Αρτηριακή Υπέρταση

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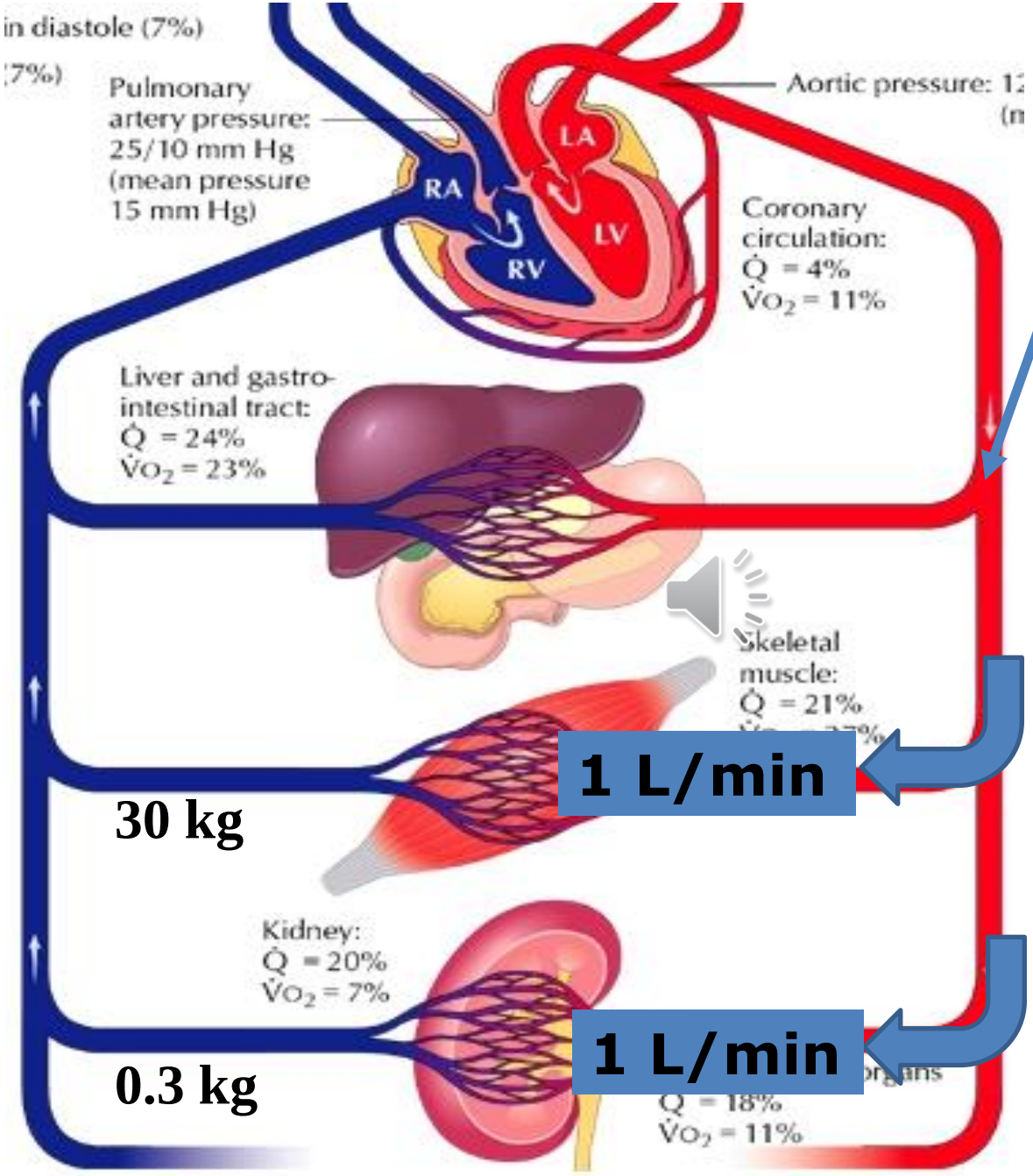
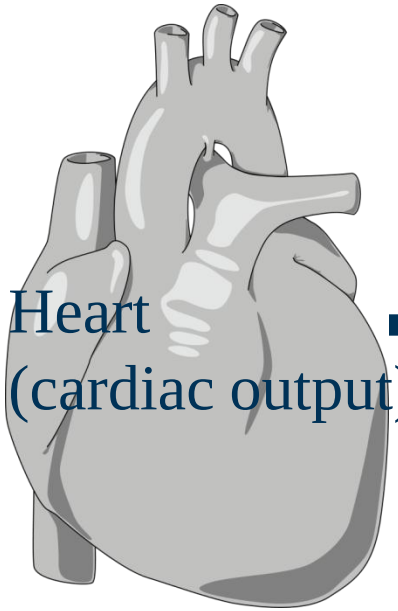
Χαϊδάρι



EFFECTIVE VOLUME

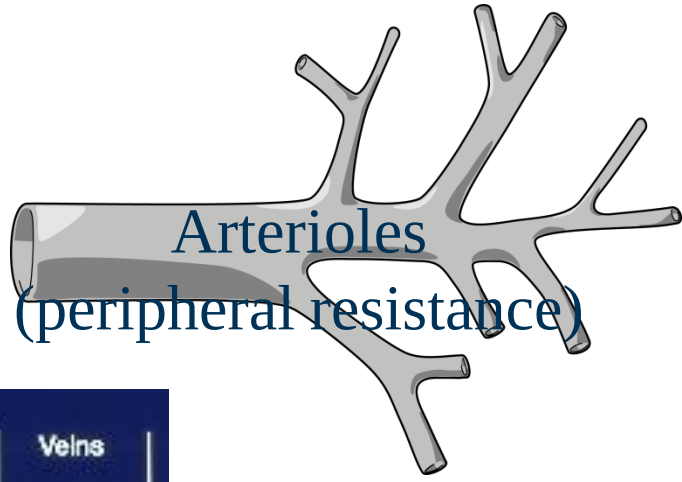
$$V = I \times R$$

Blood Pressure = Cardiac Output x Peripheral Vascular Resistance

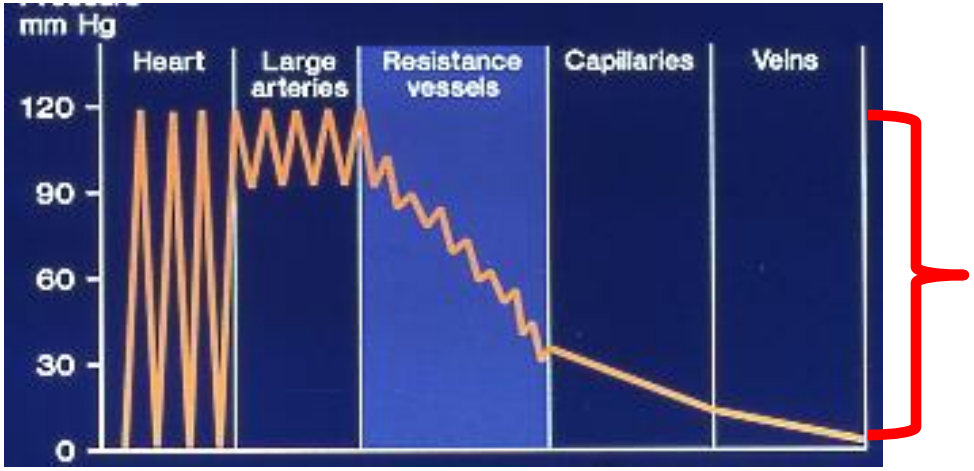


Heart
(cardiac output)

Arteries
(blood pressure)



Arterioles
(peripheral resistance)

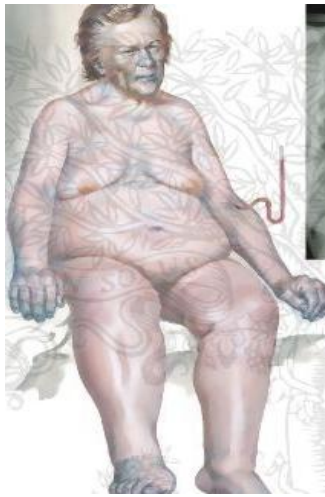


Beevers G et al. BMJ 2001; 322:912-916

ΚΛΟΑ

Μάζα Να κ.φ.

ευογκαιμία



ΧΡΟΝΙΩΣ

ΟΞΕΩΣ

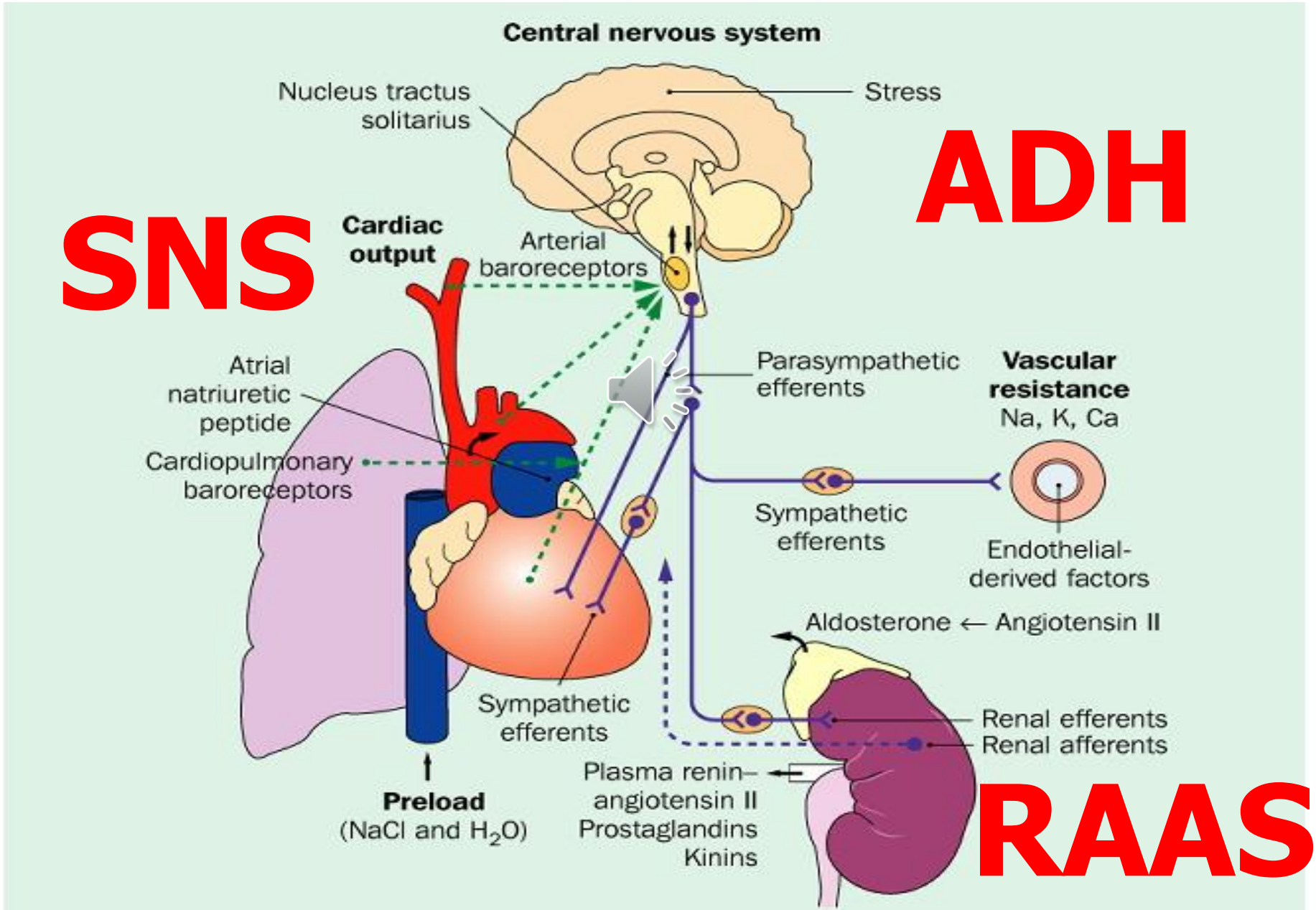
Μάζα Να ↑

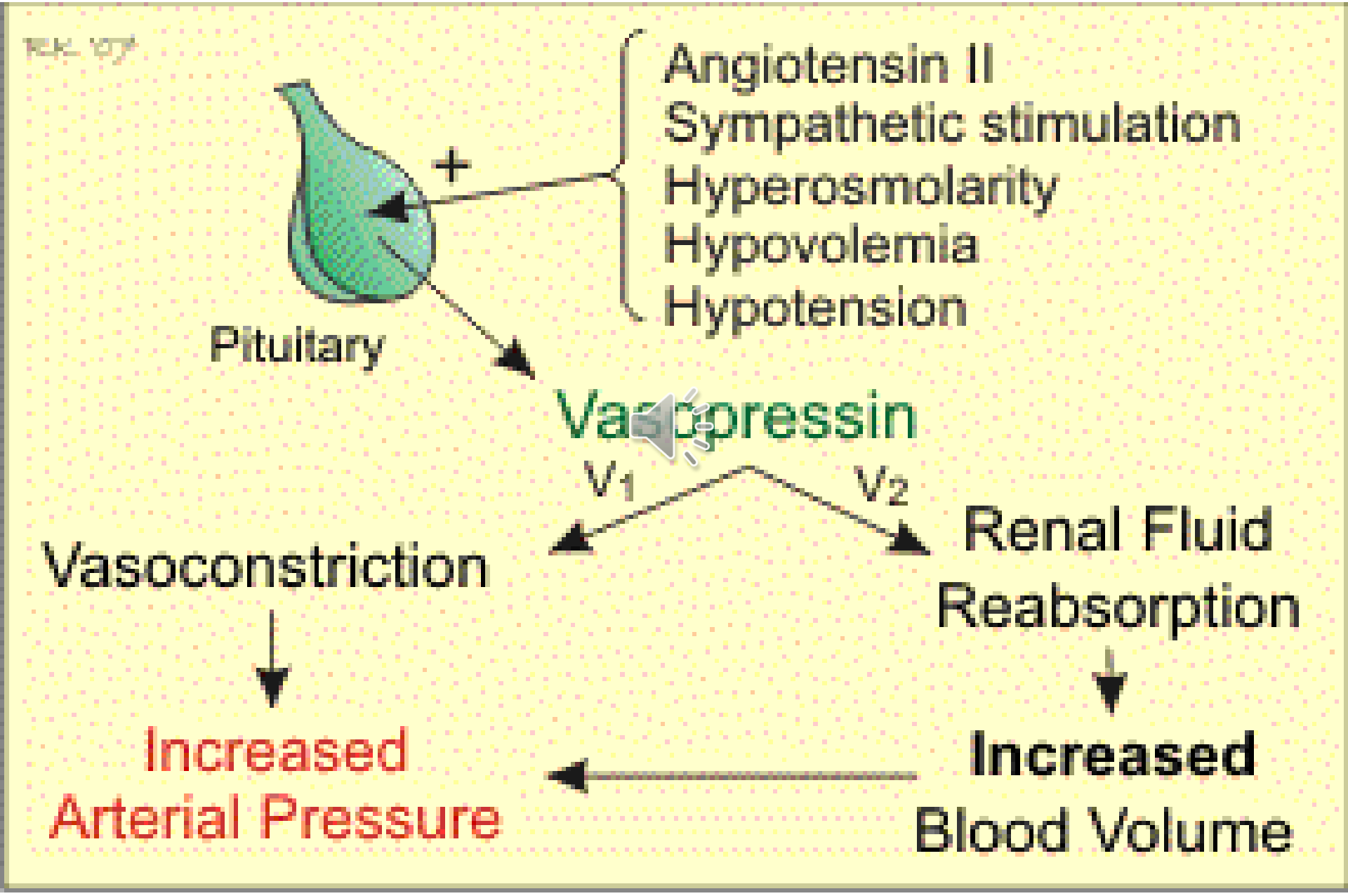
Μάζα Να ↓

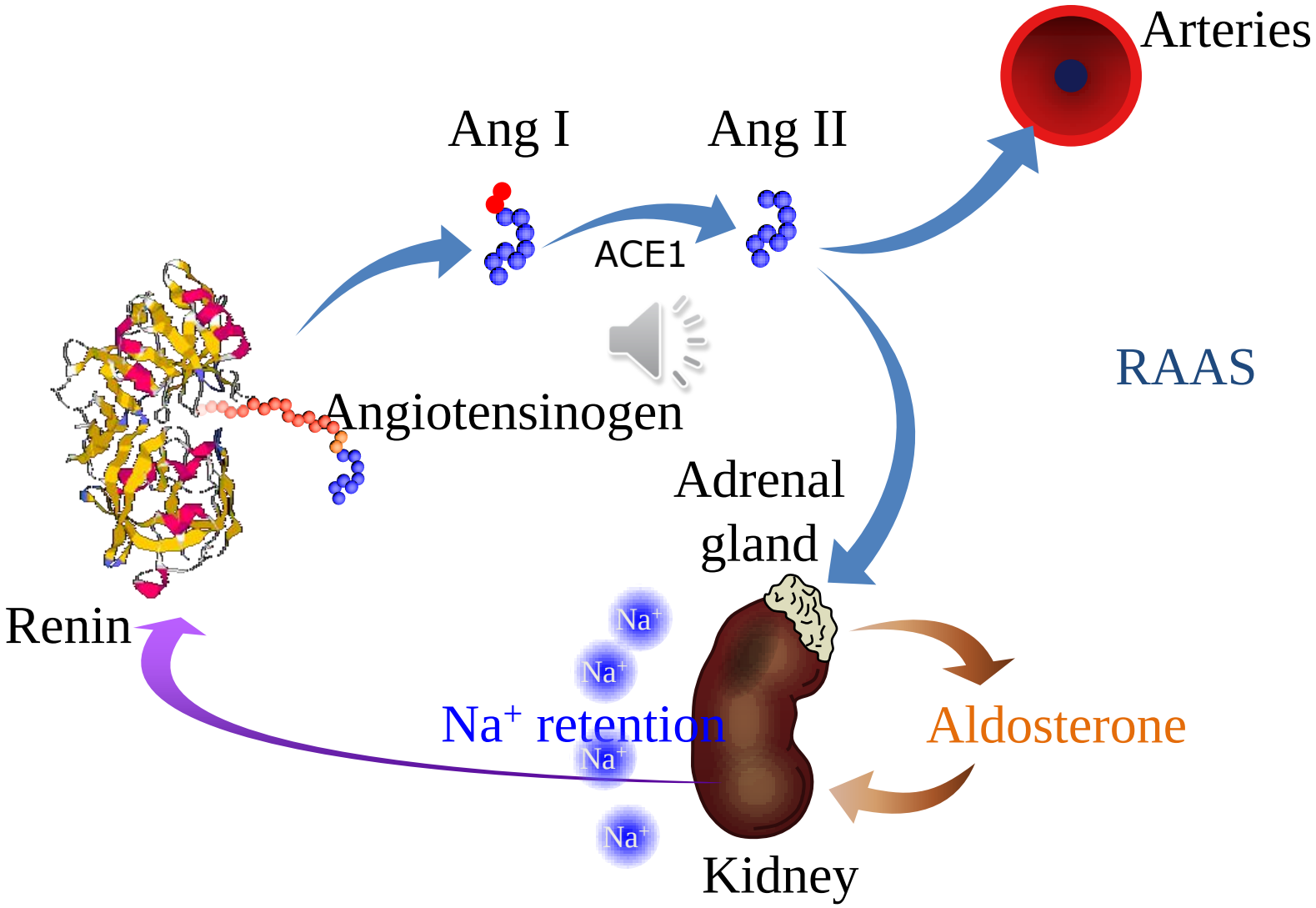
υπερογκαιμία

υποογκαιμία

Πίεση ενσφηνώσεως


Central nervous system
Nucleus tractus solitarius
Stress
ADH
SNS
Cardiac output
Arterial baroreceptors
Atrial natriuretic peptide
Cardiopulmonary baroreceptors
Parasympathetic efferents
Vascular resistance
Na, K, Ca
Sympathetic efferents
Endothelial-derived factors
Aldosterone ← Angiotensin II
Sympathetic efferents
Renal efferents
Renal afferents
Plasma renin–angiotensin II
Prostaglandins
Kinins
RAAS
Preload
(NaCl and H_2O)


Angiotensin II
Sympathetic stimulation
Hyperosmolarity
Hypovolemia
Hypotension
+
Pituitary
Vasopressin
V1
V2
Vasoconstriction
Renal Fluid Reabsorption
Increased Arterial Pressure
Increased Blood Volume


Arteries
Ang I
Ang II
ACE1
RAAS
Angiotensinogen
Adrenal gland
Renin
Na+
Na+
Na+ retention
Na+
Na+
Aldosterone
Kidney

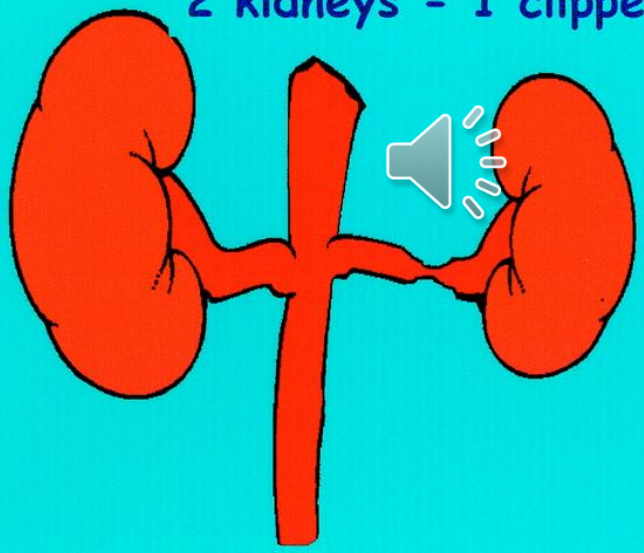
Sympathetic Nervous System

- Sympathetic system activation produces
  - vasoconstriction
  - reflex tachycardia
  - increased cardiac output
- The actions of the sympathetic system are rapid and account for **second to second blood pressure control**

GOLDBLATT HYPERTENSION

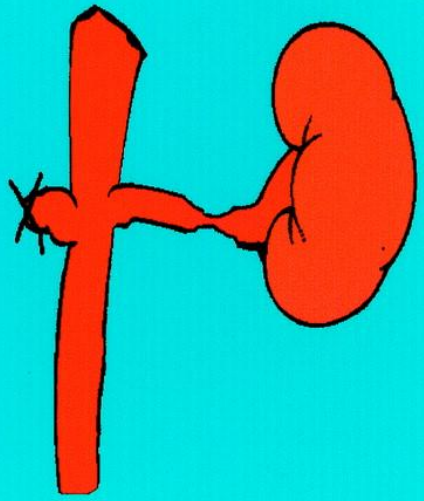
Experimental Models

2 kidneys - 1 clipped



BP	Renin	Volume
High	High	Normal or decreased

1 kidney - 1 clipped

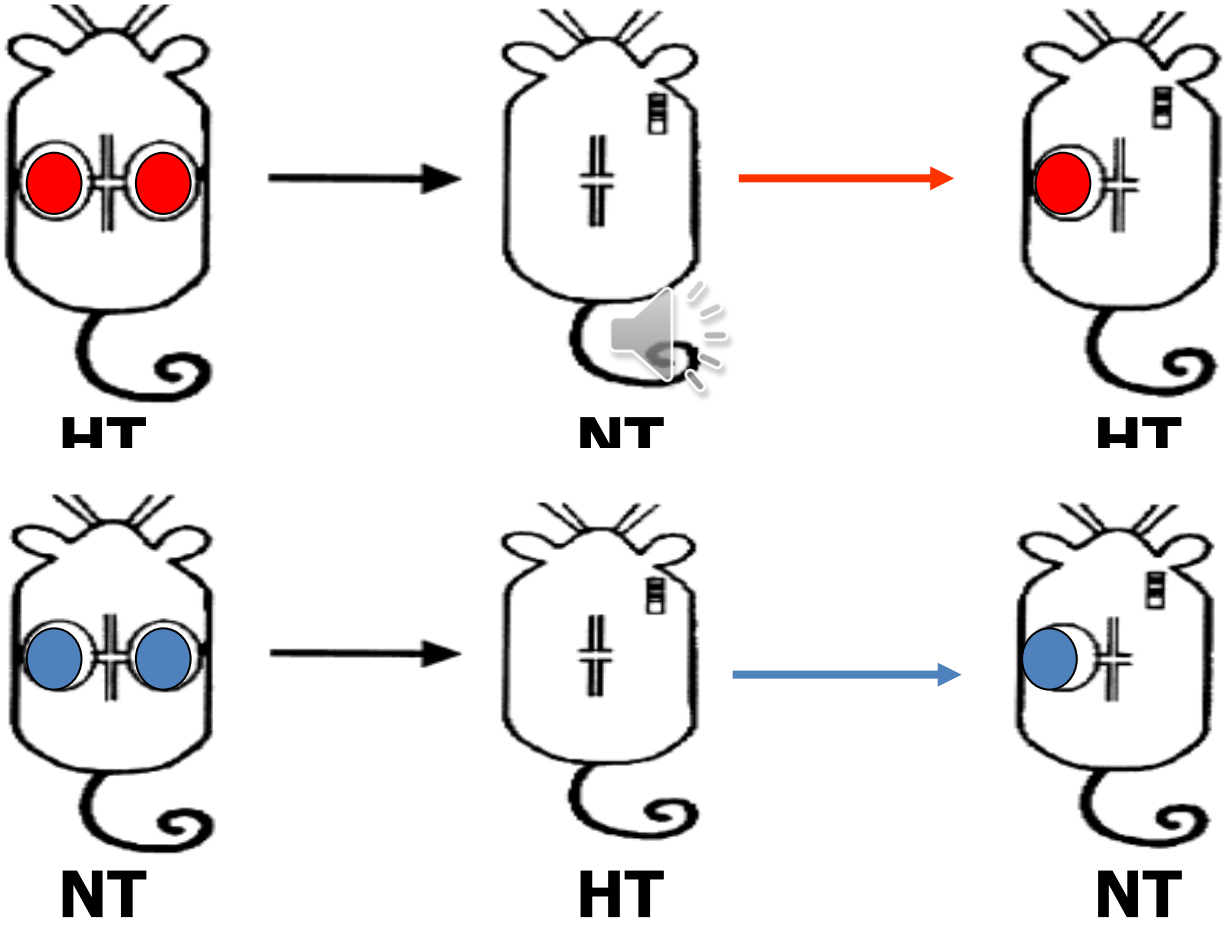


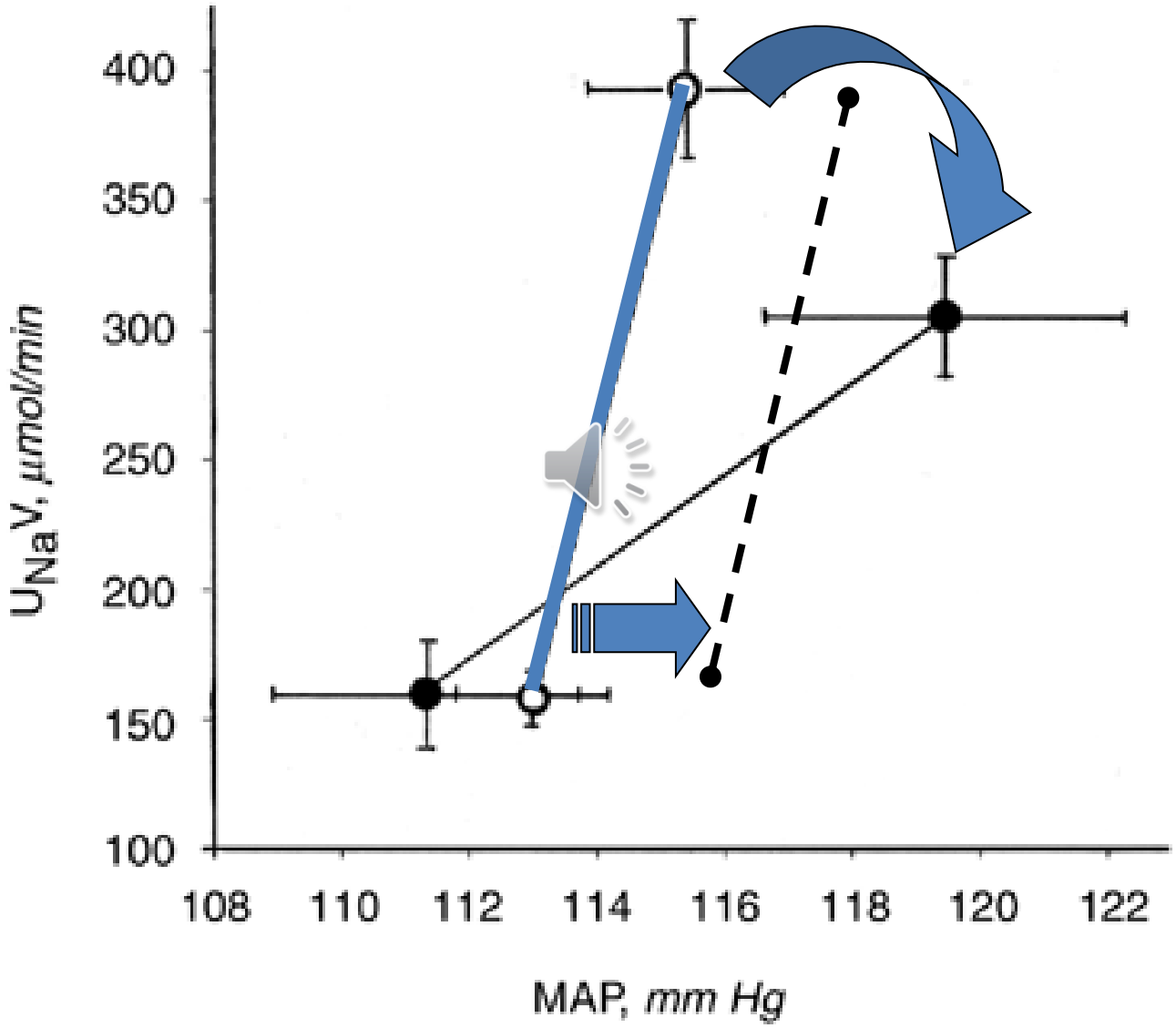
BP	Renin	Volume
High	Normal	High

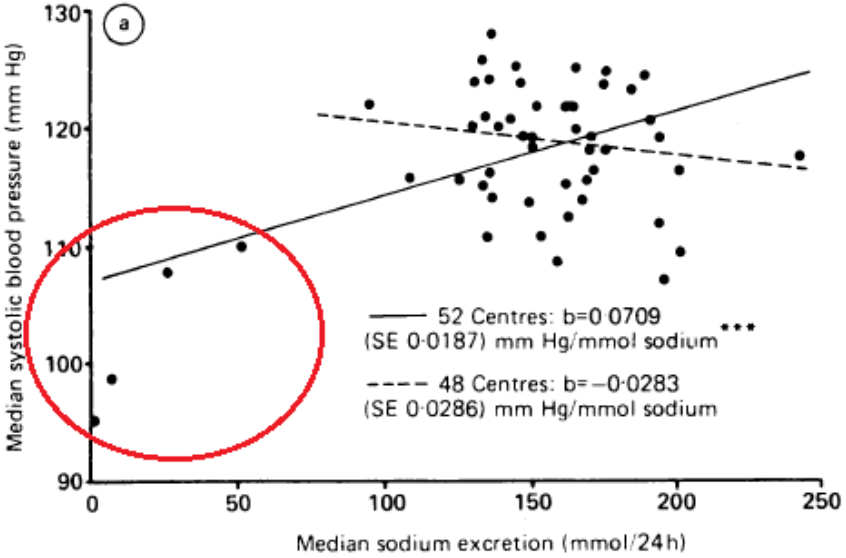
i.e. inappropriately decreased

In this short paper, I have tried to explain the elation that we felt when we first realized that the kidney-fluid mechanism for controlling the arterial pressure has an infinite feedback gain property. Because of this, all the other pressure control mechanisms, none of which has ever been shown to have a similar infinite gain property, must themselves alter the kidney-fluid mechanism if they are to succeed in causing long-term changes in the arterial pressure. We have not been able to refute this principle despite many experiments over the

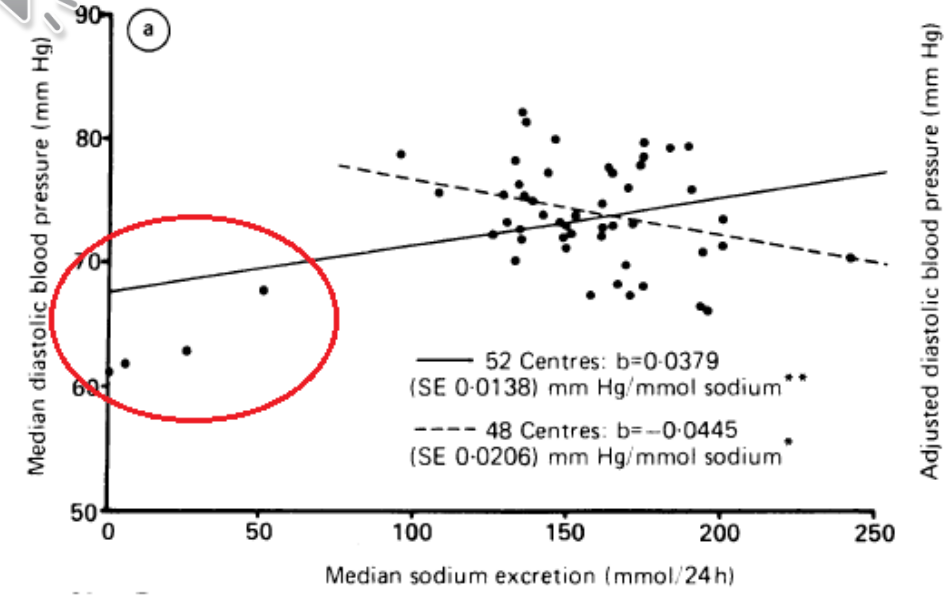
Hypertension travels along with the kidney!



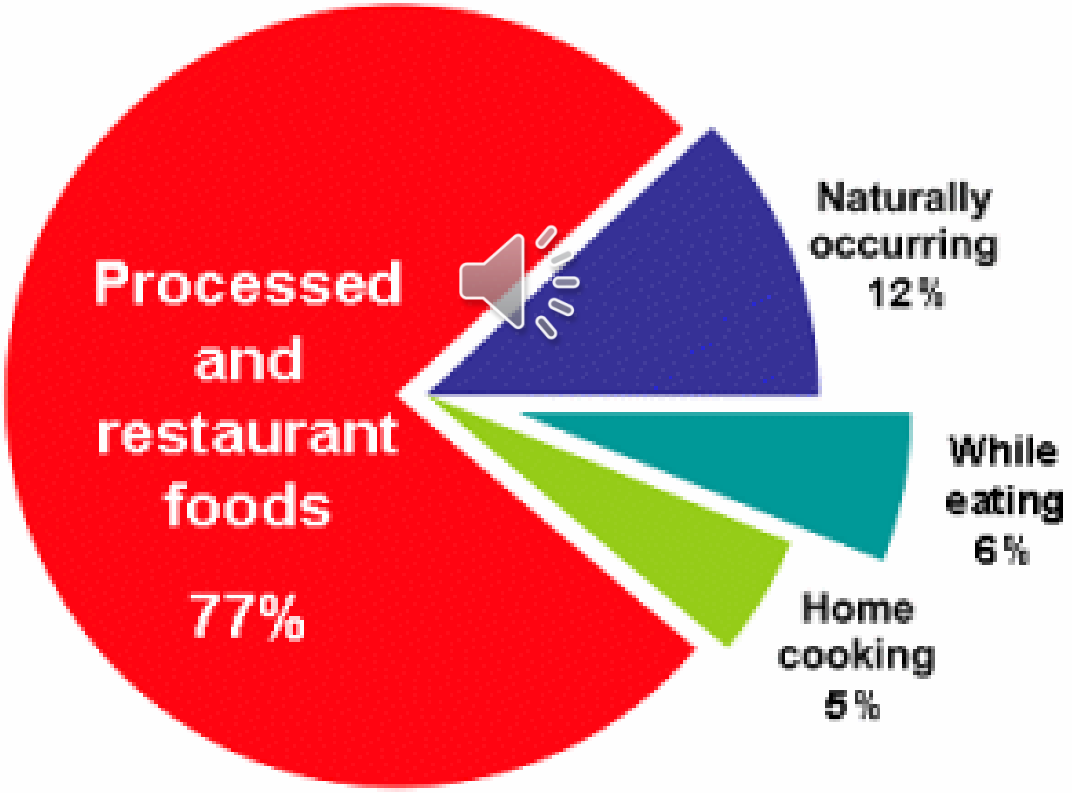

400
350
300
250
200
150
100
$U_{Na}V$, *µmol/min*
108
110
112
114
116
118
120
122
MAP, *mm Hg*

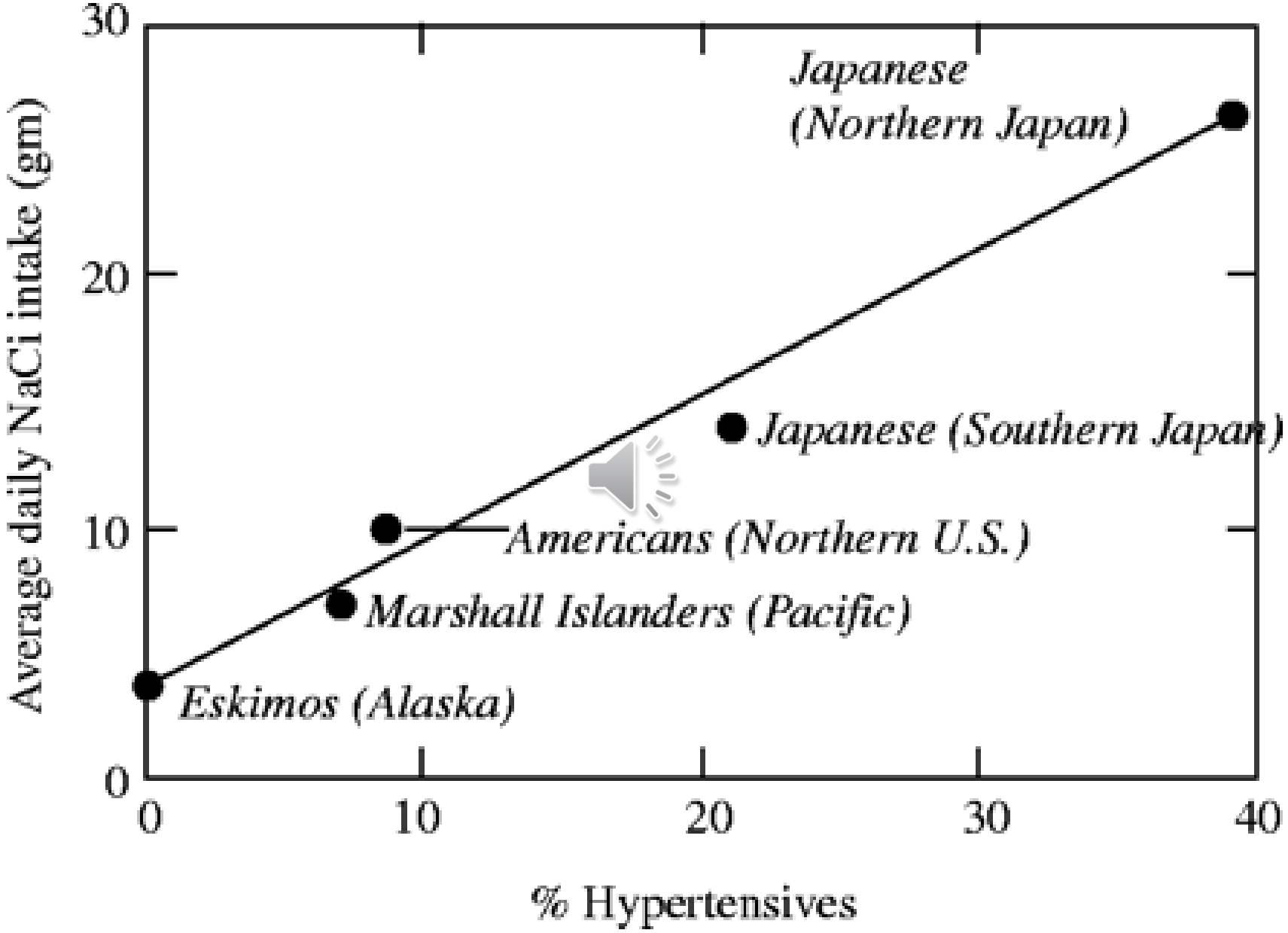

a
Median systolic blood pressure (mm Hg)
130
120
110
100
90
0
50
100
150
200
250
Median sodium excretion (mmol/24h)
52 Centres: b=0 0709
(SE 0·0187) mm Hg/mmol sodium***
48 Centres: b=−0·0283
(SE 0·0286) mm Hg/mmol sodium

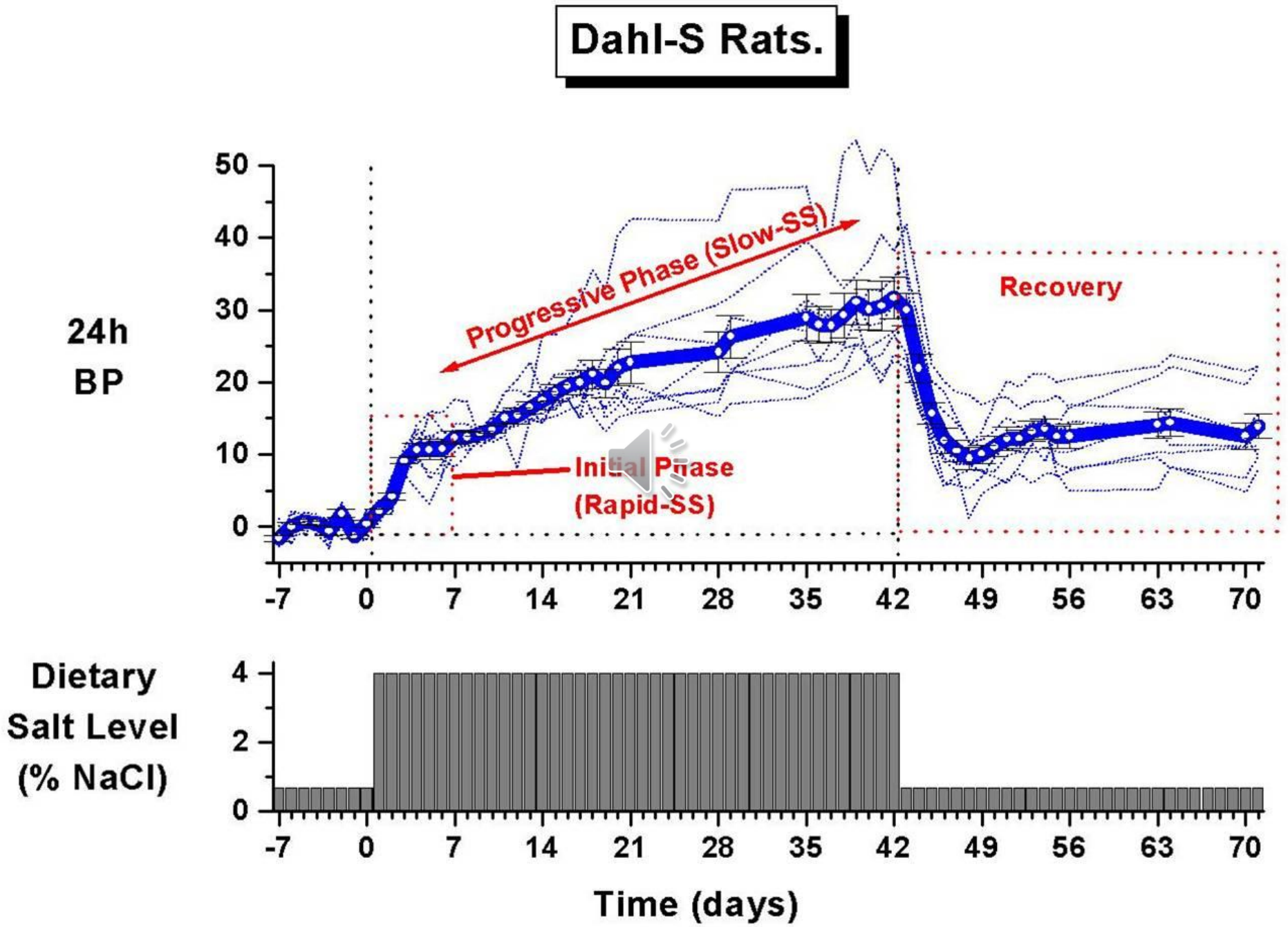

Adjusted systolic blood pressure (mm Hg)


a
Median diastolic blood pressure (mm Hg)
90
80
70
60
50
0
50
100
150
200
250
Median sodium excretion (mmol/24h)
52 Centres: b=0·0379
(SE 0·0138) mm Hg/mmol sodium**
48 Centres: b=−0·0445
(SE 0·0206) mm Hg/mmol sodium*
Adjusted diastolic blood pressure (mm Hg)

Most Sodium Comes from Processed and Restaurant Foods




Average daily NaCl intake (gm)
30
20
10
0
0
10
20
30
40
% Hypertensives
Japanese
(Northern Japan)
Japanese (Southern Japan)
Americans (Northern U.S.)
Marshall Islanders (Pacific)
Eskimos (Alaska)


Dahl-S Rats.
24h
BP
50
40
30
20
10
0
Progressive Phase (Slow-SS)
Recovery
Initial Phase
(Rapid-SS)
-7
0
7
14
21
28
35
42
49
56
63
70
Dietary
Salt Level
(% NaCl)
4
2
0
Time (days)

Denton D et al. The effect of increased salt intake on blood pressure in chimpanzees.
Nat Med 1995;1:1009-16.

- Humans share 98.4% genetic identity with chimpanzees
- By adding up to 15 g of NaCl daily, SBP increased by 33 mm Hg and DBP by 10 mm Hg
- The increases were reversed after withdrawal of the sodium chloride supplement.

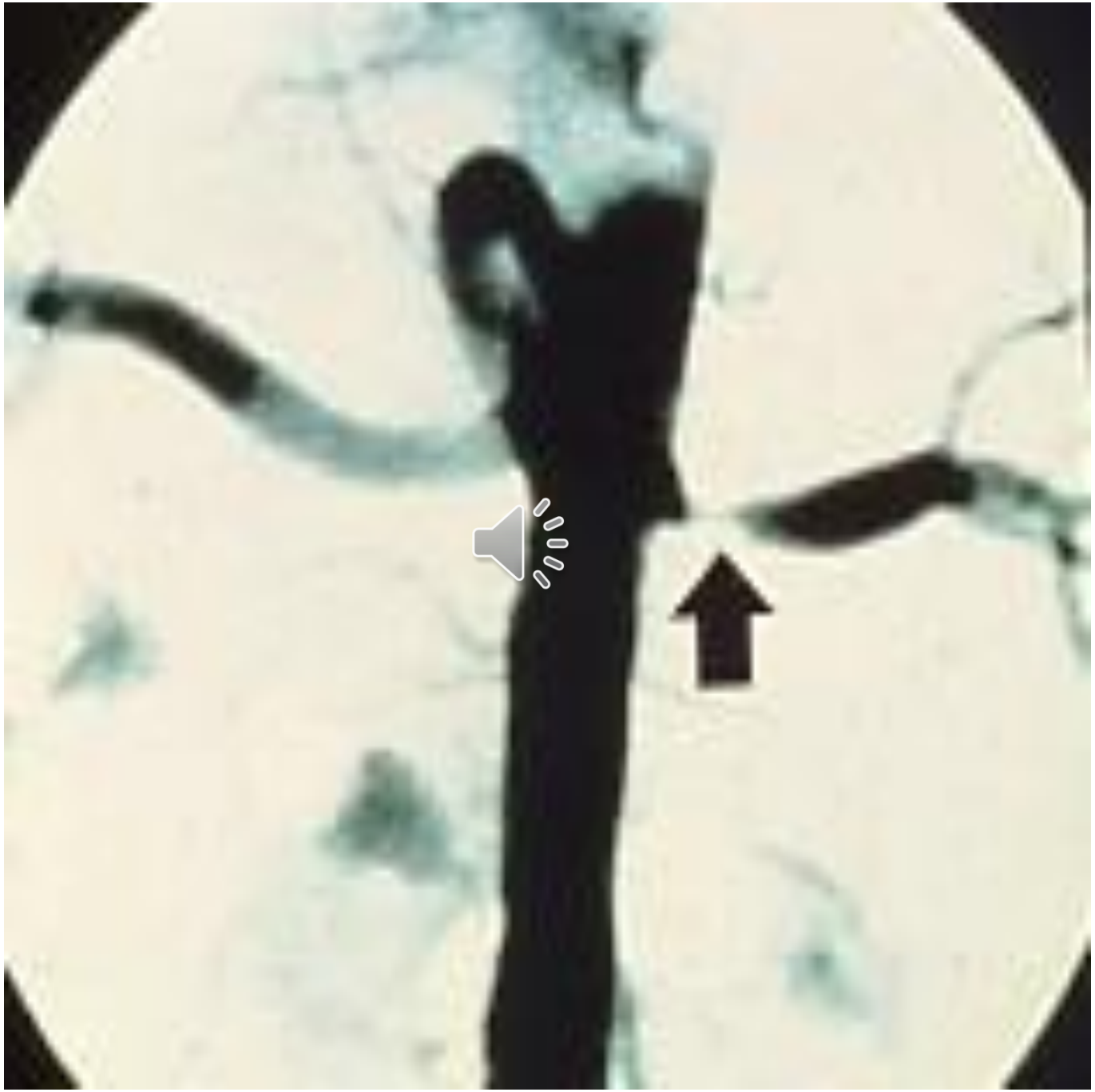
Relatively salt-sensitive groups of people

- Individuals > 50-60 yo
- Blacks
- Hypertensive patients
- Obese people with metabolic syndrome and DM
- Patients with CKD

Prevalence of Hypertension in US by Obesity Class and Sex

BMI(kg/m^2)	<18.5	18.5-24.9	25-29.9	30-34.9	35-39.9	≥40
	underweight	normal	overweight	obesity class 1	obesity class2	obesity class 3

Must A et al. JAMA 1999; 282:1523-1529



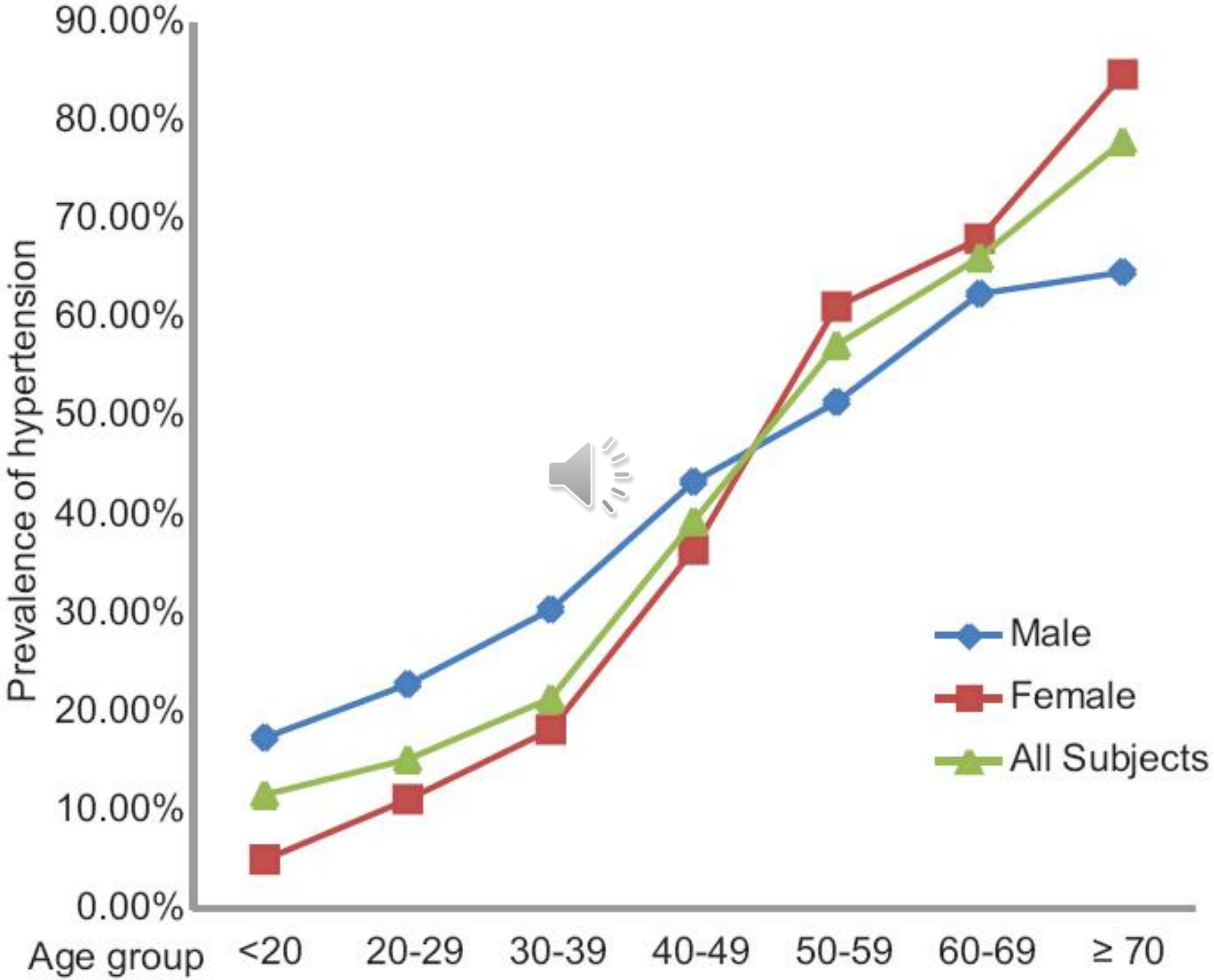
Office BP measurement - 1

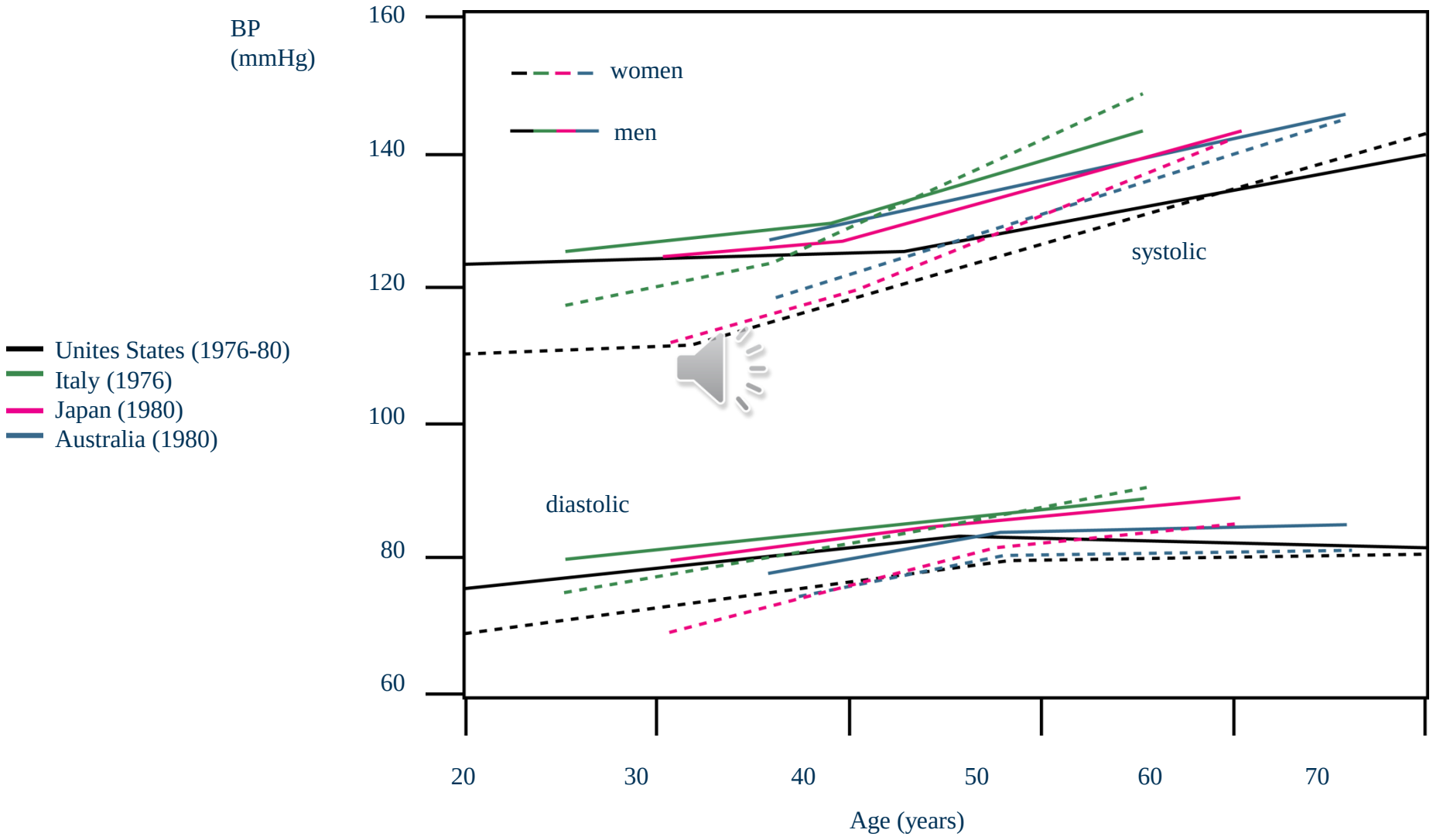
Patients should be seated comfortably in a quiet environment for 5 min before beginning BP measurements.
Three BP measurements should be recorded, 1–2 min apart, and additional measurements only if the first two readings differ by > 10 mmHg. BP is recorded as the average of the last two BP readings.
Additional measurements may have to be performed in patients with unstable BP values due to arrhythmias, such as in patients with AF, in whom manual auscultatory methods should be used as most automated devices have not been validated for BP measurement in patients with AF.
Use a standard bladder cuff (12–13 cm wide and 35 cm long) for most patients, but have larger and smaller cuffs available for larger (arm circumference > 32 cm) and thinner arms, respectively.
The cuff should be positioned at the level of the heart with the back and arm supported, to avoid muscle contraction and isometric-exercise dependent increases in BP.
When using auscultatory methods, use phase I and V (sudden reduction/disappearance) Korotkoff sounds to identify SBP and DBP, respectively.
Measure BP in both arms at the first visit to detect possible between-arm differences. Use the arm with the higher value as the reference.

Classification of office BP and definitions of hypertension grade

Category	Systolic (mmHg)		Diastolic (mmHg)
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

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104


90.00%
80.00%
70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
Prevalence of hypertension
Age group
<20
20-29
30-39
40-49
50-59
60-69
≥ 70
Male
Female
All Subjects



Lip G and Bakris G. Handbook Hypertension Management. CMG

Definitions of hypertension according to office, ambulatory, and home BP levels

Category	Systolic (mmHg)		Diastolic (mmHg)
Office BP	≥ 140	and/or	≥ 90
Ambulatory BP			
Daytime (or awake) mean	≥ 135	and/or	≥ 85
Night-time (or asleep) mean	≥ 120	and/or	≥ 70
24-h mean	≥ 130	and/or	≥ 80
Home BP mean	≥ 135	and/or	≥ 85

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Routine work-up for evaluation of hypertensive patients

Routine laboratory tests
Haemoglobin and/or haematocrit
Fasting blood glucose and glycated HbA_{1c}
Blood lipids: total cholesterol, LDL cholesterol, HDL cholesterol
Blood triglycerides
Blood potassium and sodium
Blood uric acid
Blood creatinine and eGFR
Blood liver function tests
Urine analysis: microscopic examination; urinary protein by dipstick test or, ideally, albumin:creatinine ratio
12-lead ECG

10-year CV risk categories (SCORE system)

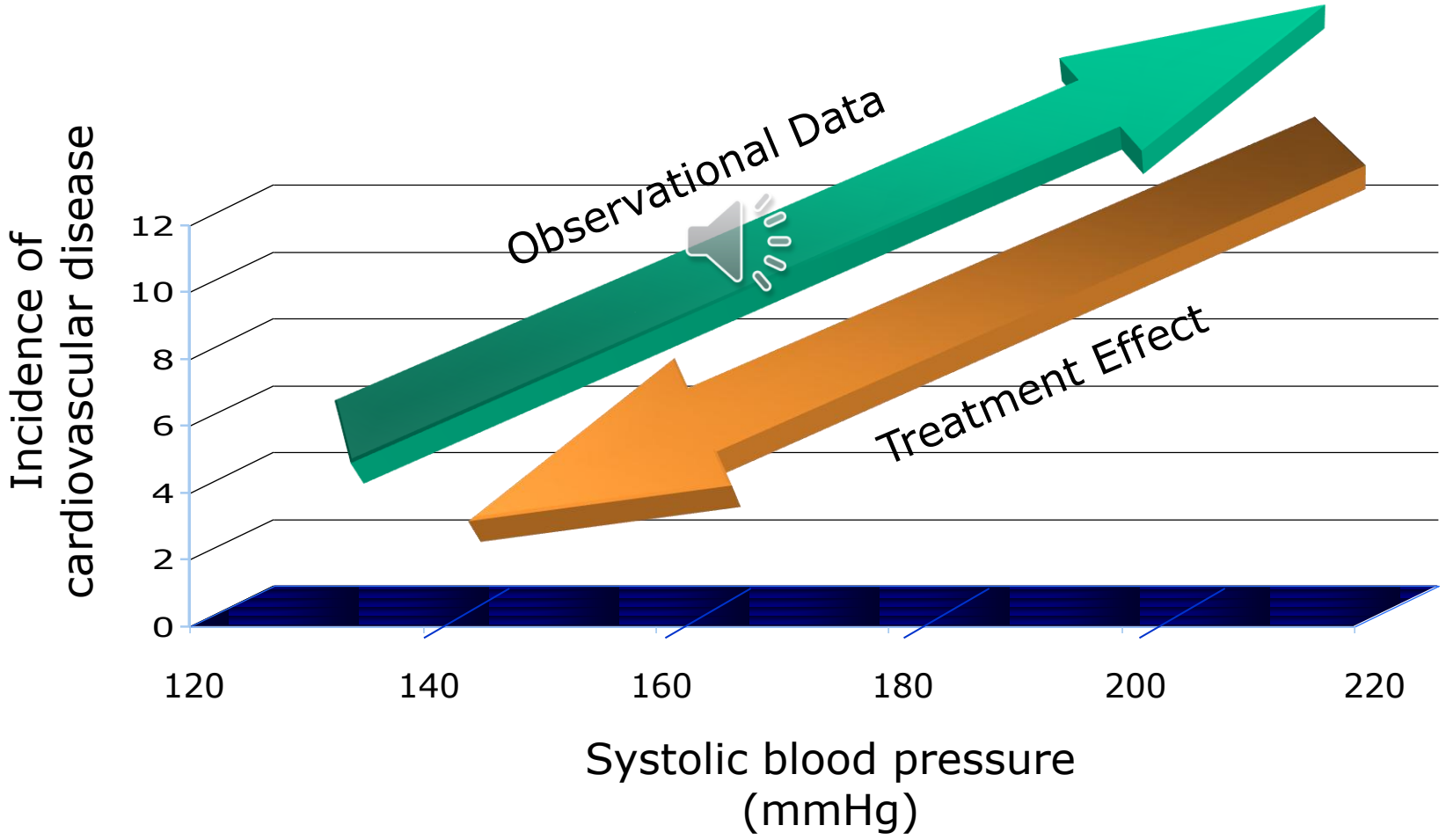
Very high risk	**People with any of the following:** **Documented CVD, either clinical or unequivocal on imaging.** • **Clinical CVD** includes acute myocardial infarction, acute coronary syndrome, coronary or other arterial revascularization, stroke, TIA, aortic aneurysm and PAD. • **Unequivocal documented CVD on imaging** includes significant plaque (i.e. ≥ 50% stenosis) on angiography or ultrasound. It does not include increase in carotid intima-media thickness. • **Diabetes mellitus with target organ damage**, e.g. proteinuria or a with a major risk factor such as grade 3 hypertension or hypercholesterolaemia • **Severe CKD** (eGFR < 30 mL/min/1.73 m²) • **A calculated 10-year SCORE of ≥ 10%**
High risk	**People with any of the following:** • **Marked elevation of a single risk factor**, particularly cholesterol > 8 mmol/L (> 310 mg/dL) e.g. familial hypercholesterolaemia, grade 3 hypertension (BP ≥ 180/110 mmHg) • **Most other people with diabetes mellitus** (except some young people with type 1 diabetes mellitus and without major risk factors, that may be moderate risk) • **Hypertensive LVH** • **Moderate CKD (eGFR 30–59 mL/min/1.73 m²)** • **A calculated 10-year SCORE of 5–10%**
Moderate risk	**People with:** • **A calculated 10-year SCORE of 1% to < 5%** • **Grade 2 hypertension** • **Many middle-aged people** belong to this category
Low risk	**People with:** • **A calculated 10-year SCORE of < 1%**

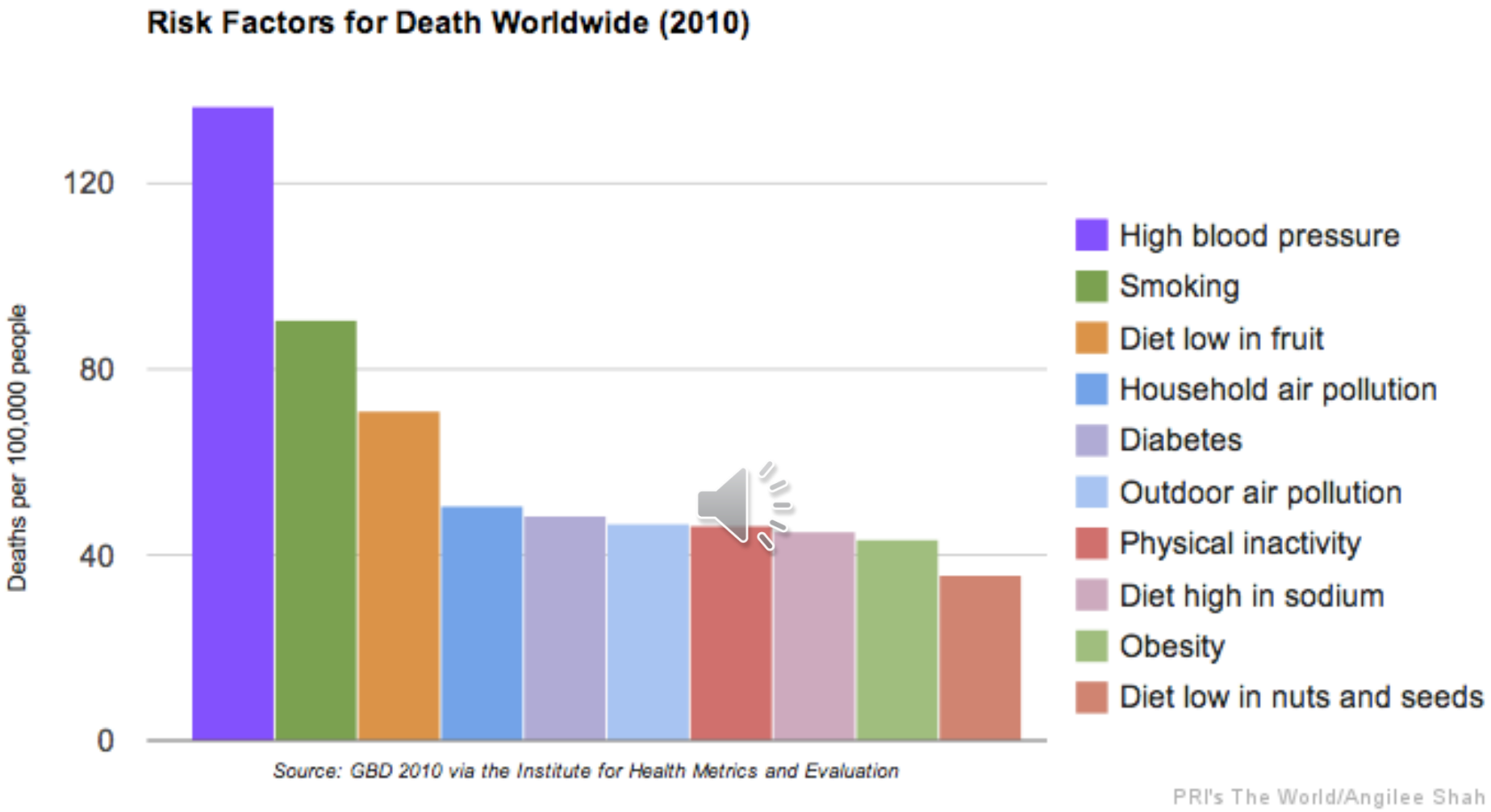
Classification of hypertension stages according to BP levels, presence of CV risk factors, HMOD, or comorbidities

Hypertension disease staging	Other risk factors, HMOD, or disease	BP (mmHg) grading			
		High-normal SBP 130–139 DBP 85–89	Grade 1 SBP 140–159 DBP 90–99	Grade 2 SBP 160–179 DBP 100–109	Grade 3 SBP ≥ 180 DBP ≥ 110
Stage 1 (uncomplicated)	No other risk factors	Low risk	Low risk	Moderate risk	High risk
	1 or 2 risk factors	Low risk	Moderate risk	Moderate to high risk	High risk
	≥ 3 risk factors	Low to moderate risk	Moderate to high risk	High risk	High risk
Stage 2 (asymptomatic disease)	HMOD, CKD grade 3, or diabetes mellitus without organ damage	Moderate to high risk	High risk	High risk	High to very high risk
Stage 3 (established disease)	Established CVD, CKD grade ≥ 4, or diabetes mellitus with organ damage	Very high risk	Very high risk	Very high risk	Very high risk

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

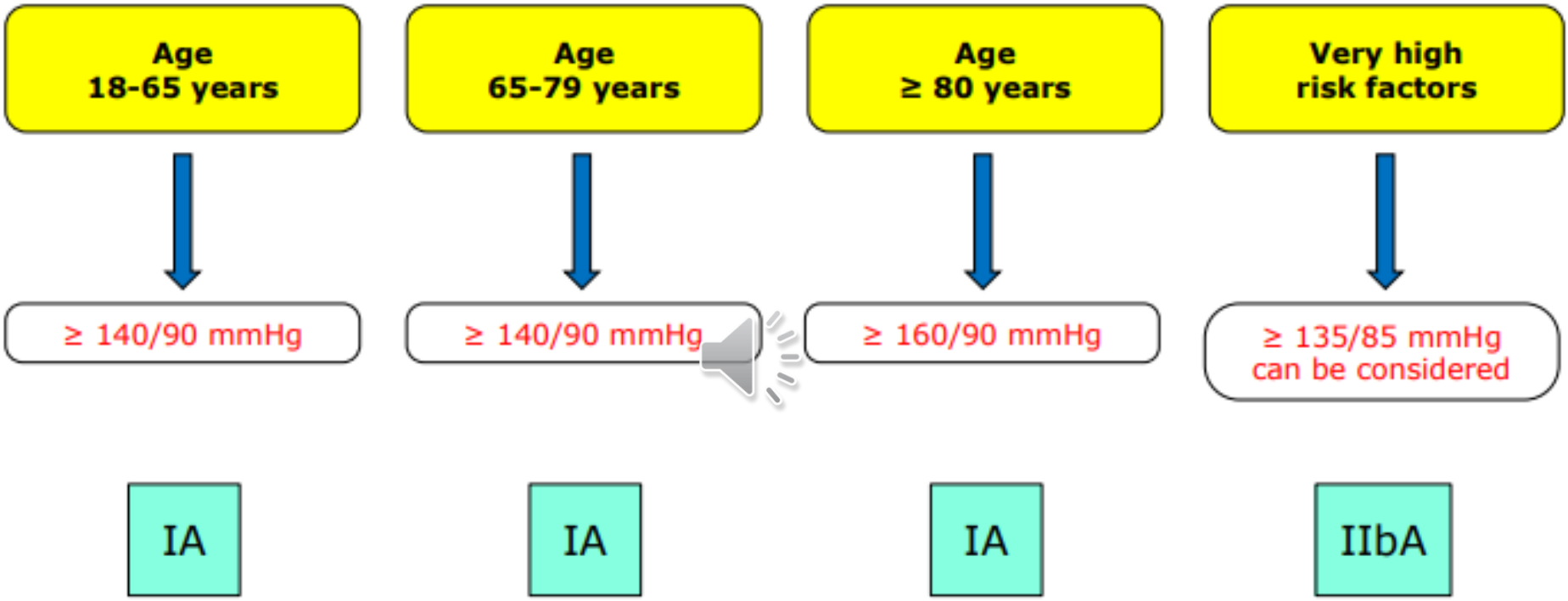
Hypertension Treatment Effect Mirrors Observational Data





Apart antibiotics, anti-hypertensives are the single most important therapy contributing to rising life expectancies.

Summary of office BP thresholds for treatment



ESC European Society of Cardiology

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

ESH Europe Societ Hyper

Office BP treatment target range

Age 18-65 years

- First SBP <140 mmHg
- Aim for SBP 130 mmHg or lower if tolerated
- DBP <80-70 mmHg
- Do not go <120/70 mmHg

IA

Age >65-79 years*

- First SBP <140 mmHg
- Aim for SBP 130 mmHg
- DBP <80-70 mmHg
- Do not go <130/70 mmHg

IA

Age ≥ 80 years*

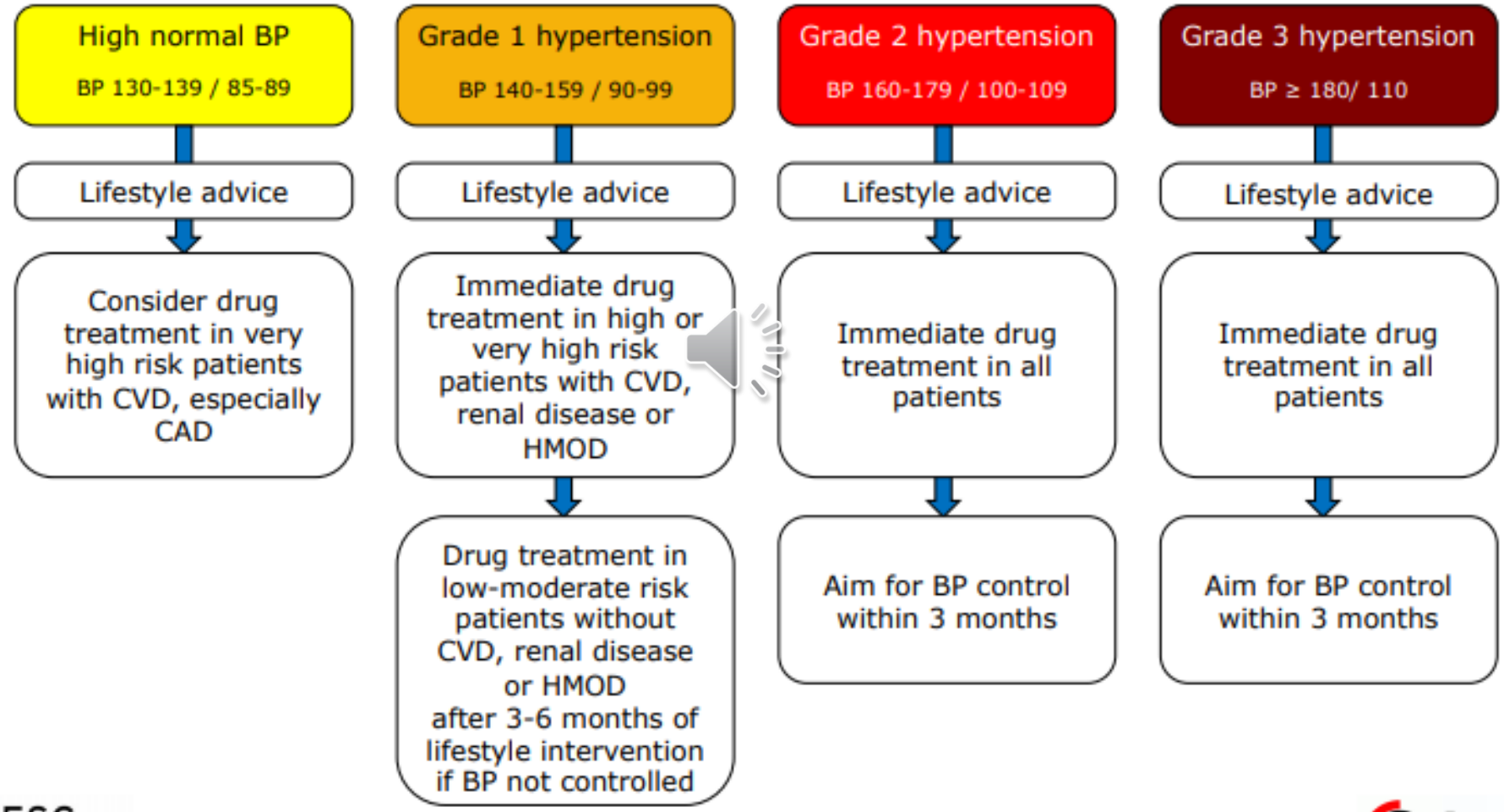
- First SBP <140 mmHg
- Aim for SBP 130 mmHg
- DBP <80-70 mmHg
- Do not go <130/70 mmHg

IA

* Consider frailty/independence/tolerability of treatment

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Initiation of BP-lowering treatment (lifestyle changes and medication) at different initial office BP levels

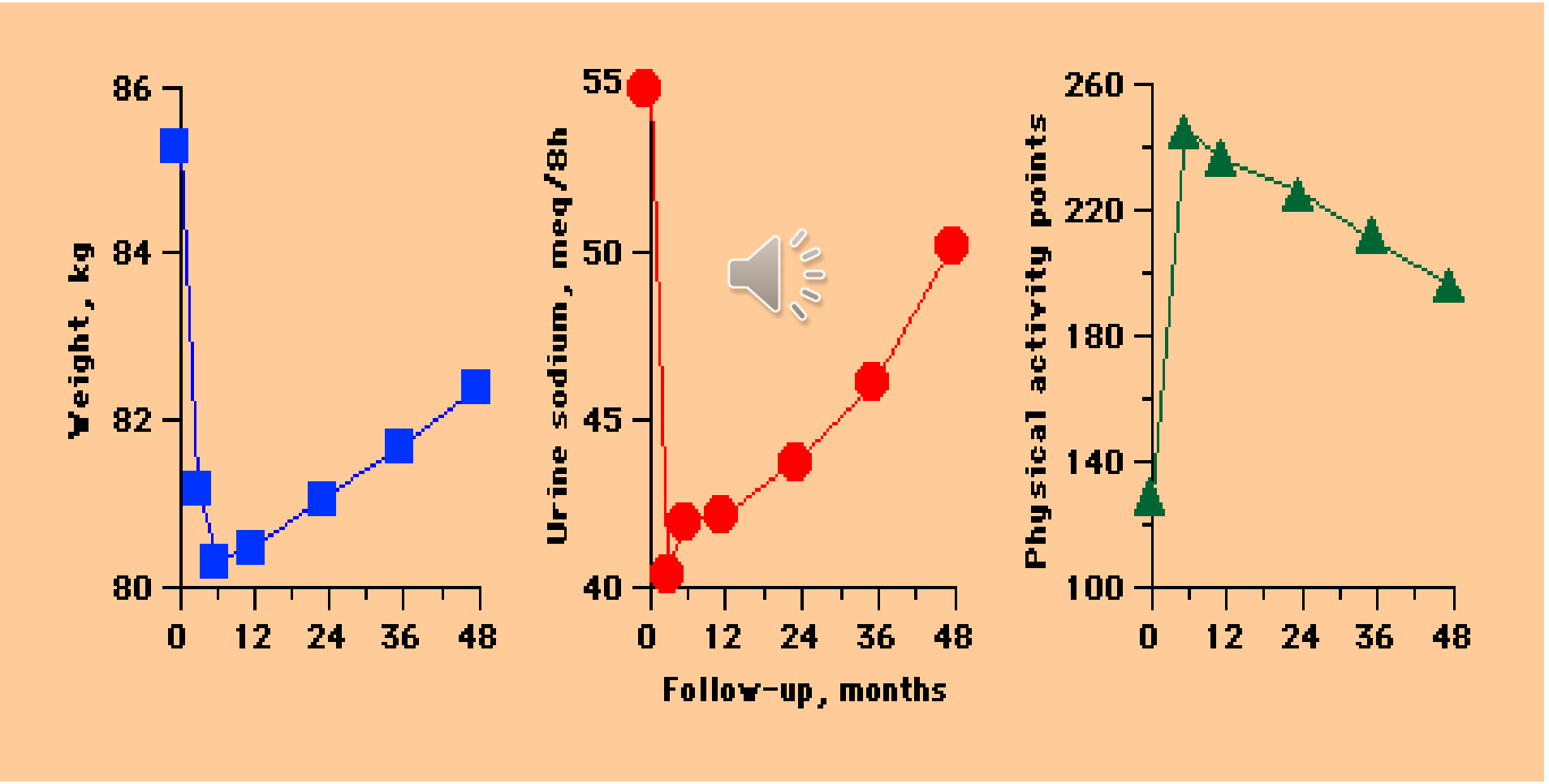


Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Adoption of lifestyle changes in patients with hypertension

Recommendations	Class	Level
Salt restriction to < 5 g per day is recommended.	I	A
It is recommended to restrict alcohol consumption to: • Less than 14 units per week for men. • Less than 8 units per week for women.	I	A
It is recommended to avoid binge drinking.	III	C
Increased consumption of vegetables, fresh fruits, fish, nuts, unsaturated fatty acids (olive oil), low consumption of red meat, and consumption of low-fat dairy products are recommended.	I	A
Body-weight control is indicated to avoid obesity (BMI > 30 kg/m^2 or WC > 102 cm in men and > 88 cm in women) and aim at a healthy BMI (about 20–25 kg/m^2) and WC values (< 94 cm in men and < 80 cm in women) to reduce BP and CV risk.	I	A
Regular aerobic exercise (e.g. at least 30 min of moderate dynamic exercise on 5–7 days per week) is recommended.	I	A
Smoking cessation and supportive care and referral to smoking cessation programs are recommended.	I	B

force of HABIT



Diminished compliance with nonpharmacologic therapy over time Changes

1. Η επίτευξη άριστης ρύθμισης έχει μεγαλύτερη σημασία στη μείωση του κινδύνου
2. Στις περισσότερες περιπτώσεις χρειάζονται 2-3 φάρμακα

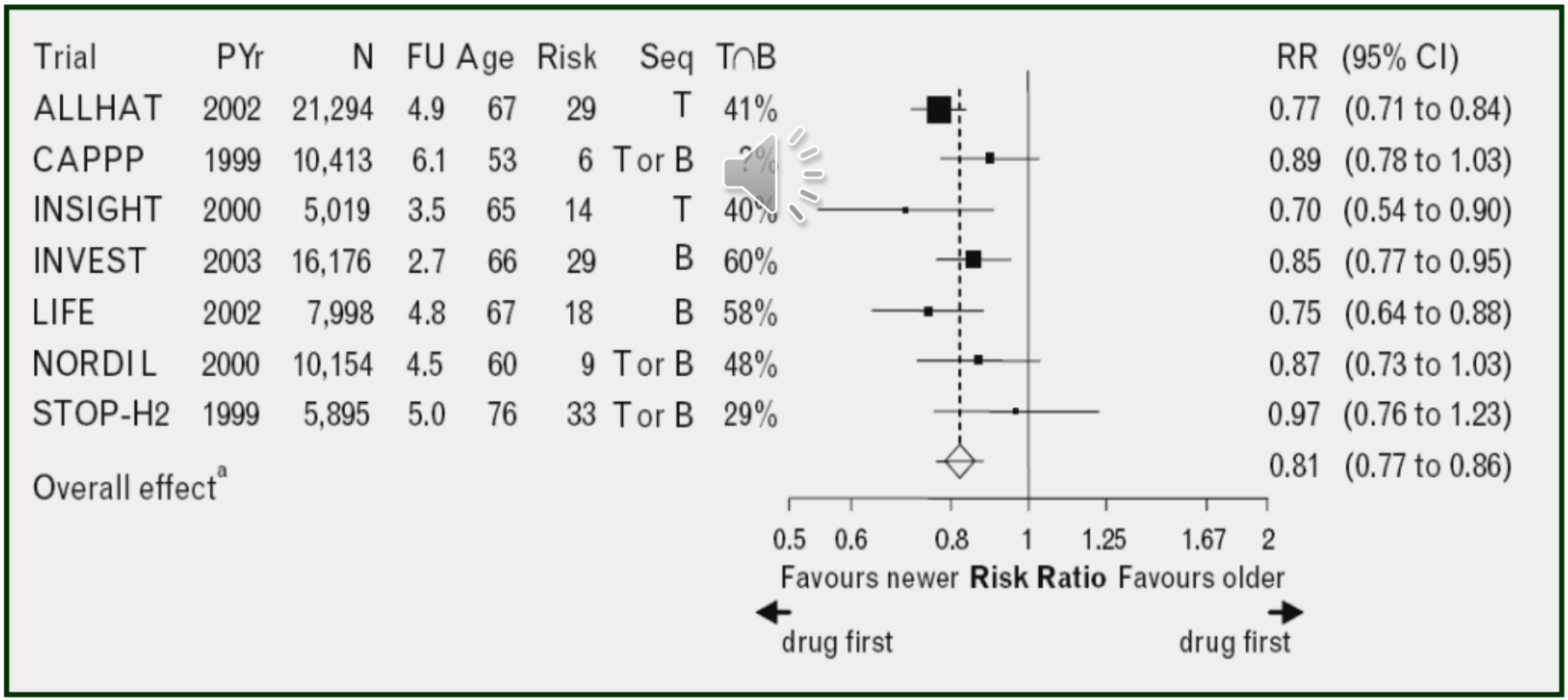
Φάρμακα 1ης γραμμής

- Θειαζιδικά διουρητικά
- Αναστολείς ΜΕΑ
- Ανταγωνιστές Ca
- Ανταγωνιστές αγγειοτασίνης
- β-Αποκλειστές ***

ΠΡΟΤΙΜΗΣΗ***: *σε ειδικές ενδείξεις*
ΑΠΟΦΥΓΗ: *σε ↑ κίνδυνο εμφάνισης διαβήτη, ηλικιωμένους*

Το διαβητογόνο δυναμικό των συνδυασμών θειαζιδικού τύπου διουρητικού και β-αποκλειστή σε ασθενείς με υπέρταση

Με συνδυασμό β-αποκλειστή και θειαζιδικού
→ **RR = 1.19 (1.14-1.23) για διαβήτη Τ2** συγκριτικά με άλλες αντιυπερτασικές θεραπείες που δεν χρησιμοποιούν αυτό το συνδυασμό



Mason JM, *J Hypertens*. 2005

Αντιϋπερτασικά φάρμακα
Επιλογή φαρμάκων

Φάρμακα δεύτερης γραμμής

(Λιγότερες αποδείξεις από μεγάλες μελέτες)

- Α1 αποκλειστές
- Κεντρικώς δρώντα φάρμακα (α2 αγωνιστές, τροποποιητές της ιμιδαζολίνης)
- Ανταγωνιστές της αλδοστερόνης

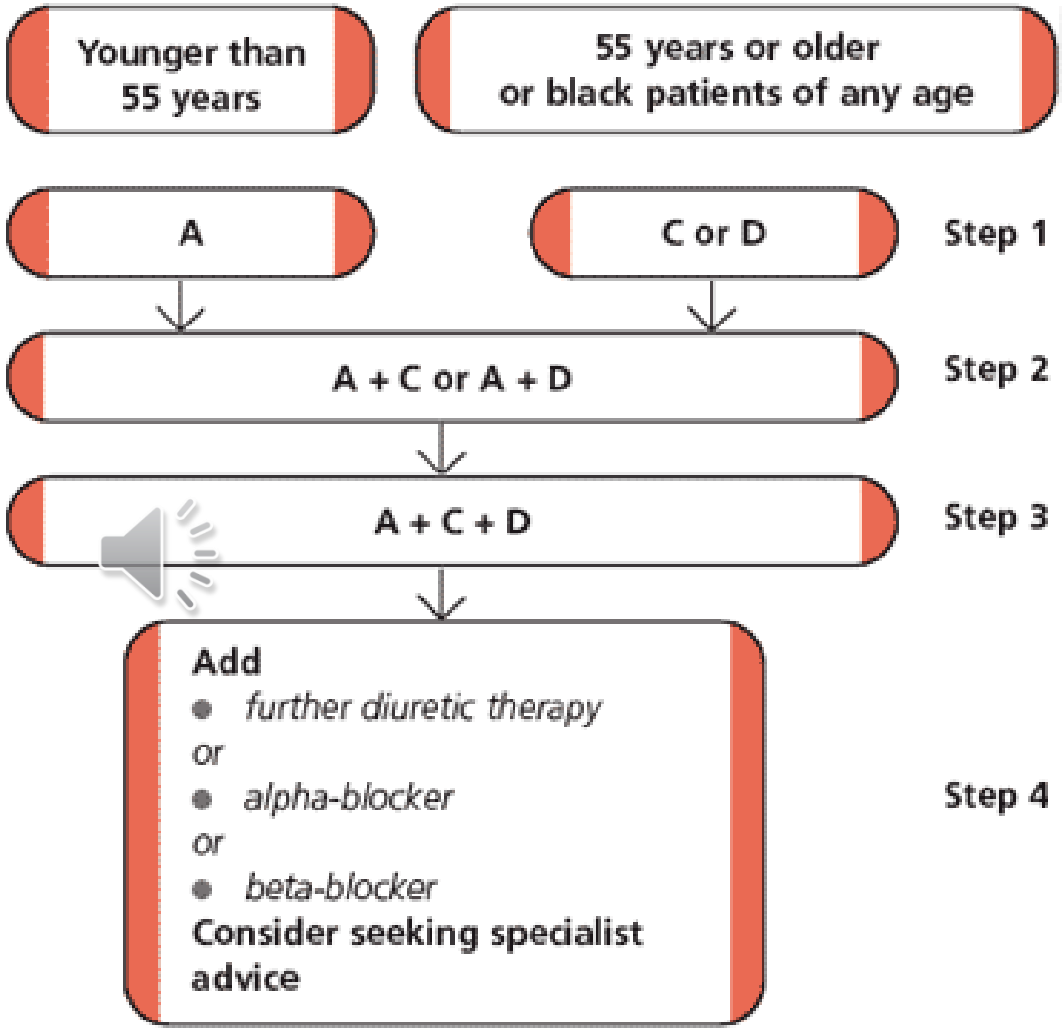
Compelling and possible contraindications to the use of specific antihypertensive drugs

Drug	Contraindications	
	Compelling	**Possible**
Diuretics (thiazides/thiazide-type, e.g. chlorthalidone and indapamide)	• Gout	• Metabolic syndrome • Glucose intolerance • Pregnancy • Hypercalcemia • Hypokalemia
Beta-blockers	• Asthma • Any high-grade sino-atrial or atrioventricular block • Bradycardia (heart rate < 60 beats per min)	• Metabolic syndrome • Glucose intolerance • Athletes and physically active patients
Calcium antagonists (dihydropyridines)		• Tachyarrhythmia • Heart failure (HFrEF, class III or IV) • Pre-existing severe leg oedema
Calcium antagonists (verapamil, diltiazem)	• Any high-grade sino-atrial or AV block • Severe LV dysfunction (LV EF < 40%) • Bradycardia (heart rate < 60 beats per min)	• Constipation
ACE inhibitors	• Pregnancy • Previous angioneurotic oedema • Hyperkalemia (potassium > 5.5 mmol/L) • Bilateral renal artery stenosis	• Women of child-bearing potential without reliable contraception
ARBs	• Pregnancy • Hyperkalemia (potassium > 5.5 mmol/L) • Bilateral renal artery stenosis	• Women of child-bearing potential without reliable contraception

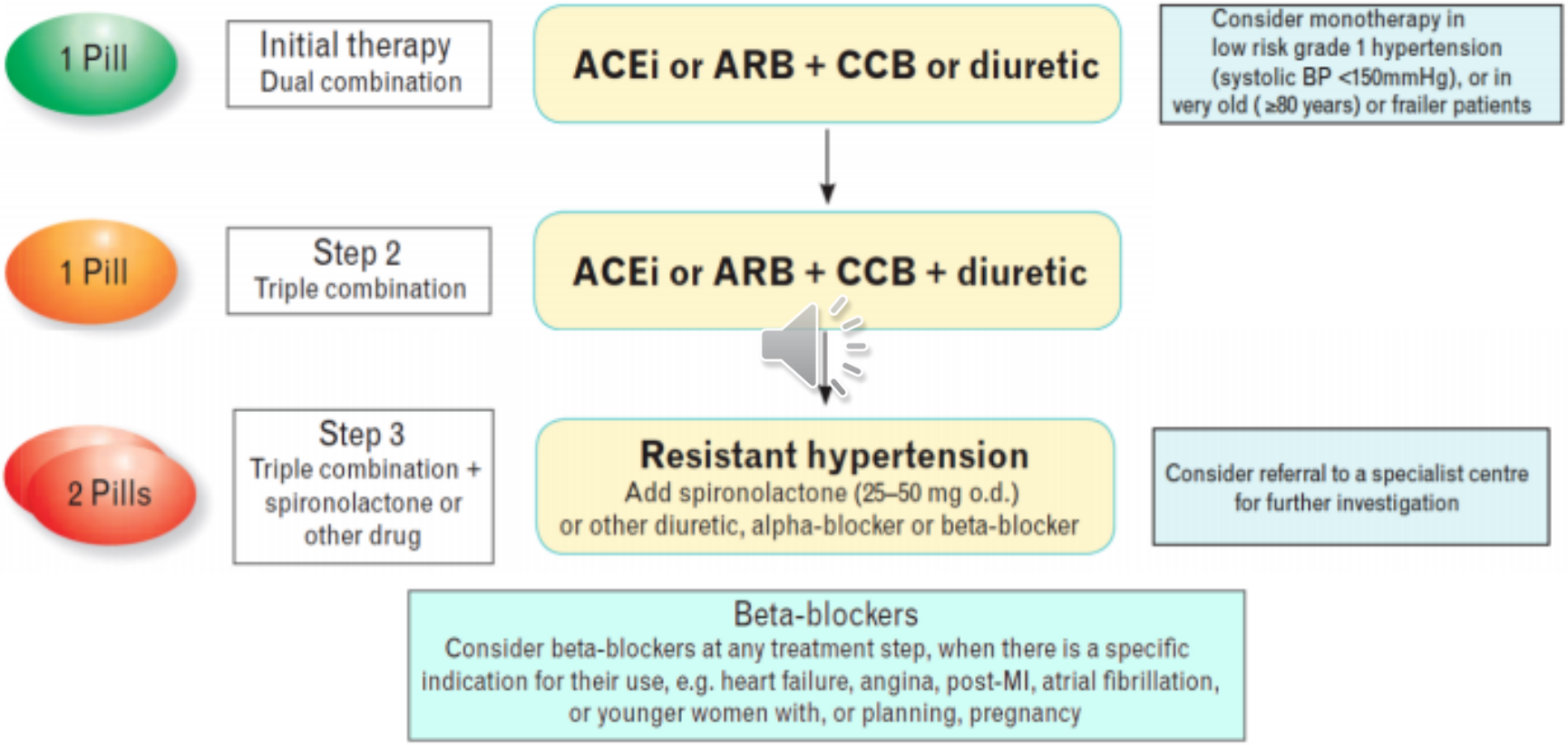
Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Abbreviations:
A = ACE inhibitor
(consider angiotensin-II receptor antagonist if ACE intolerant)
C = calcium-channel blocker
D = thiazide-type diuretic

Black patients are those of African or Caribbean descent, and not mixed-race, Asian or Chinese patients



Core drug-treatment strategy for uncomplicated hypertension



The core algorithm is also appropriate for most patients with HMOD, cerebrovascular disease, diabetes, or PAD

Sensitivity to detect treatment-induced changes, reproducibility and operator independence, time to changes, and prognostic value of changes provided by markers of HMOD

Marker of HMOD	Sensitivity to changes	Reproducibility and operator independence	Time to changes	Prognostic value of the change
LVH by ECG	Low	High	Moderate (> 6 months)	Yes
LVH by echocardiogram	Moderate	Moderate	Moderate (> 6 months)	Yes
LVH by CMR	High	High	Moderate (> 6 months)	No data
eGFR	Moderate	High	Very slow (years)	Yes
Urinary albumin excretion	High	Moderate	Fast (weeks to months)	Moderate
Carotid IMT	Very low	Low	Slow (> 12 months)	No
PWV	High	Low	Fast (weeks to months)	Limited data
Ankle–brachial index	Low	Moderate	Slow (> 12 months)	Moderate

Resistant hypertension characteristics, secondary causes, and contributing factors

Characteristics of patients with resistant hypertension	Causes of secondary resistant hypertension	Drugs and substances that may cause raised BP
Demographics • Older age (especially > 75 years) • Obesity • More common in black people • Excess dietary sodium intake • High baseline BP and chronicity of uncontrolled hypertension	**More common causes** • Primary hyperaldosteronism • Atherosclerotic renovascular disease • Sleep apnoea • CKD	**Prescribed drugs** • Oral contraceptives • Sympathomimetic agents (e.g. decongestants in proprietary cold remedies) • Non-steroidal anti-inflammatory drugs • Cyclosporin • Erythropoietin • Steroids (e.g. prednisolone, hydrocortisone) • Some cancer therapies
Concomitant disease • HMOD: LVH and/or CKD • Diabetes • Atherosclerotic vascular disease • Aortic stiffening and isolated systolic hypertension	**Uncommon causes** • Phaeochromocytoma • Fibromuscular dysplasia • Aortic coarctation • Cushing's disease • Hyperparathyroidism	**Non-prescription drugs** • Recreational drugs (e.g. cocaine, amphetamines, anabolic steroids) • Excess liquorice ingestion • Herbal remedies (e.g. ephedra, ma huang)

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Primary hyperaldosteronism

2/3 bilateral hyperplasia,

1/3 adenoma (Conn' syndrome)

M:F => 1:2, 30-50 yo

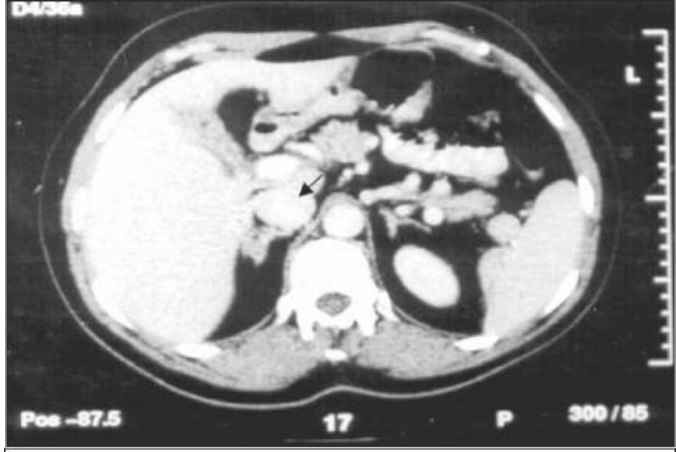
-Hypertension

-Hypokalemia (95%)

ή K+ 3.4-3.7 meq/L

-Metabolic Alkalosis

-Low Renin - High Aldo



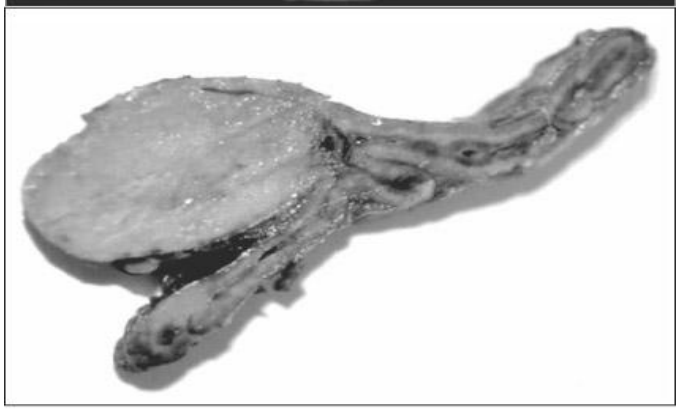


Fig. 4 - Aspecto macroscópico da glândula supra-renal-renal e vesícula biliar. A supra-renal mediu 4,7 x 4,5 x 1,5 cm e apresentou nódulo único medindo 1,5 cm de diâmetro. A vesícula biliar não apresentou alterações.

Pheochromocytoma

- 0.01-0.1% of HTN population
  - Found in 0.5% of those screened
- M = F
- 3rd to 5th decades of life
- Rare, investigate only if clinically suspicion:
  - Signs or Symptoms
  - Severe HTN, HTN crisis
  - Refractory HTN (> 3 drugs)
  - HTN present @ age < 20 or > 50 ?
  - Adrenal lesion found on imaging (ex. Incidentaloma)

Pheo: Signs & Symptoms

- The five P's:
  - Pressure (HTN) 90%
  - Pain (Headache) 80%
  - Perspiration 71%
  - Palpitation 64%
  - Pallor 42%
    - » Paroxysms (the sixth P!)
- The Classical Triad:
  - Pain (Headache), Perspiration, Palpitations
  - Lack of all 3 virtually excluded diagnosis of pheo in a series of > 21,0000 patients

Pheo: ‘Rule of 10’

- 10% extra-adrenal (closer to 15%)
- 10% occur in children
- 10% familial (closer to 20%)
- 10% bilateral or multiple (more if familial)
- 10% recur (more if extra-adrenal)
- 10% malignant
- 10% discovered incidentally

Localization: Imaging

- CT abdomen
  - Adrenal pheo SEN 93-100%
  - Extra-adrenal pheo SEN 90%
- MRI

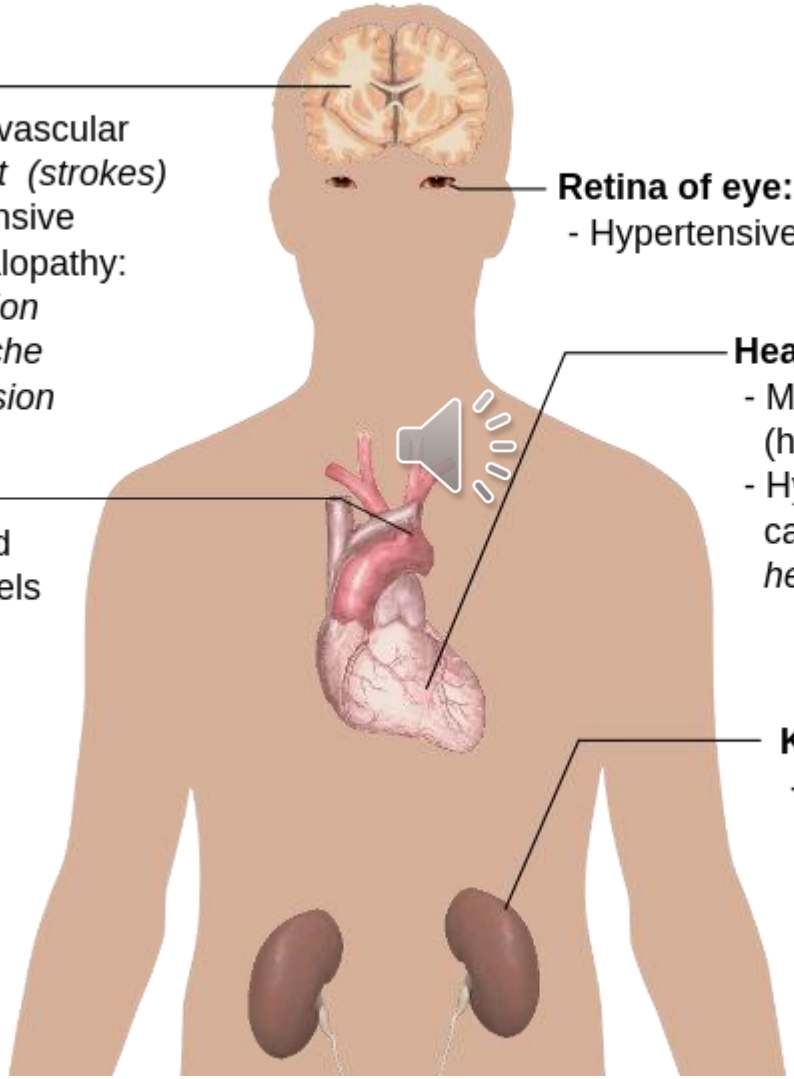
  - > SEN than CT for extra-adrenal pheo

Pheo Management

- Prior to 1951, reported mortality for excision of pheochromoyctoma 24 - 50 %
  - **HTN crisis, arrhythmia, MI, stroke**
  - **Hypotensive shock**
- **Currently, mortality:** 0 - 2.7 %
  - Preoperative preperation, α-blockade?
  - New anesthetic techniques?
    - » Anesthetic agents
    - » Intraoperative monitoring: arterial line, EKG monitor, CVP line, Swan-Ganz
- **Experienced & Coordinated team:**
  - Endocrinologist, Anesthesiologist and Surgeon

Main complications of persistent

High blood pressure



Brain:
- Cerebrovascular *accident (strokes)*
- Hypertensive encephalopathy:
  -confusion
  -headache
  -convulsion

Retina of eye:
- Hypertensive retinopathy

Heart:
- Myocardial infarction (heart attack)
- Hypertensive cardiomyopathy: *heart failure*

Blood:
- Elevated sugar levels

Kidneys:
- Hypertensive nephropathy: *chronic renal failure*

Hypertensive emergencies requiring immediate BP lowering with i.v. drug therapy

Clinical presentation	Time line and target for BP reduction	First-line treatment	Alternative
Malignant hypertension with or without acute renal failure	Several hours Reduce MAP by 20–25%	Labetalol Nicardipine	Nitroprusside Urapidil
Hypertensive encephalopathy	Immediately reduce MAP by 20–25%	Labetalol Nicardipine	Nitroprusside
Acute coronary event	Immediate reduce SBP to < 140 mmHg	Nitroglycerine Labetalol	Urapidil
Acute cardiogenic pulmonary oedema	Immediately reduce SBP to < 140 mmHg	Nitroprusside or nitroglycerine (with loop diuretic)	Urapidil (with loop diuretic)
Acute aortic dissection	Immediately reduce SBP to < 120 mmHg and heart rate to < 60 bpm	Esmolol AND nitroprusside or nitroglycerine or nicardipine	Labetalol OR metoprolol
Eclampsia and severe pre-eclampsia/HELLP	Immediately reduce SBP to < 160 mmHg and DBP to < 105 mmHg	Labetalol or nicardipine and magnesium sulphate	Consider delivery

Ευχαριστώ για την προσοχή σας!