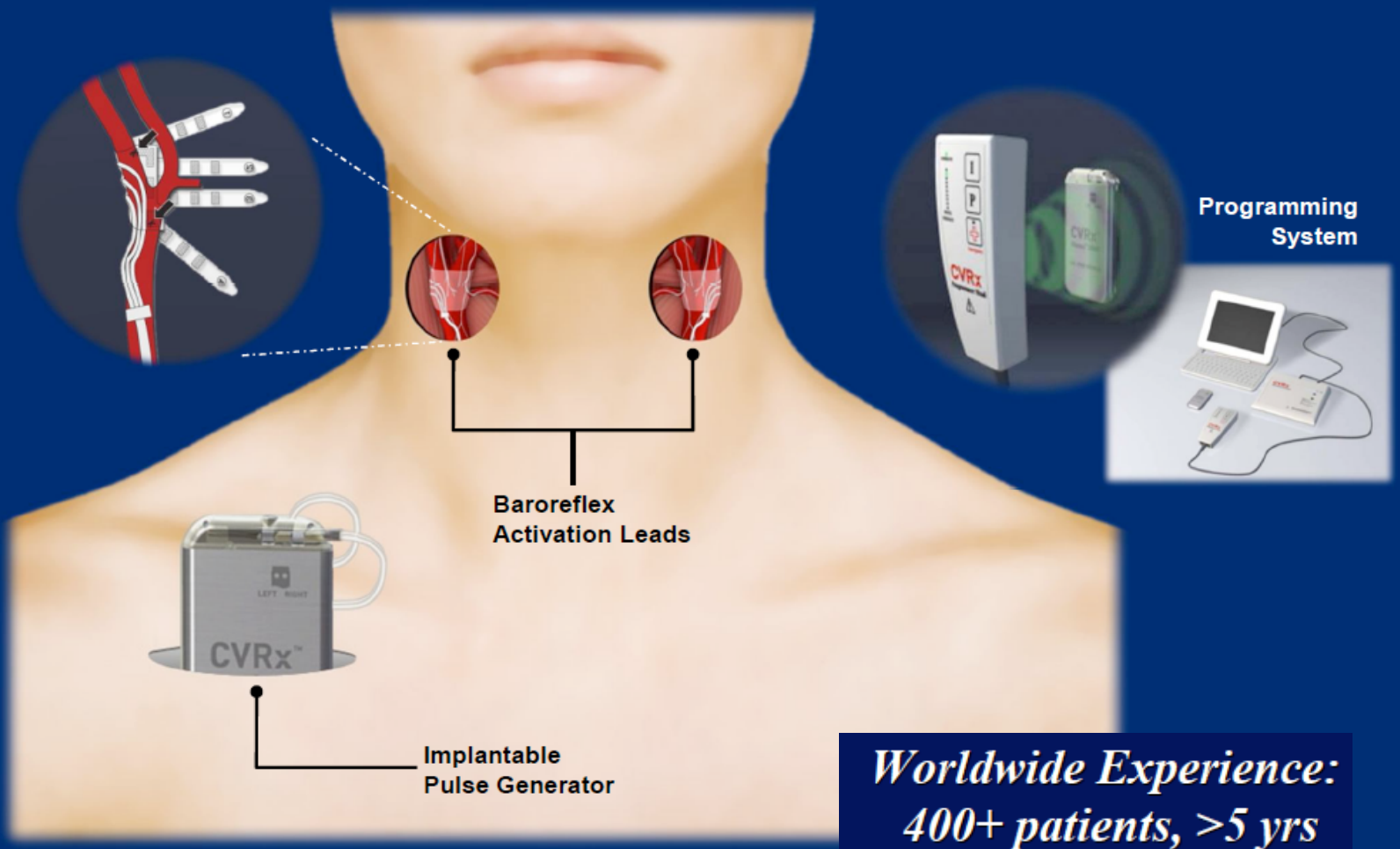
Rheos system



Actions of renal sympathetic afferent and efferent nerves



Baroreflex Activation Therapy (BAT)
The 1st Generation Rheos® System



Worldwide Experience: 400+ patients, >5 yrs