

My favorite hypertensive patients

Entertaining you is
Friedrich C. Luft

37 year-old woman with fairly severe hypertension

- Negative family history, normal pregnancy
- Receives HCTZ, Amlodipine, and Valsartan
BP still 150/100 dips but slightly
- Physical exam is OK, fundi look normal
- Urine status +1 Prot
- Na 142, K 3.6, Cl 102, HCO₃ 27 (mmol/l),
PaCO₂ 41 mm Hg, pH 7.42
- Creatinine 88 μmol/l
- What now?

Searching for 1° ALDO

- Hypokalemia
- Resistant hypertension
- History of resistance
- Ald/Renin Quotient (ARR) Screening
 - Weinberger and Fineberg. Arch Intern Med 1993

Evaluation

- Outpatient morning blood sampling (sitting): Renin (PRA) und Aldosterone
- Ideally without Meds
- SPI discontinued; BBL if possible
- ARR $>20-30$ (ng/dl per ng/ml/h)
- [ARR >554 pmol/l per ng/ml/h]
- 24-hour urine für ALDO (>12 $\mu\text{g}/24$ h) helpful

Further evaluation advocated by some

- Fludrocortisone Suppression: 4 days
0.6 mg 4 x daily; PAC >5 ng/dl
- Salt diet >200 mmol Na/daily; 24-hour
urine ALDO >12-14 $\mu\text{g}/24\text{ h}$
- 2 L 0.9% saline over 4 hours; PAC >10
ng/dl
- Captopril suppression: 25 mg per os;
PAC >10 ng/dl after 2 hours

PAC = Plasma ALDO concentration

PRA, PA and 24 h urine ALDO
with ad libitum diet

PRA >1 ng/ml/h

and/or

Urine ALDO <12 µg/24 h

1° ALDO
ruled out

PRA <1 ng/ml/h

Urine ALDO >12 µg/24 h

PA >11 ng/dl

3 days high-salt diet

PRA <1 ng/ml/h

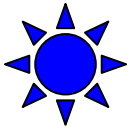
Urin ALD >12 µg/24 h

PA >11 ng/dl

1° ALDO
ruled in

Imaging for 1° ALDO

- Thin-slice CT Abdomen
 - Low sensitivity; however, if negative an operation is unlikely.
 - Adrenal vein catheterization (AVC)
 - Here you need an excellent invasive radiologist
 - (I have never encountered one radiologist who admitted that he/she was no good)

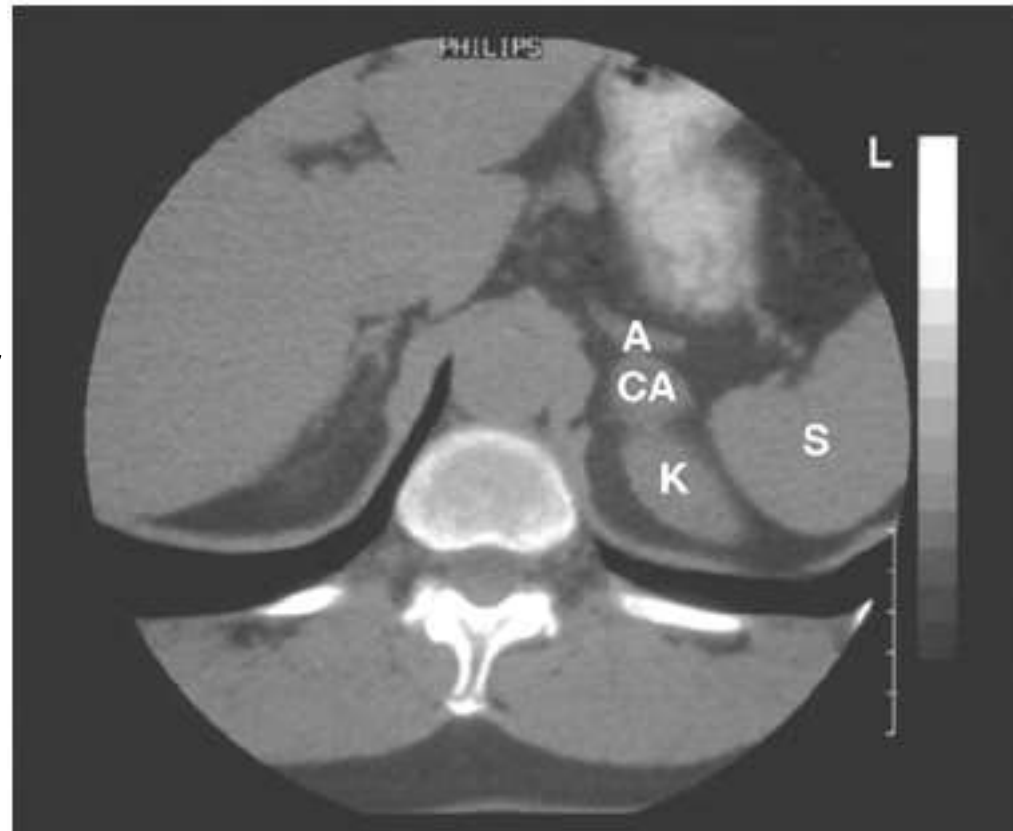


37 year-old woman with severe hypertension, hypokalemia, and ARR 41.6

Modern CT
Sensitivity >80%

„Chemical-shift“
MRI may be better

¹³¹I-6-β-iodomethyl
norcholesterol (NP-59)
Scintigraphy is an option
For adenomas <10 mm.
However, they need DEX
for 7 days



Benign
Tumors
are
hypodense
HU <10

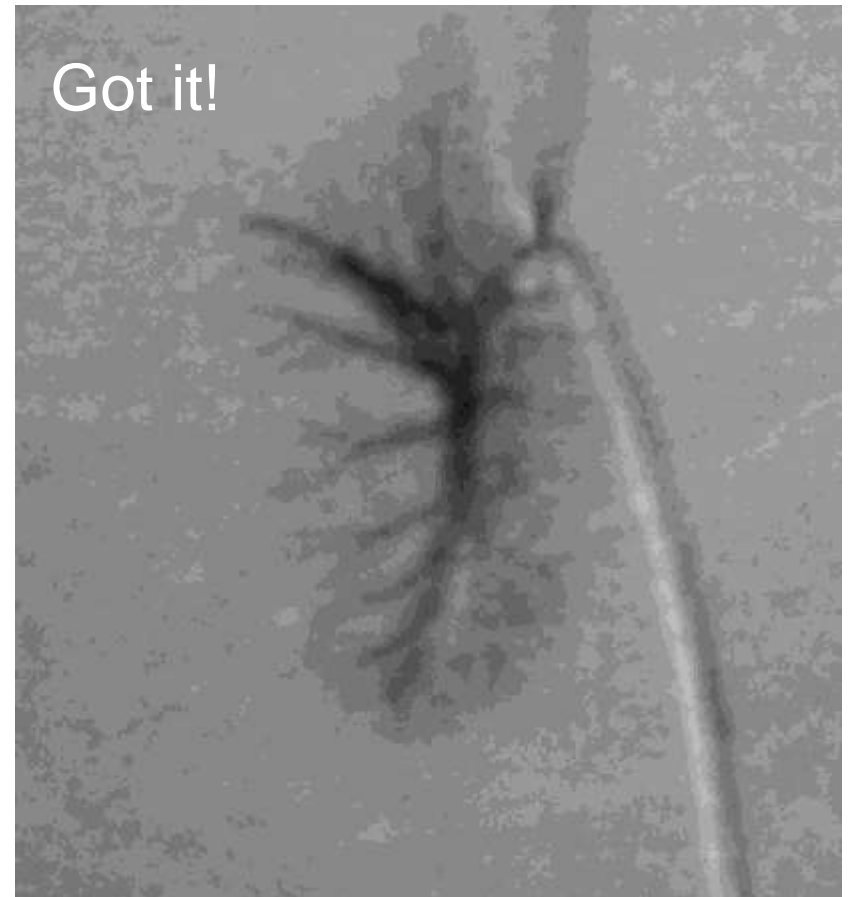
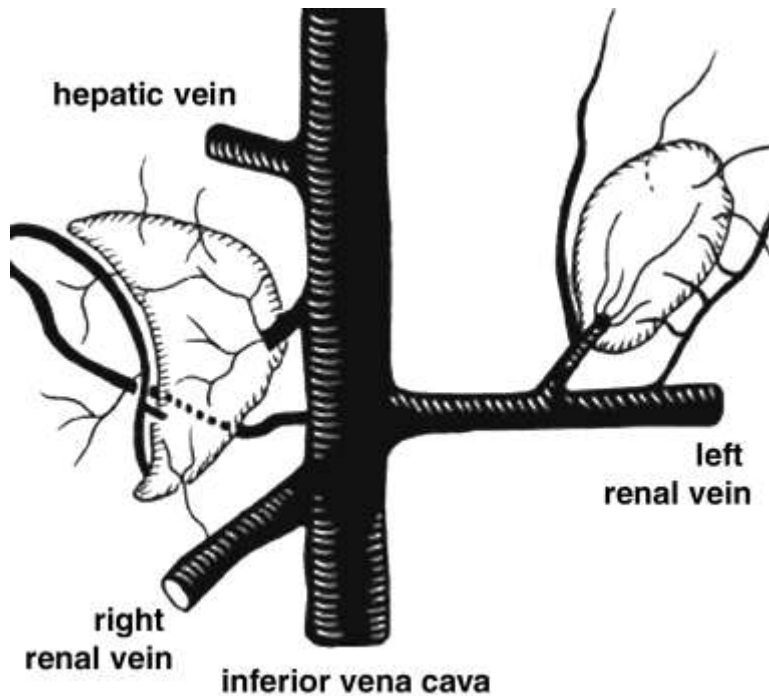
S=spleen, K=kidney, CA=Conn's Adenoma, A=adrenal

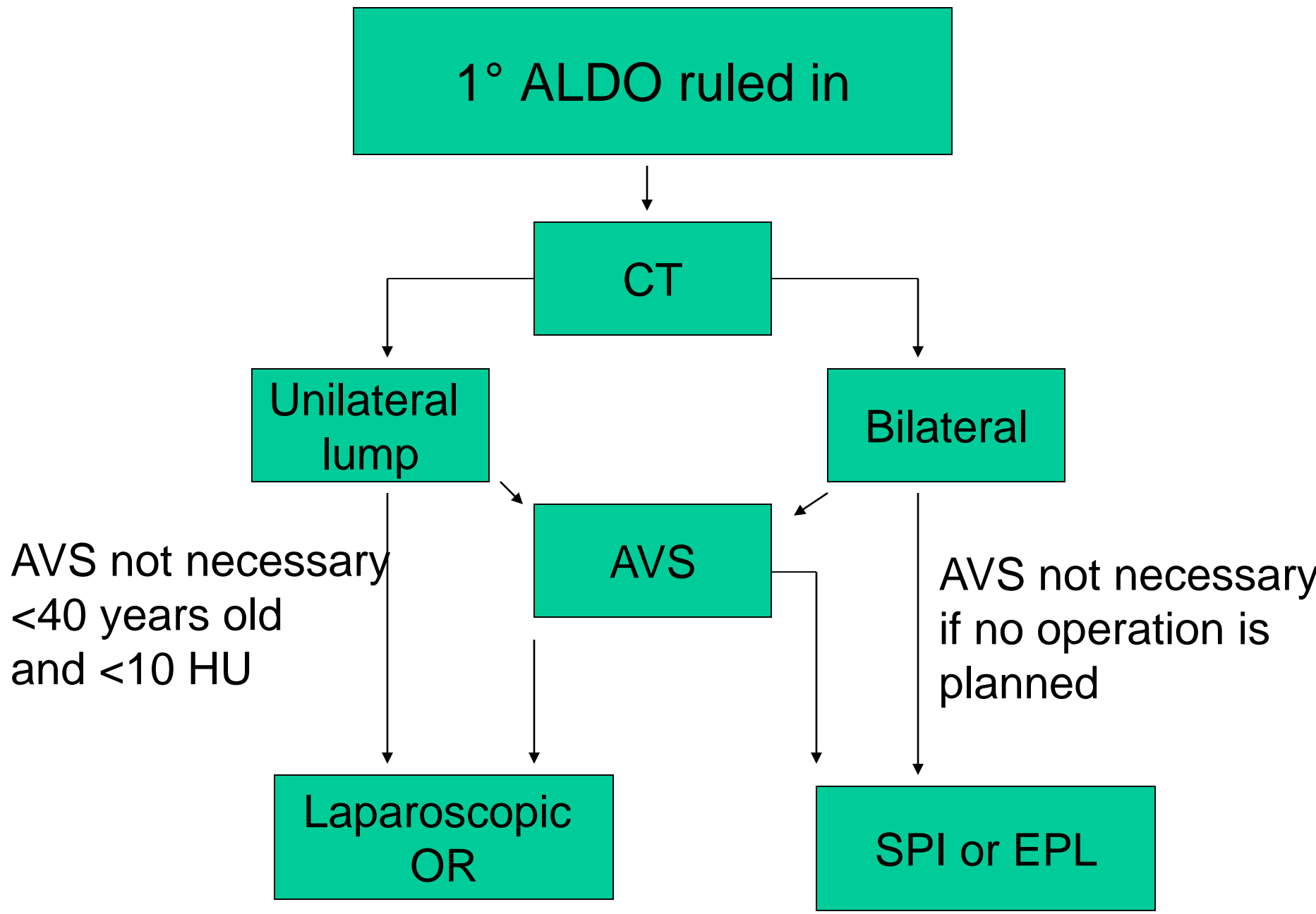
Adrenal vein sampling (AVS)

- Separating adenomas from hyperplasia
- ACTH infusion should be running
- Cortisol measured simultaneously
- Success rate (real world) 50% possible
- A tedious business

Why is AVS so difficult?

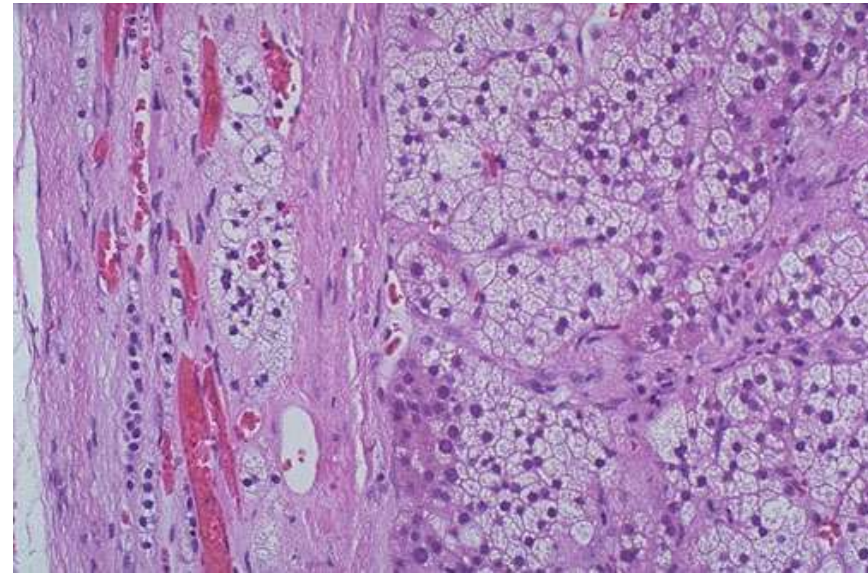
The left enters the renal vein (easy), the right enters the vena cava at an acute angle





Aldo 25 ng/dl; PRA 0.6 ng/ml/h; after high-salt diet, Urine Aldo 19 $\mu\text{g}/24\text{ h}$;

Yellow fatty Tumor



Capsule is left; Tumor looks like
Zona fasciculata
Tumor size not correlated
with PAC



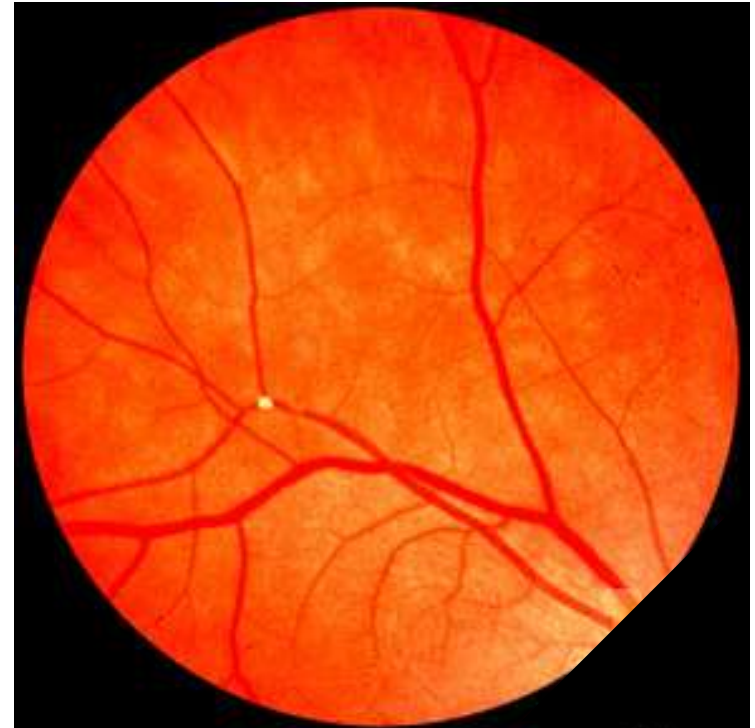
55 year-old heavy smoker

- Resistant hypertension >10 years
- Family history positive for smoking and ASCVD
- Keith and Wagner Gr II eye grounds
- Duplex: possible renal artery stenosis left
- Resistive Index (after Jörg Radermacher) <0.8

Fundi with hypertension and atherosclerosis



Copper and silver wiring with closed blood vessel



Hollenhorst Plaque
Cholesterol embolus

Clinical signs of renal artery stenosis (expert opinion)

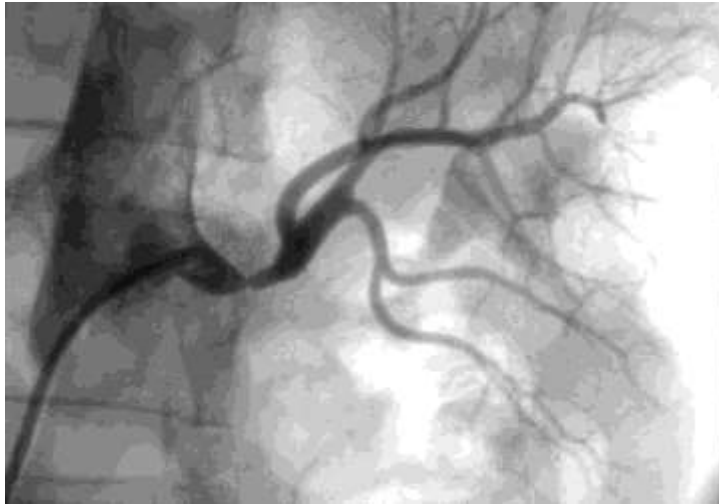
- Hypertension after age 50 years
- No + family history
- BP continually increases
- GFR decrease
- Sudden GFR decrease after ACEI oder ARB
- ASCVD in other vessels
- Flash pulmonary edema

Diagnostic tests

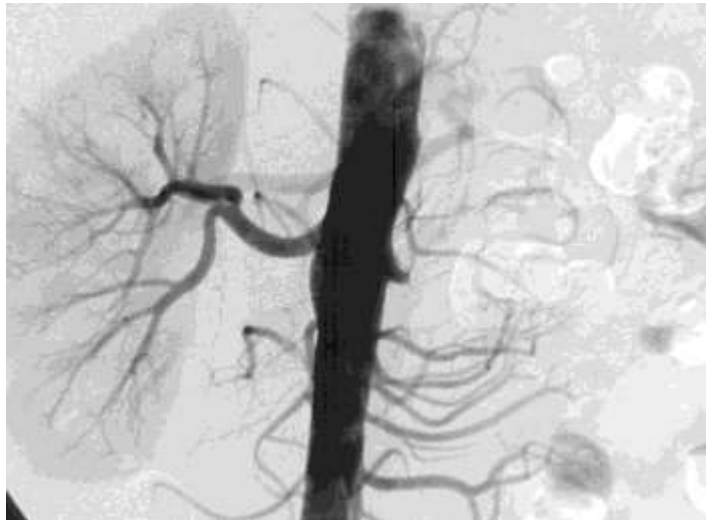
	Sensitivity	Specificity
• Captopril Scan	90	90
• Doppler	90	90
• MRI-Angio	97	90
• CT	98	94
• Angiography	100	100

„Screening-Tests“ (PRA) PRA after
Captopril etc not helpful

55 year-old smoker, female
renal-artery stenosis left



Pain and creatinine increase



Gradient falls from 30 mm Hg
to zero. Usual Michael Gross result.



Much effort and Abciximab



Facit

(the kidney was
lost)

„Shit happens“

Atherosclerosis of renal artery stenosis is common

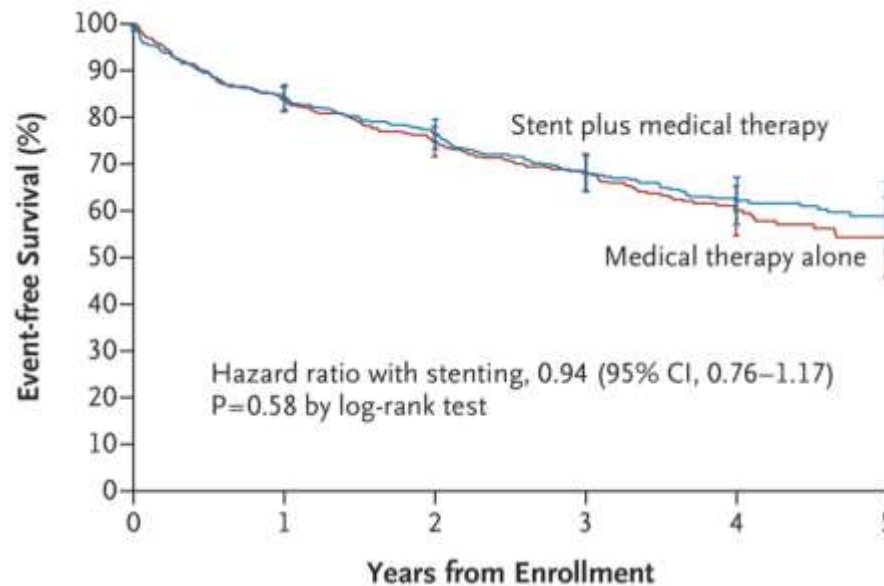
- 5% of US hypertensive patients
 - 4 000 000 cases in den US; even more in EU
- Autopsy prevalence increases with age
 - 5% at <64 years, 20% 65-74 years, 40% >75 years
- 10-40% of coronary patients
 - (J Am Soc Nephrol, Am J Cardiol and others)
- 40% peripheral vascular disease patients
 - (Ann Vasc Surg)
- I probably have it

What happens with doing nothing??

- Seven studies address this issue
- Lesions slowly progress but occlusion is actually not very common
- Progression not well correlated with GFR decreases
- Patients usually die of heart disease anyway

We were there

- Atherosclerotic renal-artery stenosis is a common problem in the elderly. Despite two randomized trials that did not show a benefit of renal-artery stenting with respect to kidney function, the usefulness of stenting for the prevention of major adverse renal and cardiovascular events is uncertain. We randomly assigned 947 participants who had atherosclerotic renal-artery stenosis and either systolic hypertension while taking two or more antihypertensive drugs or chronic kidney disease to medical therapy plus renal-artery stenting or medical therapy alone. Participants were followed for the occurrence of adverse cardiovascular and renal events (a composite end point of death from cardiovascular or renal causes, myocardial infarction, stroke, hospitalization for congestive heart failure, progressive renal insufficiency, or the need for renal-replacement therapy).



52 year-old periodic headache and tachycardia

- Five year history of this problem
- BP 140/90 that sometimes increased to 212/114 mm Hg
- Previous workups for pheo were negative
- Abdominal CT and MRI negative
- On a tilt table he became unconscious

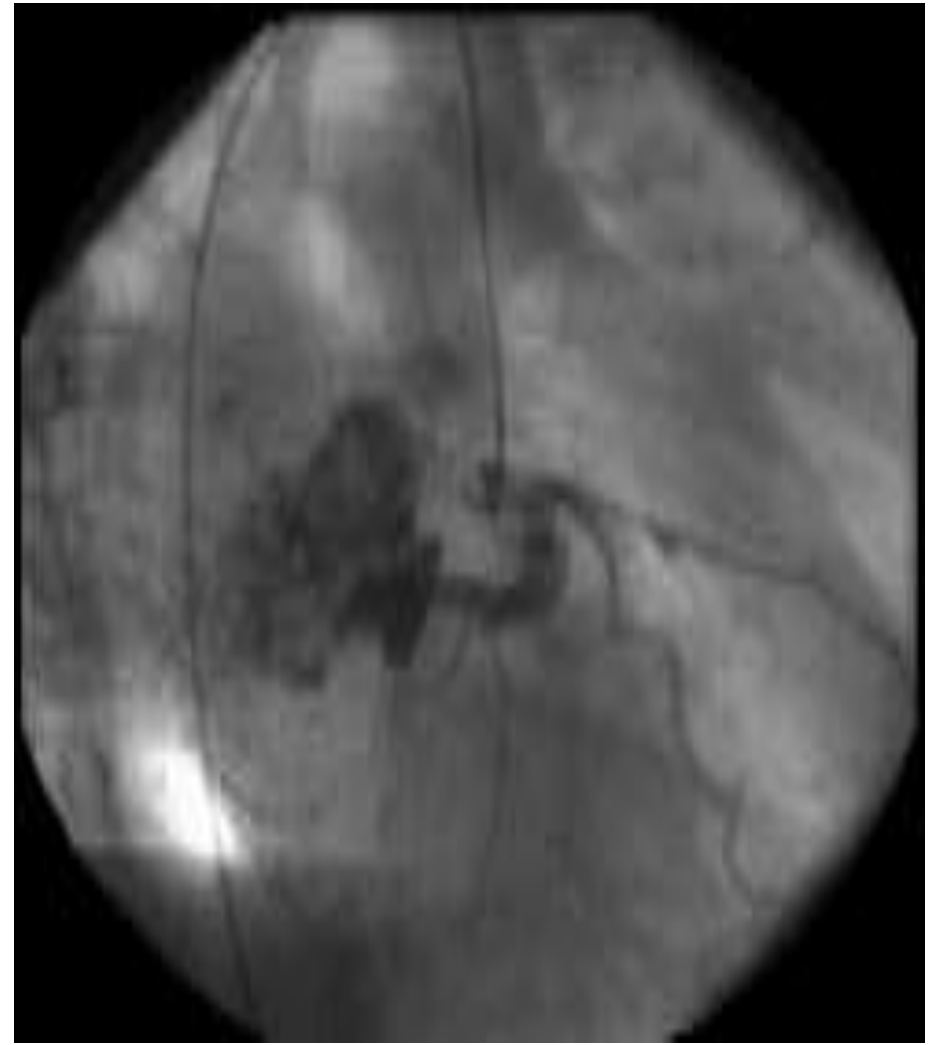
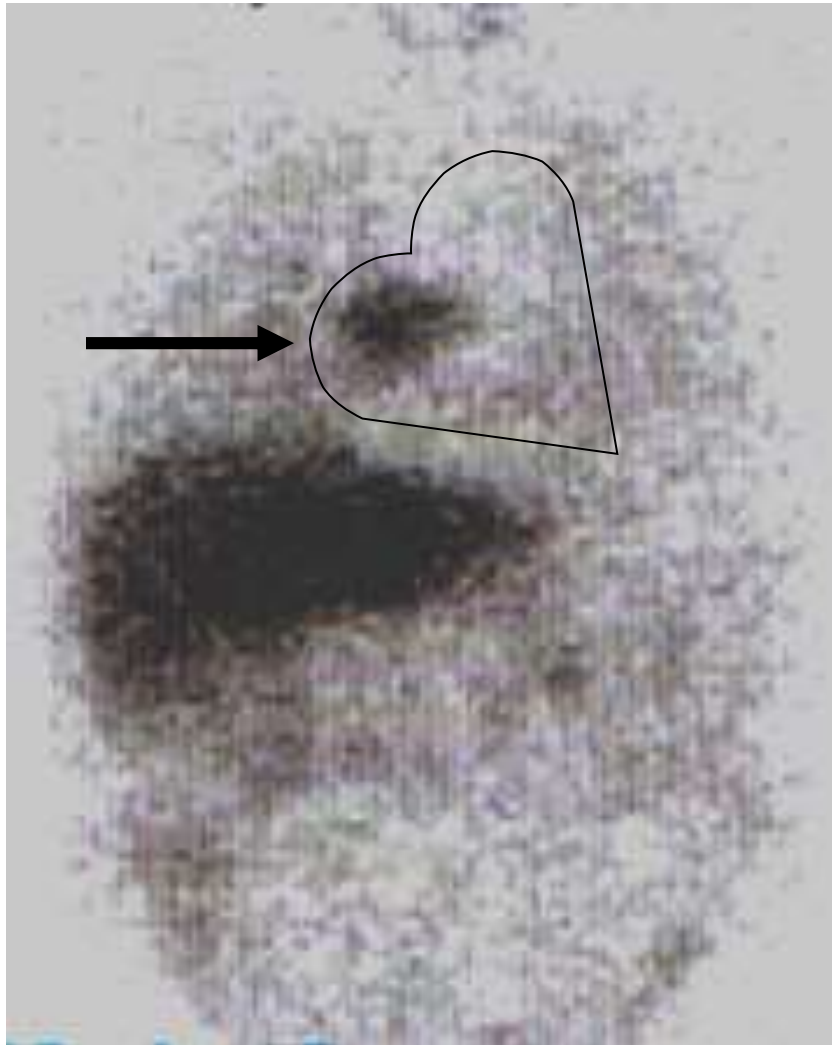
Who needs pheo „Screening“

- Hyperadrenergic „attacks“
- Resistant hypertension (25% of hypertensive patients)
- Family history (MEN2, VHL, NF-I, SDH)
- Incidentaloma workup
- Pressor episodes at anesthesia induction
- Hypertension <20 years of age
- Hypertension and dilative cardiomyopathy
- Pressure, Pain, Perspiration, Palpitation, Pallor
- 10% Extra adrenal, 10% in children, 10% multiple, 10% recurrence, 10% malignant, >10% genetic, 10% incidentaloma

Biochemical diagnosis!

- 24 h urines for metanephrine, normetanephrine
- Sensitivity 98%, Specificity 98%
- Fractionated free metanephrine
 - Sensitivity 97%, Specificity 89%
- Confounders are tricyclic anti-depressives, levodopa, ethanol, clonidine (both withdrawal), antipsychotic drugs, panic attacks, obstructive sleep apnea

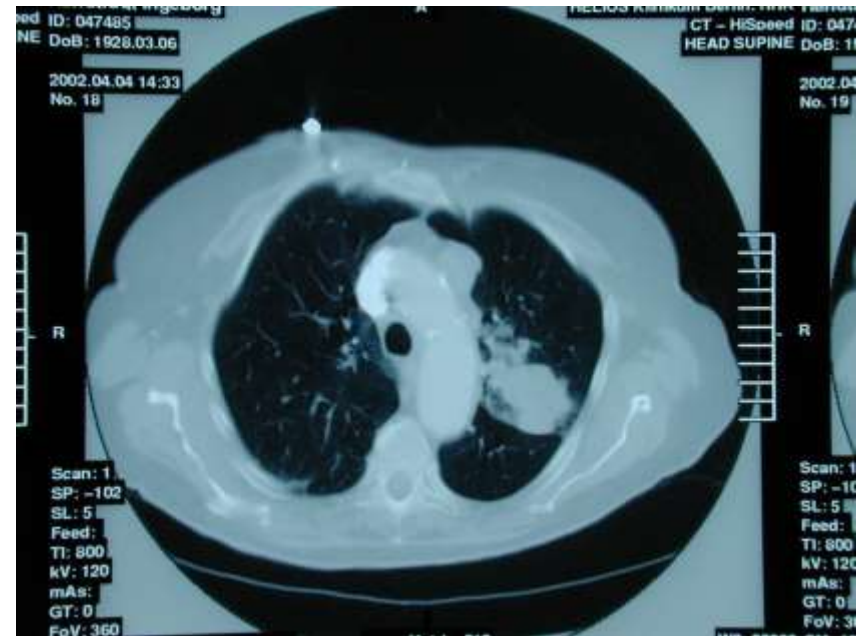
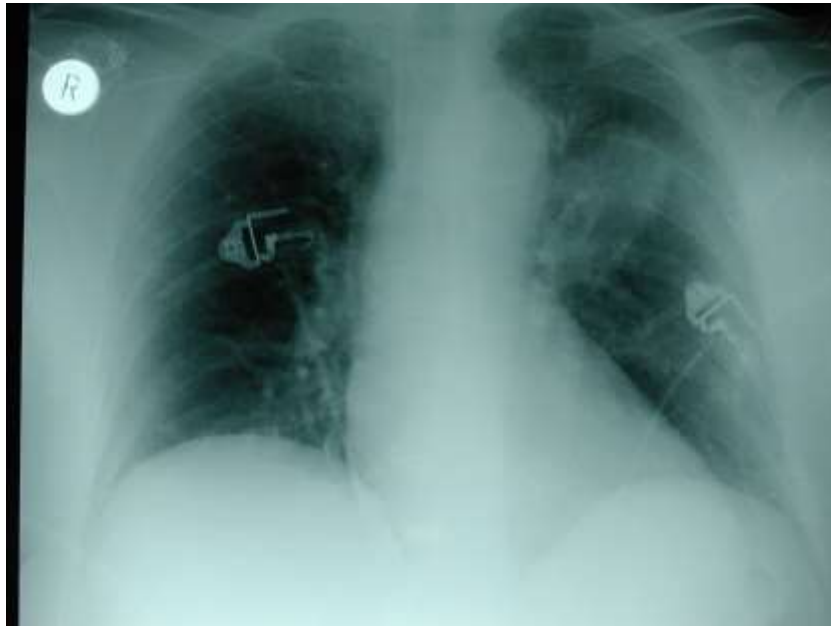
^{123}I -Meta-iodobenzylguanidine (MIBG)
Scinti, CT, MRI, CT head, neck,
somatostatin receptor scinti, PET etc.



68 year-old woman with acute coronary syndrome receives and acute stent

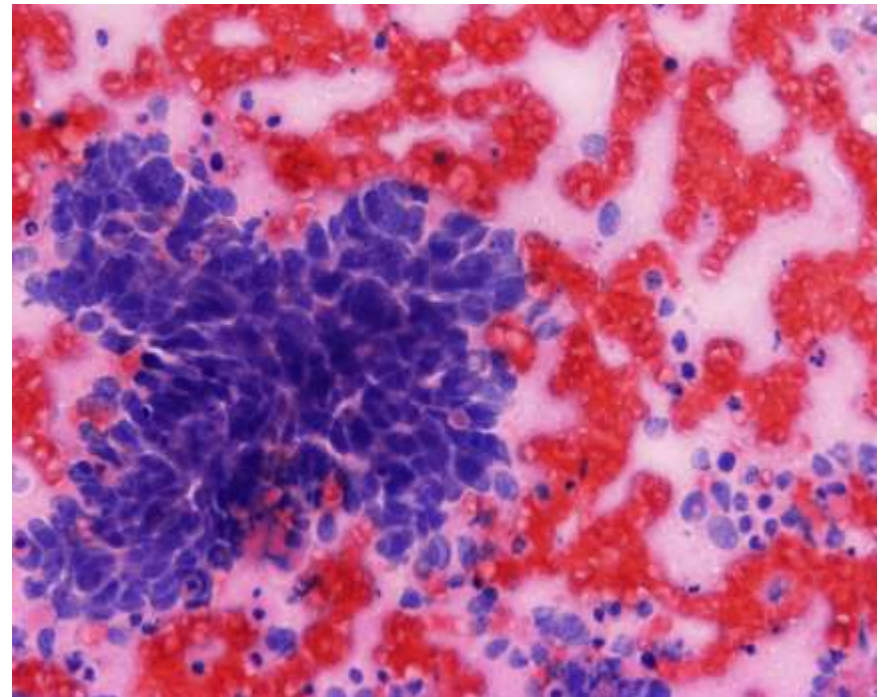
- pH 7.52, PaCO₂ 43 mm Hg, PaO₂ 82 mm Hg, Na 141, K 2.7, Cl 96, HCO₃ 36 mmol/l
- Acid-base disturbance?
- UCl, UK, UNa, UOsm, TTKG?
- TTKG = (U/P K) ÷ (U/P Osm)
- UK was 36 mmol/l UOsm was 270
- TTKG was 14-fold; thus the K loss occurs via the kidneys

The kids on ICU had not reviewed her xray. We did CT



Professional smoker, hypertensive for 10 years,
HCTZ, but no Cushing's stigmata

- PRA was low
- PA not increased
- Cortisol 2000 nmol/l
- ACTH 90 pmol/l
- No fall with Dex
- Biopsy showed „oat“

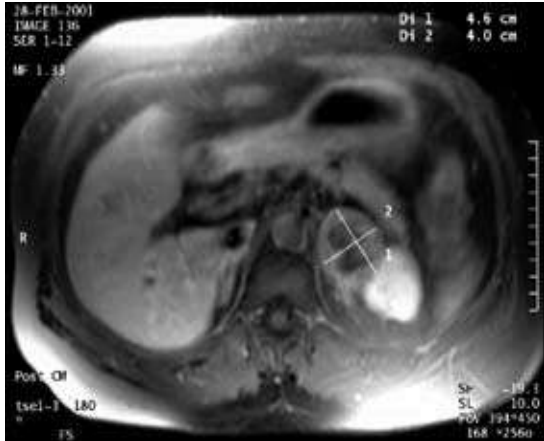


56 year-old woman with resistant hypertension and interstitial nephritis.

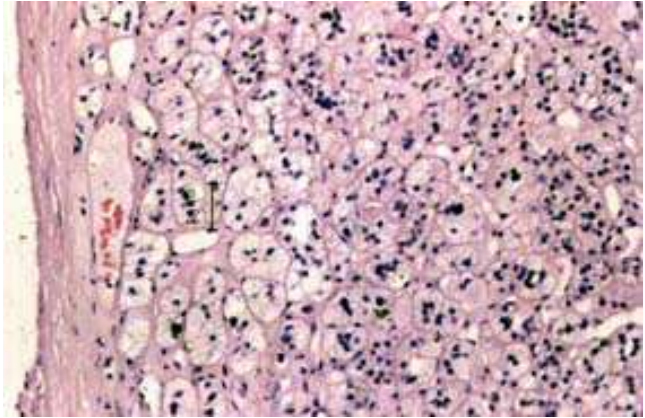
Creatinine was 290 $\mu\text{mol/l}$

- BP 170/110 mm Hg
- KW Gr III (she had a few hemorrhages and exudates)
- Urine Prot +2; Wax cylinders
- US showed a cystic adrenal mass
- What next?

Always do the most expensive test first!



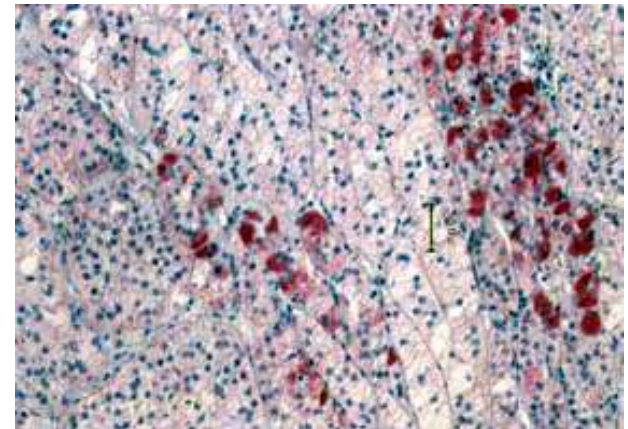
MRI



H & E



Yellow tumor confined by capsule



Melanin

The Incidentaloma, 5% of all autopsies, 10% in hypertensive patients (age dependent), >60,000 CTs at Mayo Clinic gave a 4% prevalence

Danger signs:

- Density in CT >10 Hounsfield units
- >6 cm
- >4 cm younger patients
- Cushing's, Pheo, Aldo ruled out
- I prefer doing nothing
- My young associates see that differently
- They usually win

38 year-old office worker;
BP 250/110 mm Hg

- Negative family history
- Physical examination normal
- Na 143, Cl 105, K 3.5, HCO₃ 26 (mmol/l)
- PRA <1 ng/ml/h; PA low
- Triple therapy hardly effective
- We were clueless

We sent her away for an MRI of „something or other“

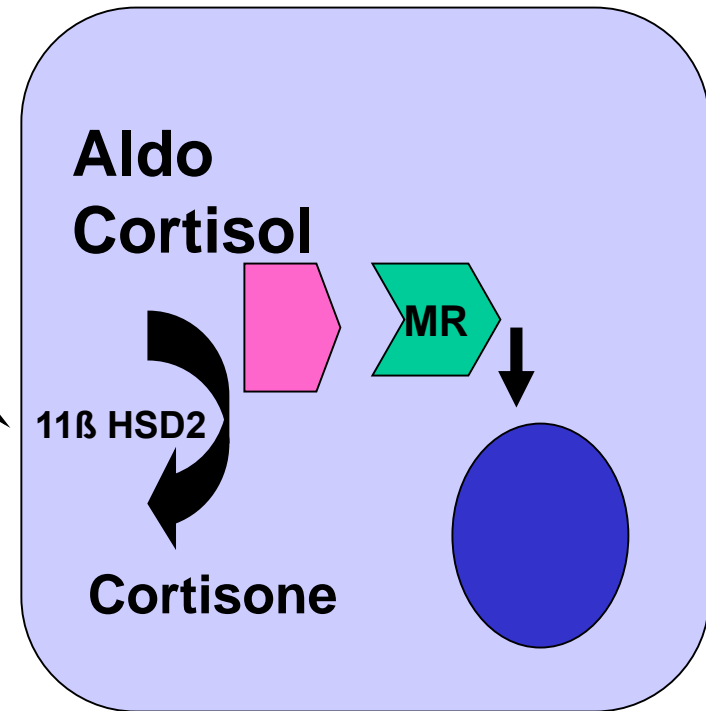
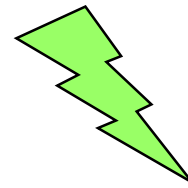


Then, we inspected the contents of her night table and personal belongings. In the process we violated at least a dozen German „data protection“ laws.

Licorice from Finland

11-Beta-hydroxysteroid Dehydrogenase-2

**Mutation or licorice inhibition.
Glycyrrhethinic acid**



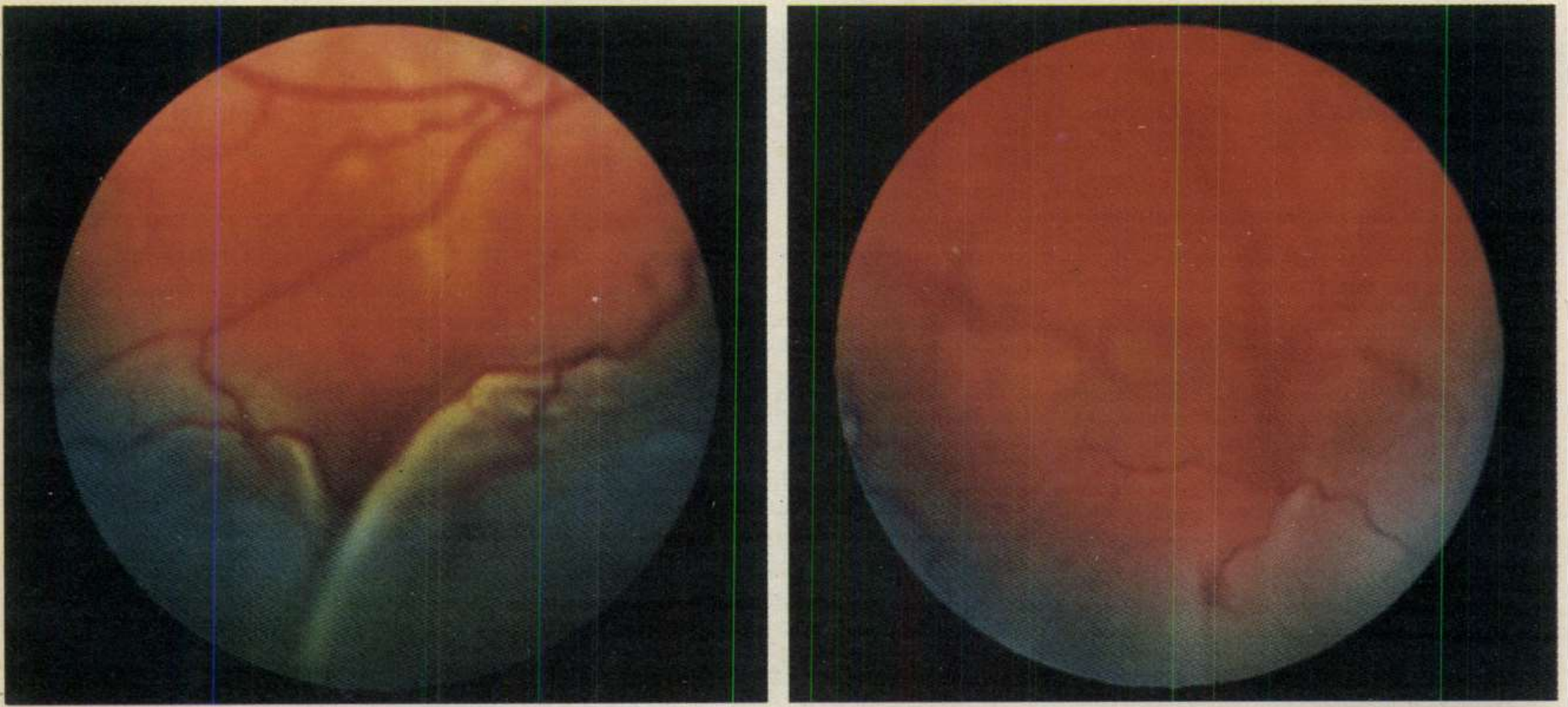
Concerns licorice,
chewing tobacco, Huangin-Tang,
host of other alternative medicinal sources
etc.

„apparent mineralocorticoid excess “

29 year-old man was sent to our emergency department by the ophthalmologic clinic for admission. Suspected „Vogt-Koyanagi-Harada-Syndrome“

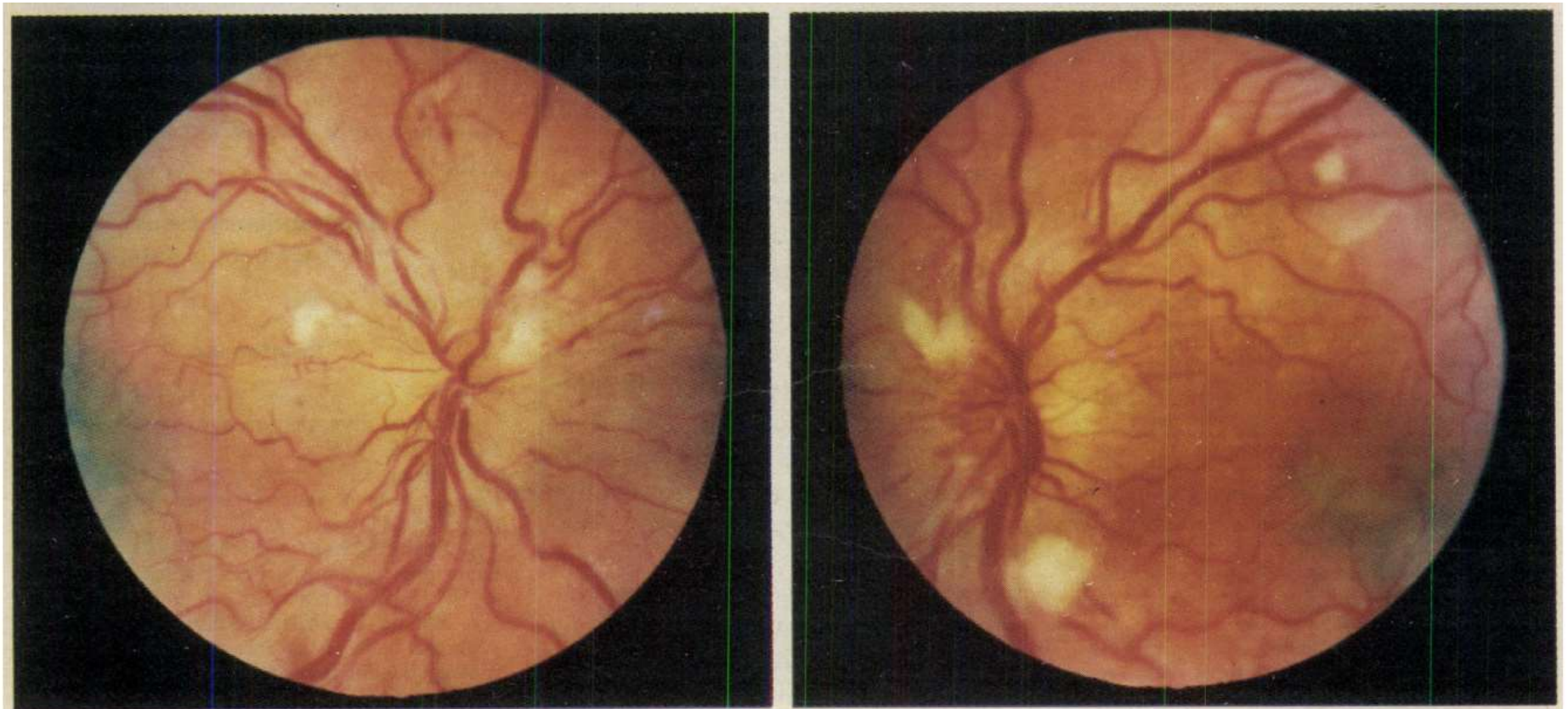
JAMA 1977

Upper panels show severe bilateral bullous retinal detachment with papilledema. Lower panels show fundi three weeks later. Retinas have reattached; papilledema remains.



After ICU, nitroprusside, furosemide, captopril, metoprolol, hydralazine, and several dialyses:

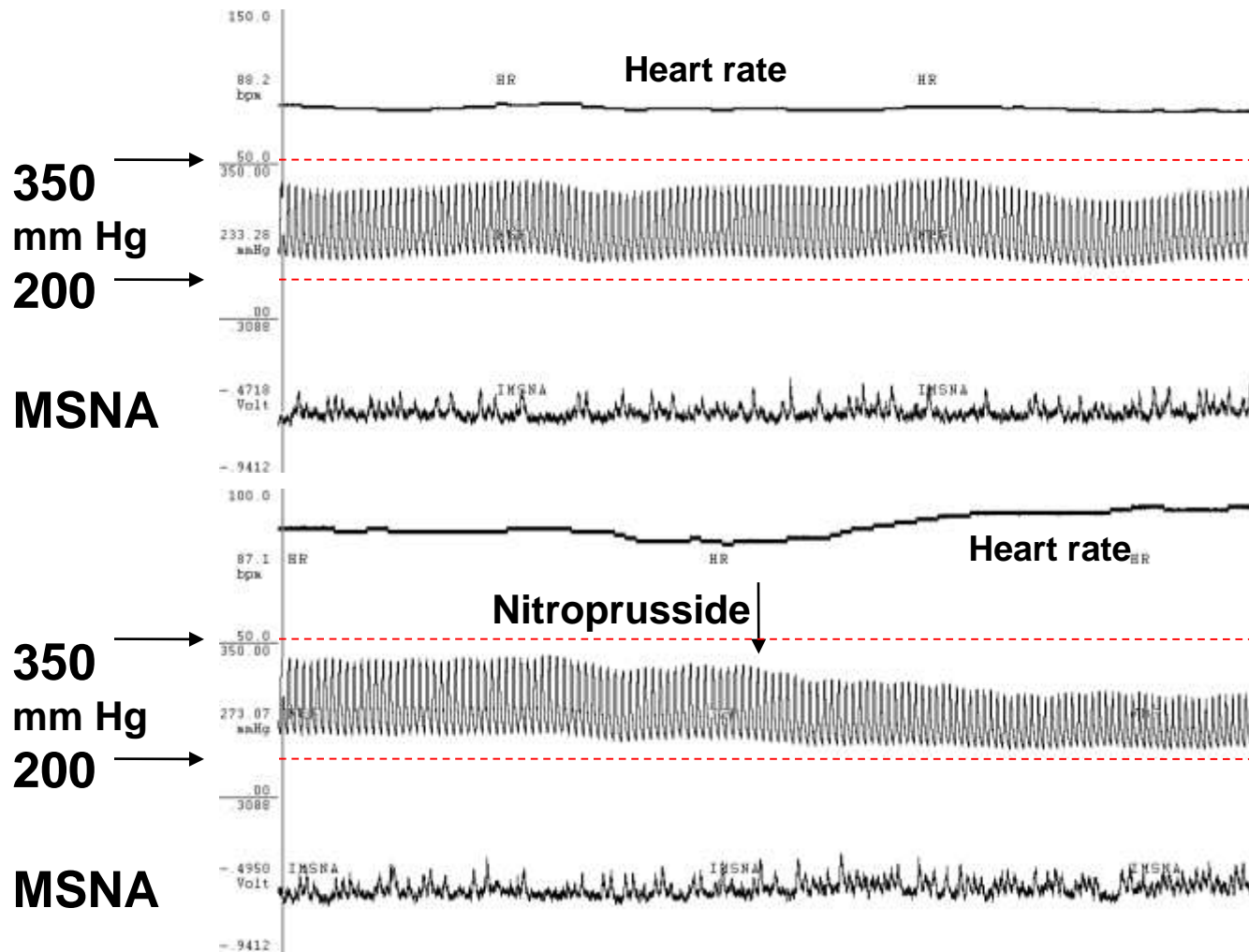
JAMA 1977



Hypertensive emergencies

- Accelerated hypertension with target-organ damage, like CNS damage and papilledema
- Flash pulmonary edema
- Suspected aortic dissection
- Acute renal failure
- Pheo crisis
- Drugs and withdrawal
- Postoperative
- Preeclampsia

65 year-old woman referred with BP 300/200 mm Hg. Both carotid arteries had been operated upon because of fibromuscular hyperplasia. One side was irradiated because of a suspected tumor

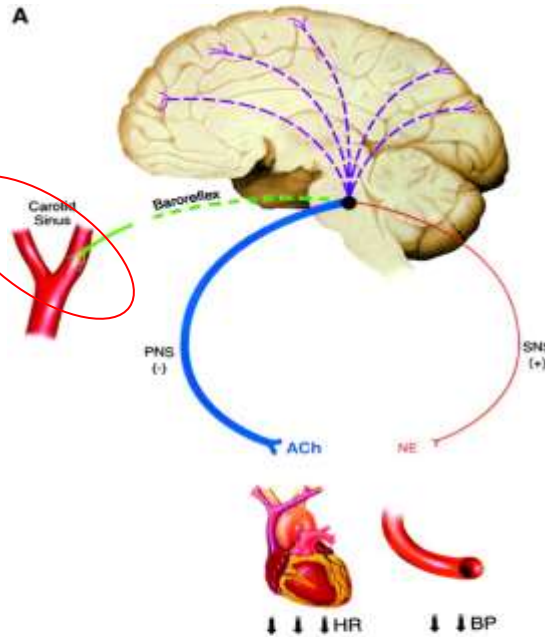


Baroreflex failure

Procaine
Anesthesia

or

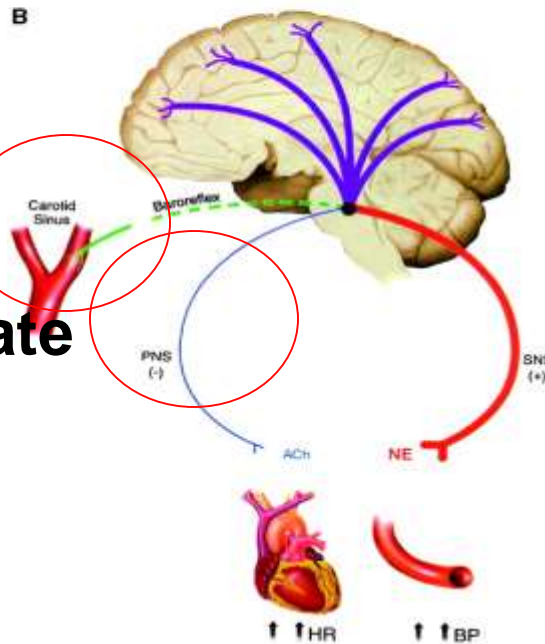
Strict
afferent
problem



Treatment is difficult

Guanethedine helped
this patient

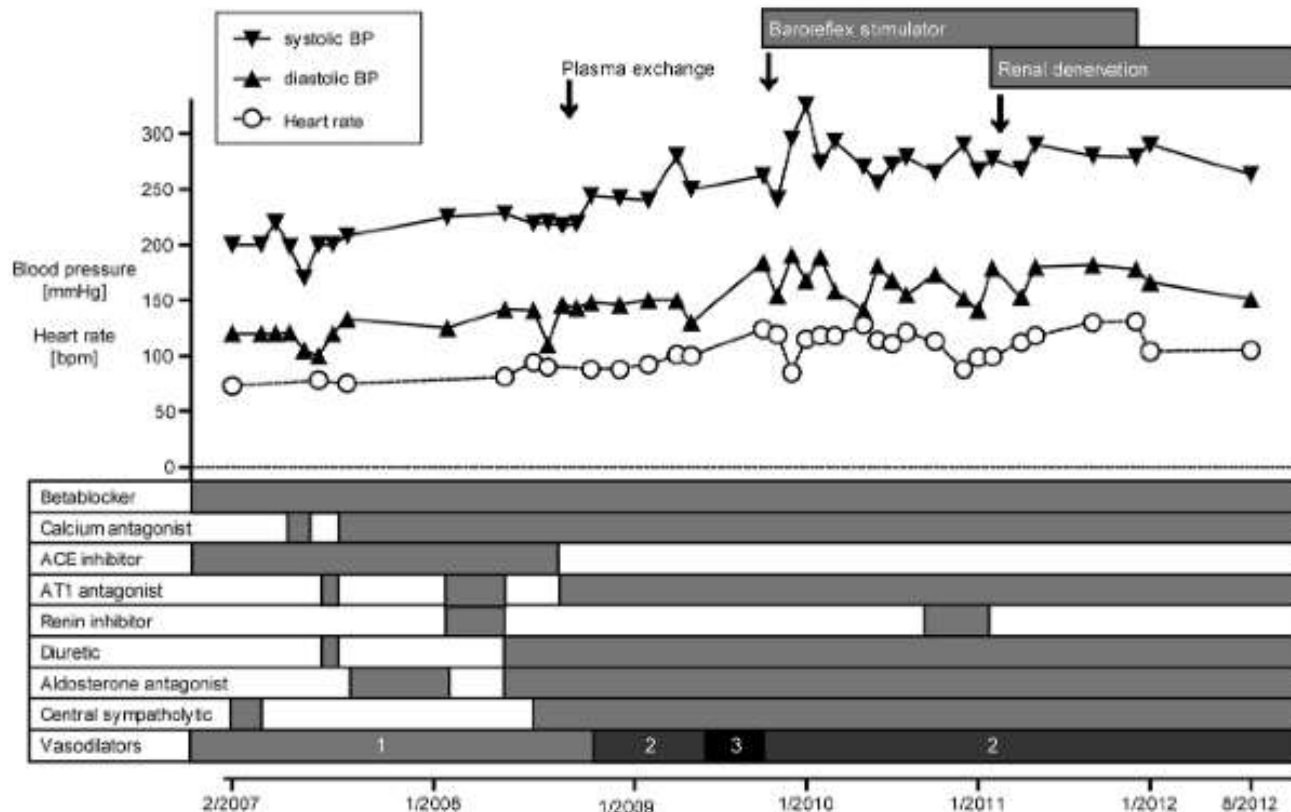
Our patient with
the „fixed“ heart rate



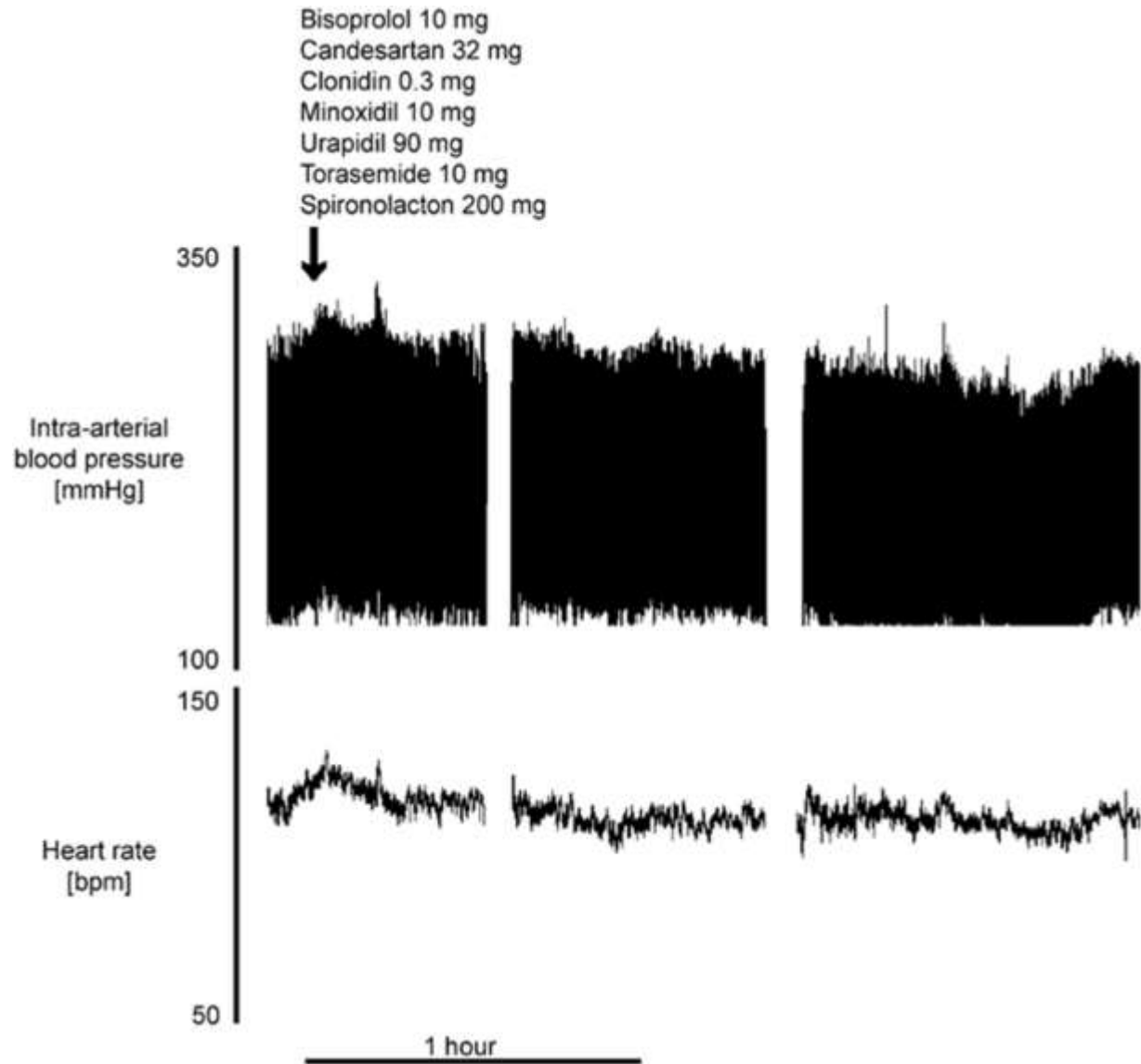
Hypertension Grand Rounds

Truly Refractory Hypertension

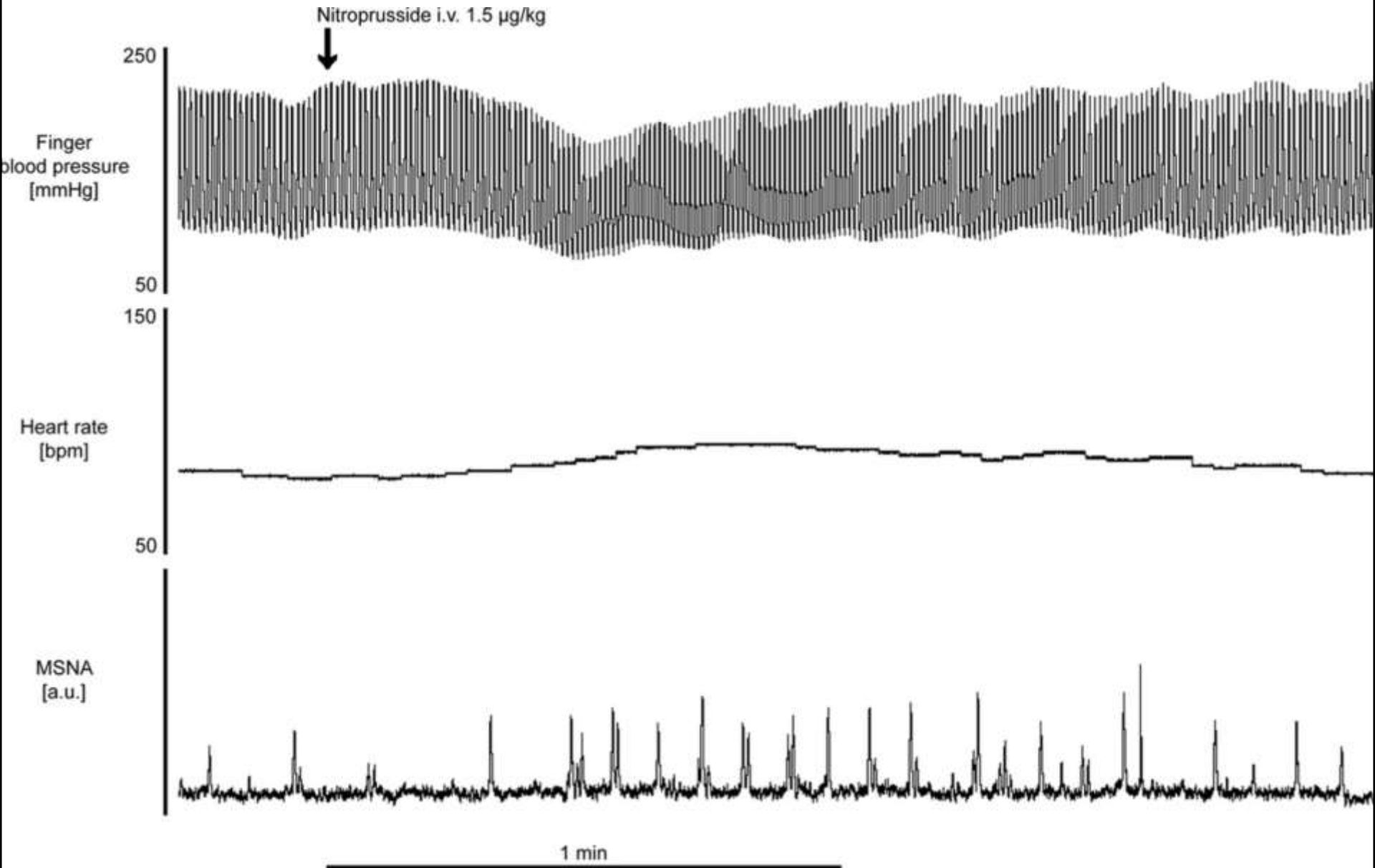
Christoph Schroeder, Karsten Heusser, Julia Brinkmann, Jan Menne, Hanno Oswald, Hermann Haller, Jens Jordan, Jens Tank, Friedrich C. Luft



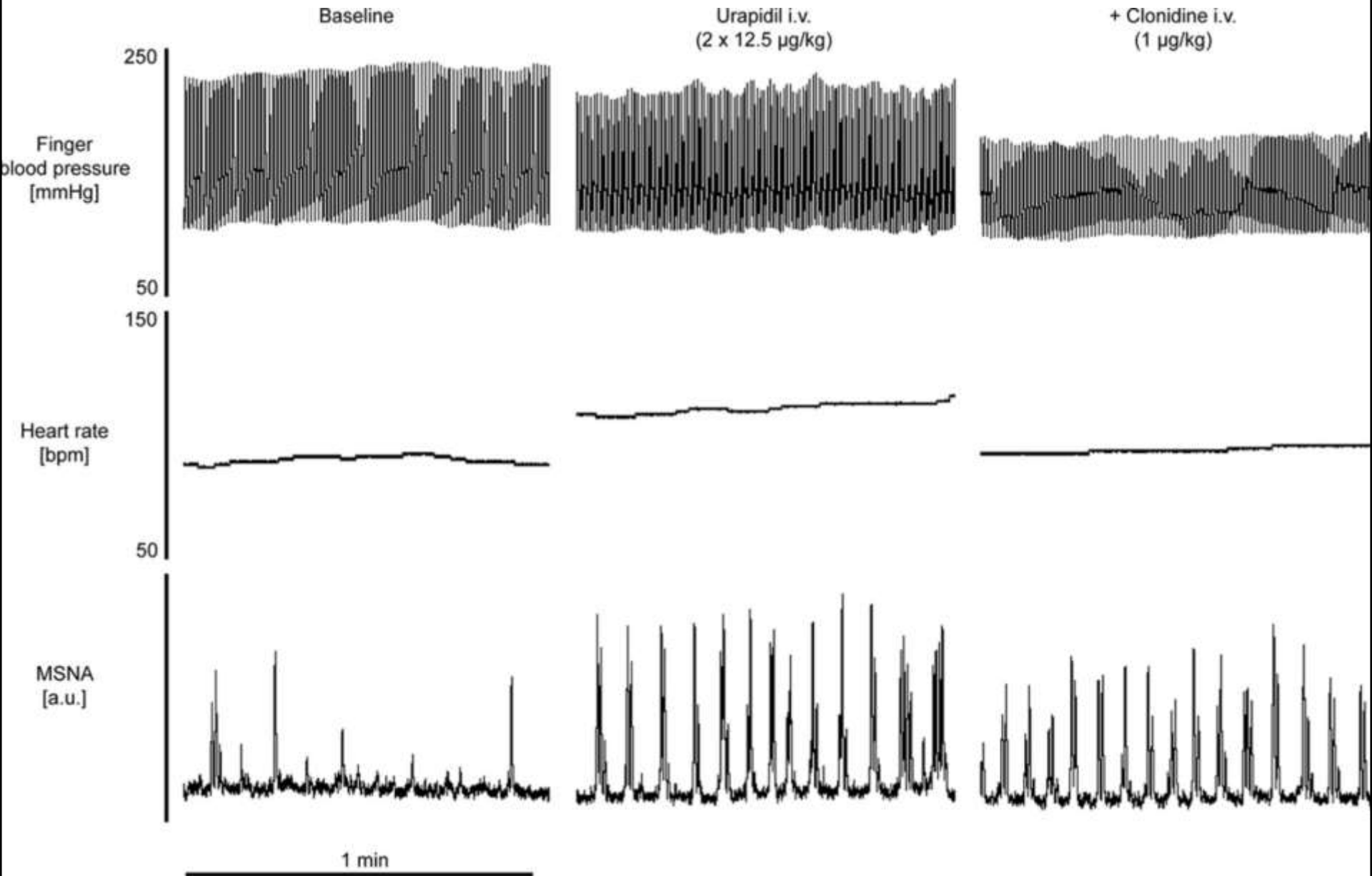
Is it true?

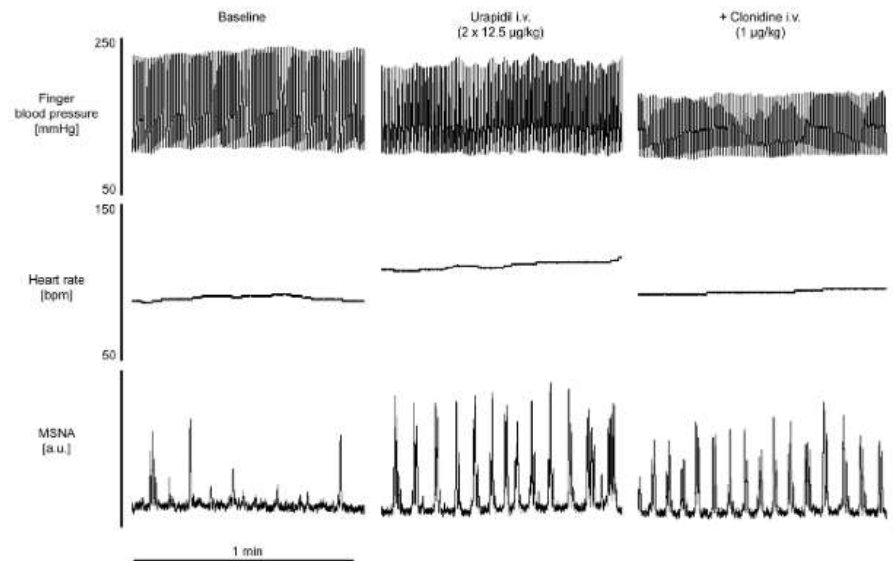
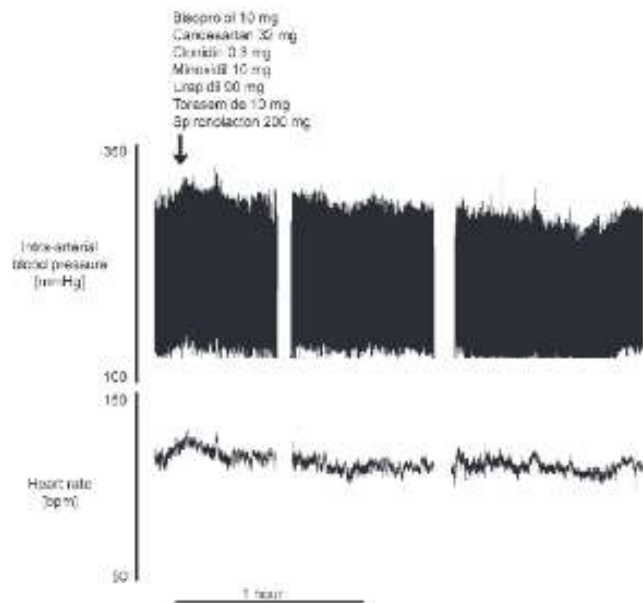


How about bolus nitroprusside?



How about iv urapidil and clonidine?





She has had (1) renal denervation, (2) carotid-sinus stimulation and now a (3) brain stimulation electrode. To my knowledge, no treatment has been satisfactory. A most sobering and humiliating experience.

Hypertension is not dull

We have an excellent armamentarium
and our importance is recognized
(we actually help people)

Improvements will be forthcoming

Interventions will be tested

The genome era will not pass us by



All very nice, but does it always work?