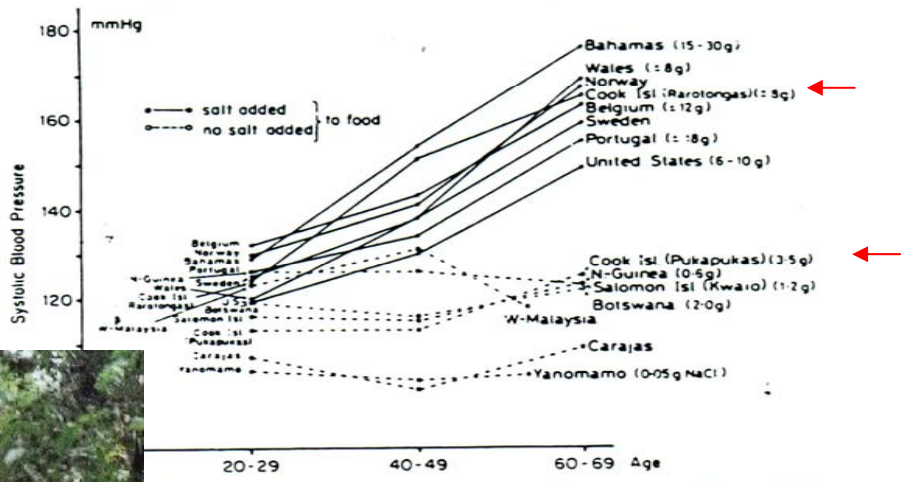
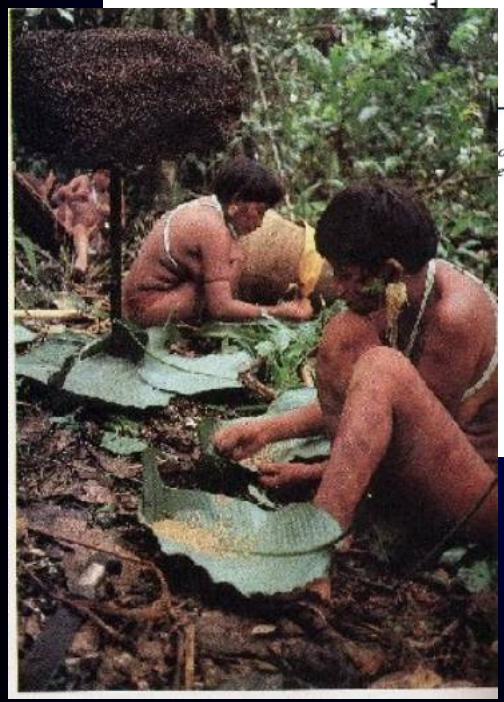
Blood pressure increases with aging only in civilizations with high salt intake



omparative international data on salt intake and blood pressure levels at varying ed from MacGregor[1] with permission.)



<u>Cook islands</u>

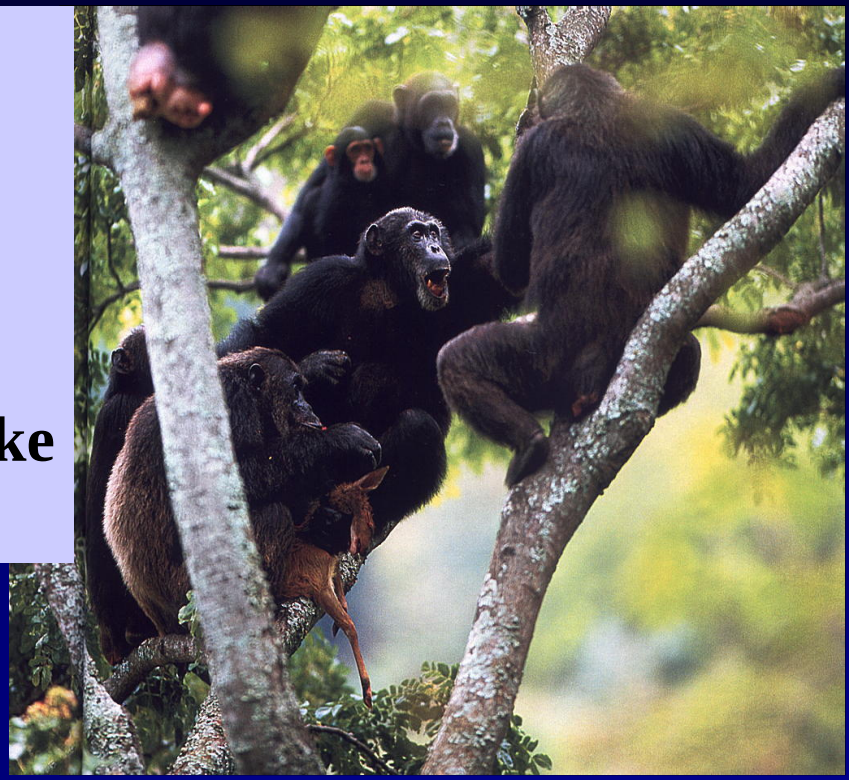
-Difference in BP and HT between highland and coast

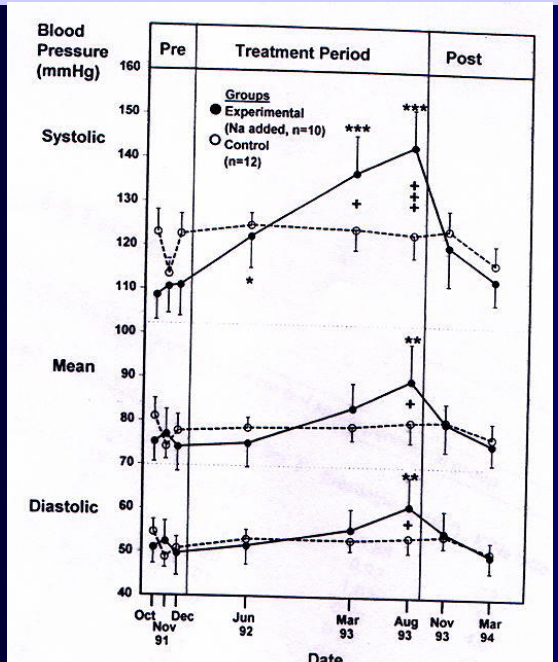
-emigrants to Hawaii – prevalence of HT higher (30%)

ANIMAL ANALOGY

-Philogenetic similarities
-99.6% coding exons
-Same amount of NaCl in milk

- no stress, same potassium intake
  BP increase with higher salt intake
- salt sensitivity in chimpanzees

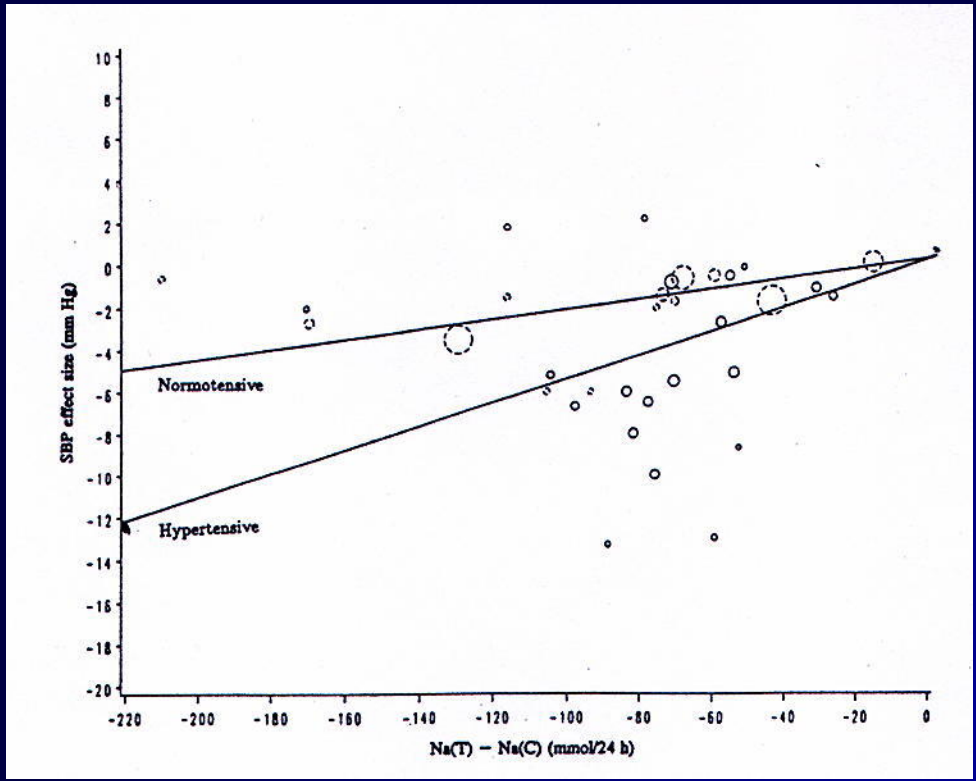




Denton, 1995

Correlation between blood pressure and salt intake

Salt intake determines BP in hypertensive and normotensive subjects

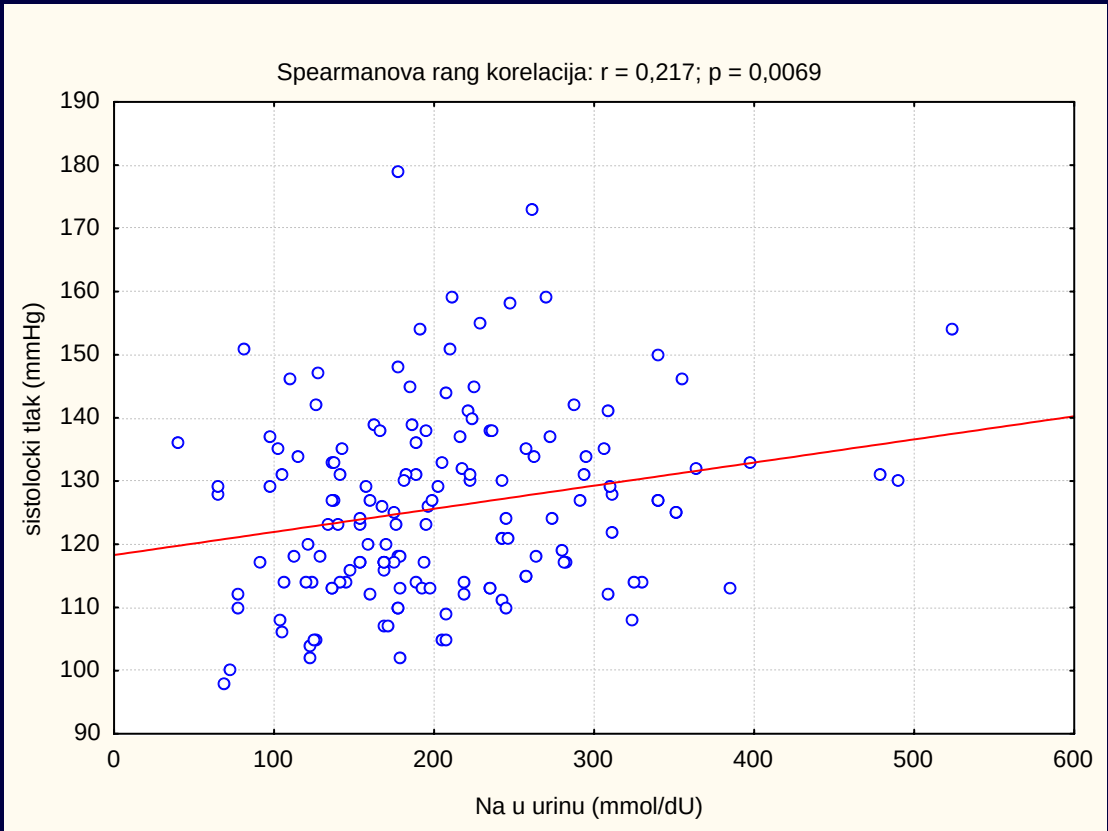


Cutler, 1997

INTERSALT study

Δ intake NaCl 100 mmol = Δ BP of 10/6 mmHg/30 years

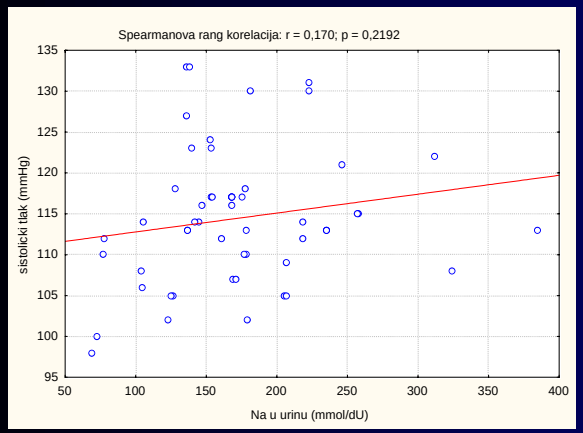
Correlation of systolic AMBP and salt intake in Croatia

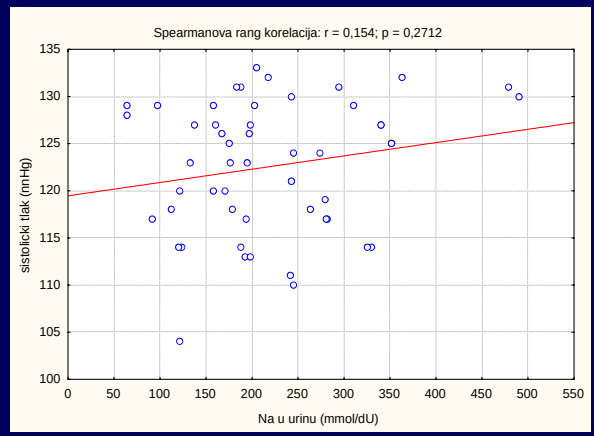


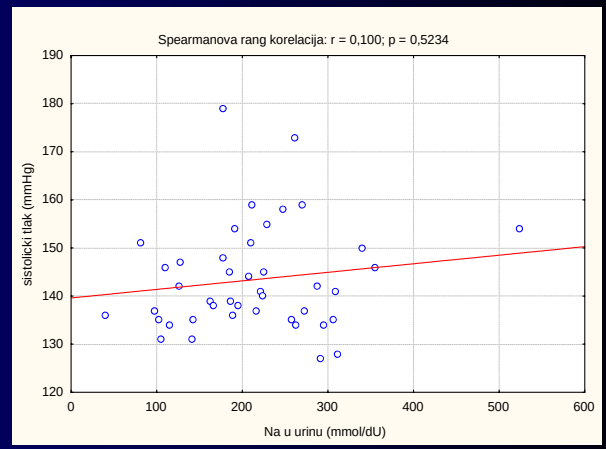
Pezo-Nikolić, Jelaković, 2008 unpublished data

Correlation of systolic AMBP and salt intake in Croatia

Normotension (N= 62)	White coat HT (N=64)	Essential HT (N=55)

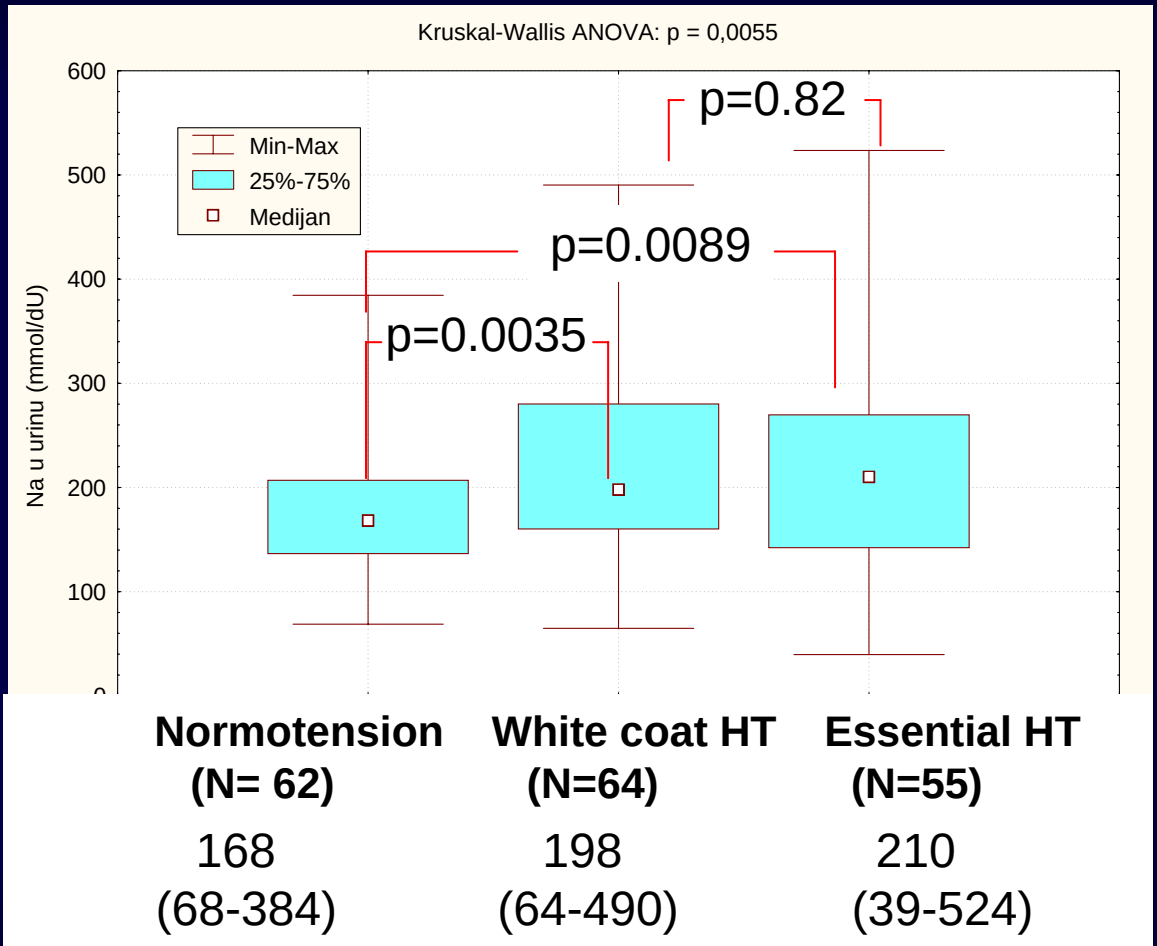




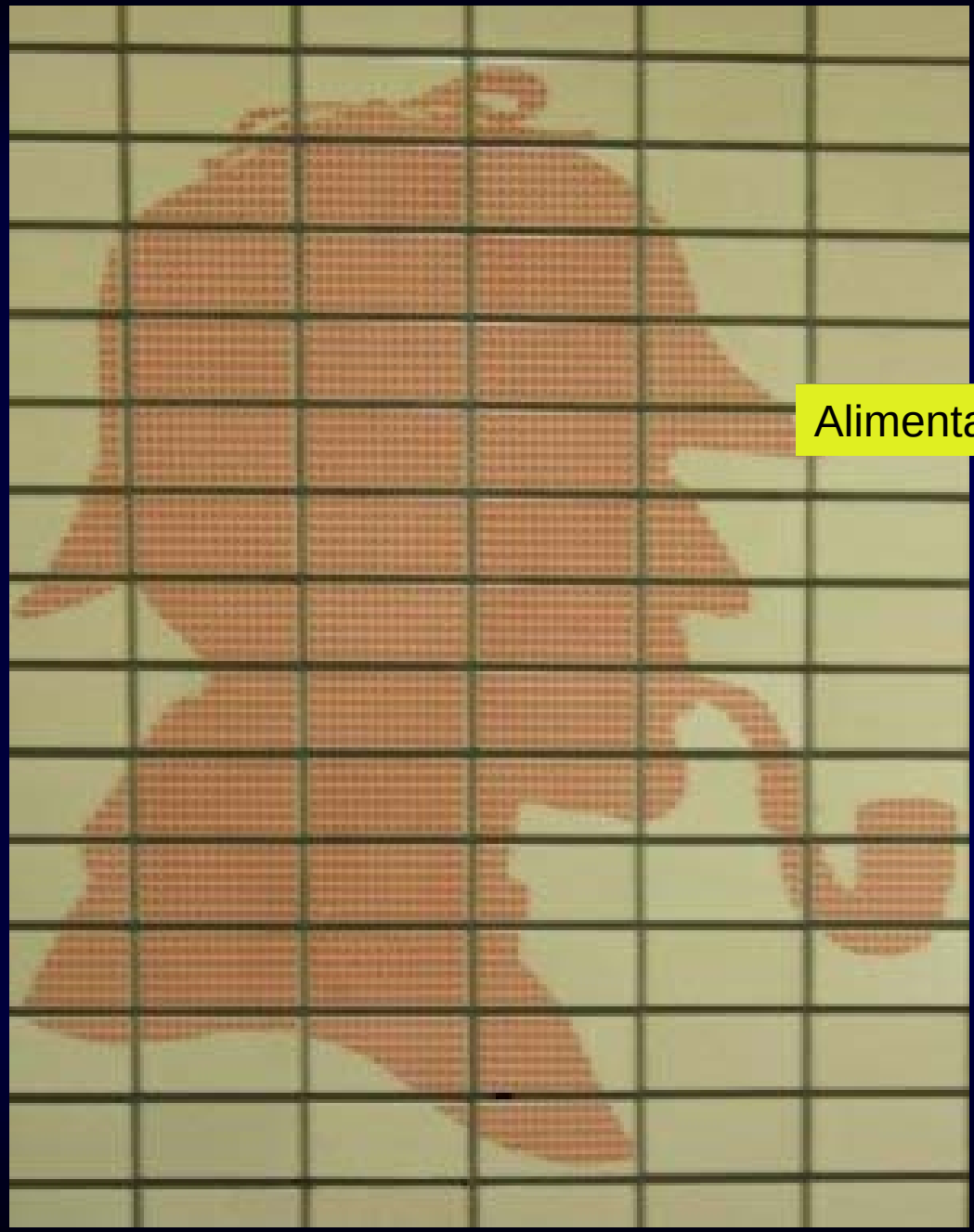


Pezo-Nikolić, Jelaković, 2008 unpublished data

24 hour sodium excretion (mmol/dU) and BP categories in Croatia



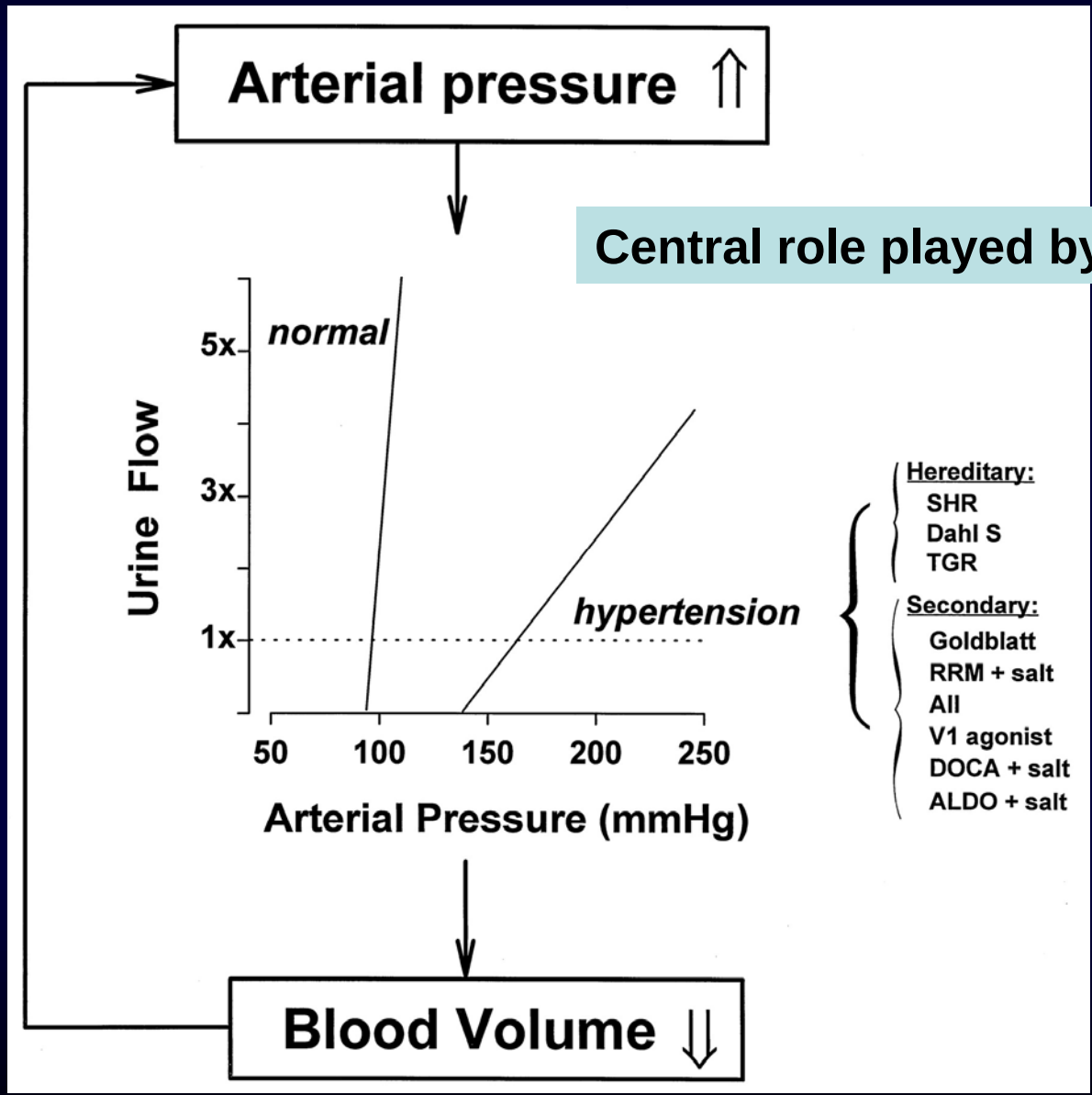
Pezo-Nikolić, Jelaković, 2008 unpblished data



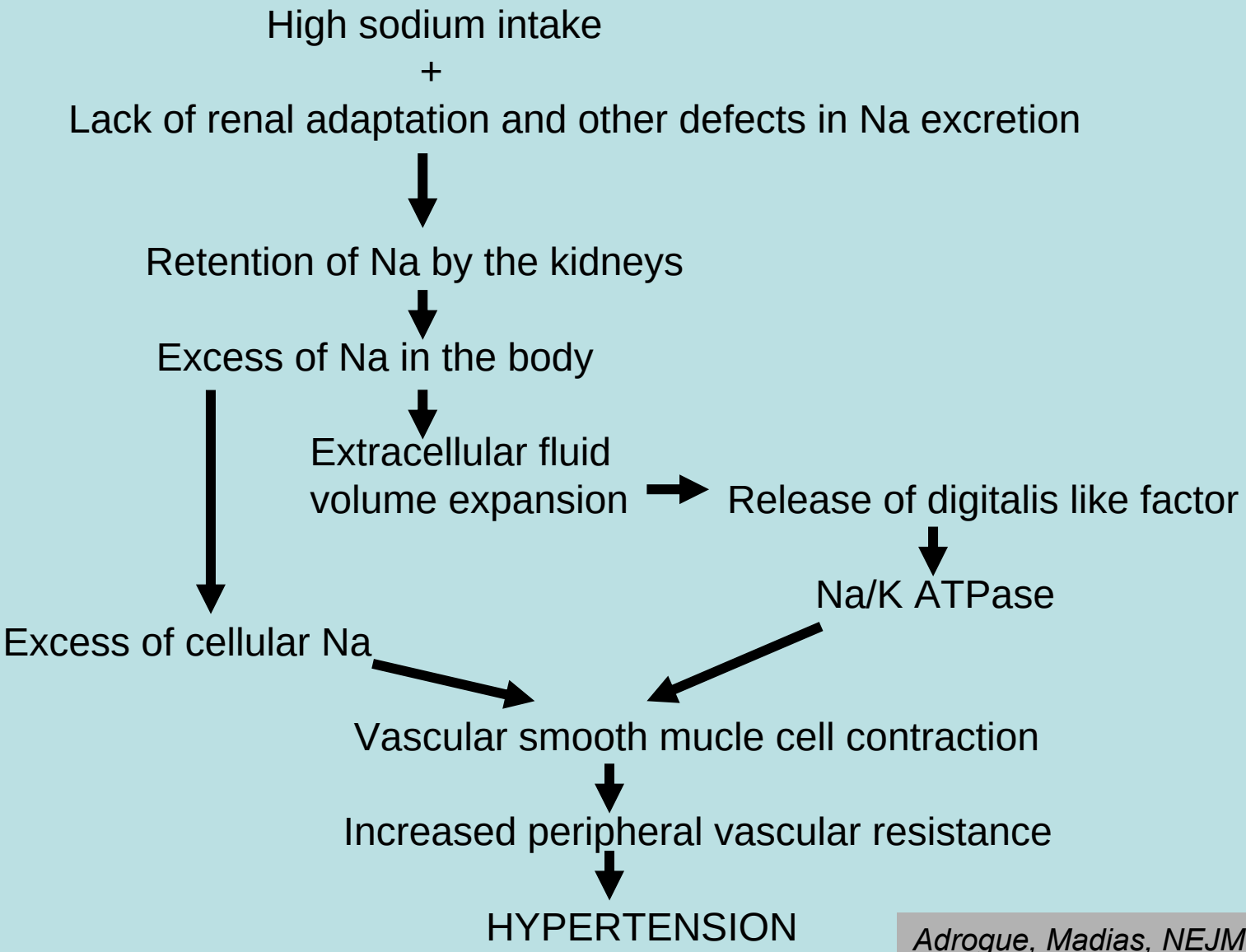
Alimentary, My Dear Watson

Doyle, Journal of Sherlock Holmes, 1898

Guytons' Pressure-Natriuresis relationship

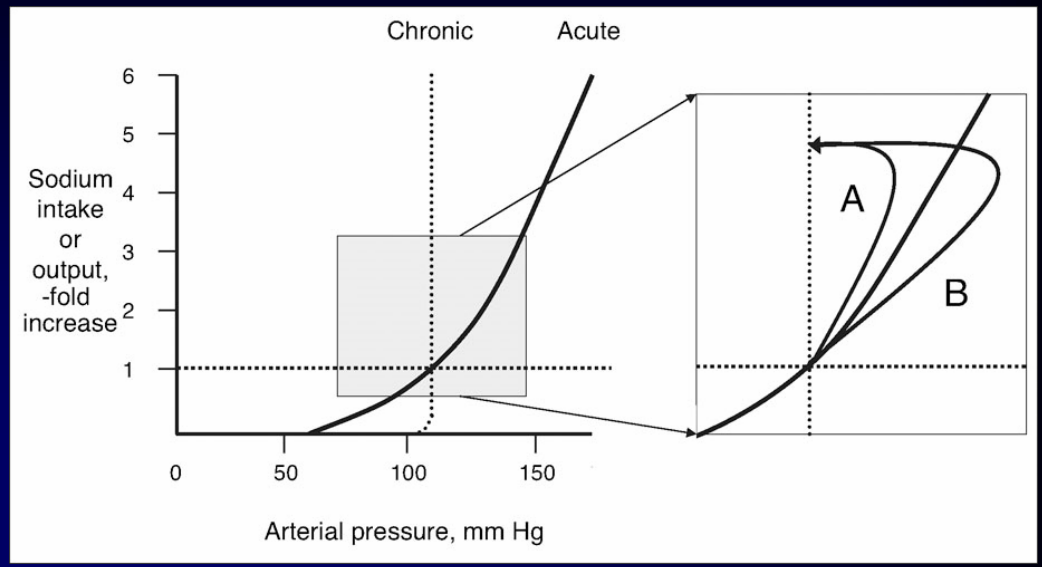


Interaction of the Modern Western Diet and the Kidneys in the Pathogenesis of Essential Hypertension



Adrogue, Madias, NEJM, 2008;35:19

Final, common pathway in hypertension



↑ kidney sodium retention

↓

↑ intravascular volume

↓

↑ cardiac output

normal perifer vascular resistance

↓

↑ blood pressure

autoregulation →

↑ perifer. vasular resistance

normal cardiac output

↓

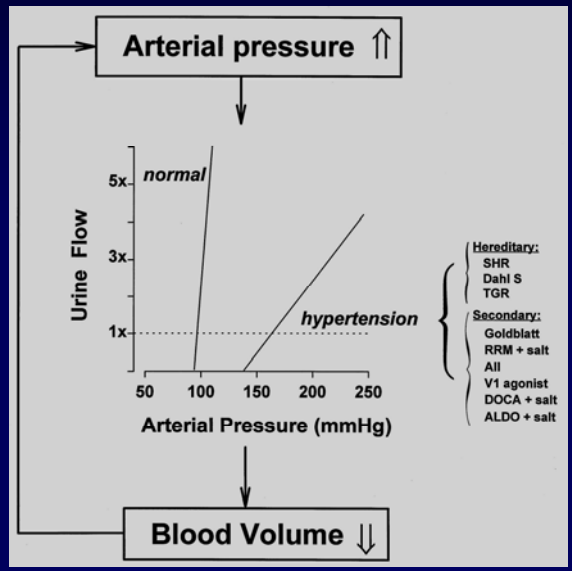
↑ blood pressure

↓

HYPERTENSION

Renal mechanisms of diminished sodium excretion

Molecular error in sodium transport



Less nephrons

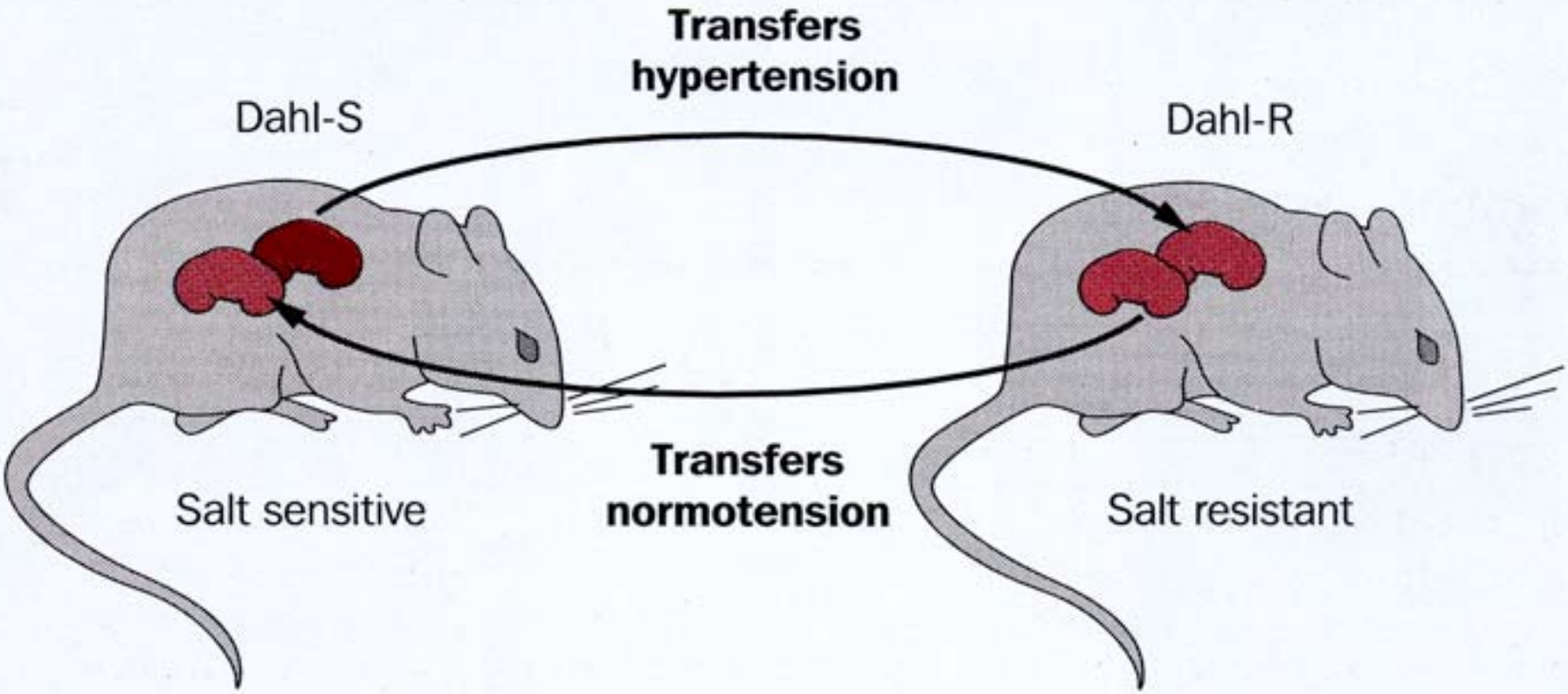
Decreased medullary circulation

Loss of peritubular blood vessels and interstitial fibrosis

Renal mechanisms of diminished sodium excretion

Mechanisms	Disorders
Reduced ultrafiltration capability	Chronic kidney disease Hypertension in blacks Sodium sensitive EH
Enhanced tubular Na reabsorption	Primary aldosteronism Diabetes mellitus Metabolic syndrome

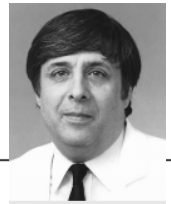
Hypertension 'follows' a transplanted kidney

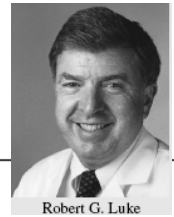


Dahl et al. Circ Res 1974;34:94-101; Dahl et al. Circ Res 1975;36:692-696
Retting et al. Hypertension 1990;15:429-434 Bianchi et al. Clin Sci Mol Med 1974;74:435-448

MILESTONES IN NEPHROLOGY

Mark A. Knepper, Feature Editor


John J. Curtis


Robert G. Luke

J Am Soc Nephrol 12: 2404–2412, 2000

REMISSION OF ESSENTIAL HYPERTENSION AFTER RENAL TRANSPLANTATION

JOHN J. CURTIS, M.D., ROBERT G. LUKE, M.B. CH.B., HARRIET P. DUSTAN, M.D., MICHAEL KASHGARIAN, M.D., JOHN D. WHELCHEL, M.D., PATRICIA JONES, R.N., AND ARNOLD G. DIETHELM, M.D.

with comments by
ROBERT G. LUKE, AND EBERHARD RITZ
m N. Engl. J. Med. 309:1009–1015, 1983

Table 1. Clinical Characteristics and Results of Blood-Pressure and Renal-Function Studies the First Time Both Were Obtained Simultaneously in the Six Black Patients with a Family History of Hypertension (See Appendix).*

PATIENT NO.	AGE/SEX	BLOOD PRESSURE	SERUM BUN/CREATININE	URINARY PROTEIN	NO. OF YEARS BEFORE ESRD THERAPY
		mm Hg	*mg/dl*		
1	29/M	240/170	13/1.3	100 mg/24 hr	4
2	36/M	180/150	23/1.7	Negative by dipstick	1.5
3	30/F	150/100	12/1.0	Negative by dipstick (<100 mg/24 hr)	5
4	27/M	185/120	35/— †	Negative by dipstick	2
5	38/F	150/100	10/0.4 (during pregnancy)	360 mg/24 hr	2
6	24/M	300/160	28/2.8	600 mg/24 hr	0.2

*BUN denotes blood urea nitrogen level, and ESRD end-stage renal disease. †Creatinine not measured.

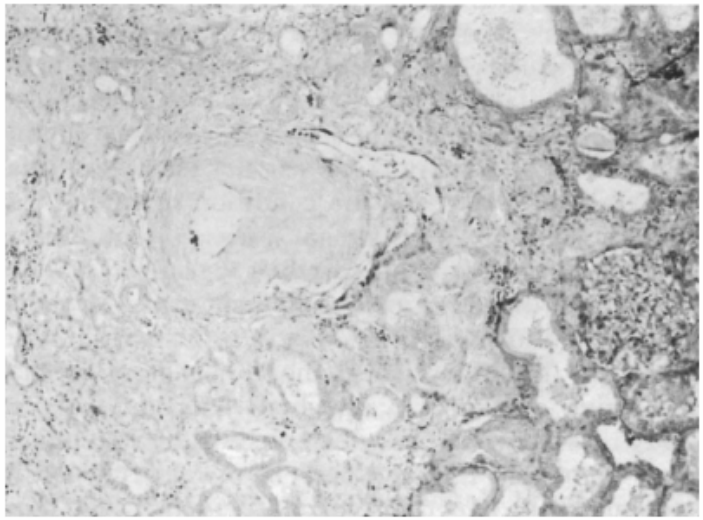
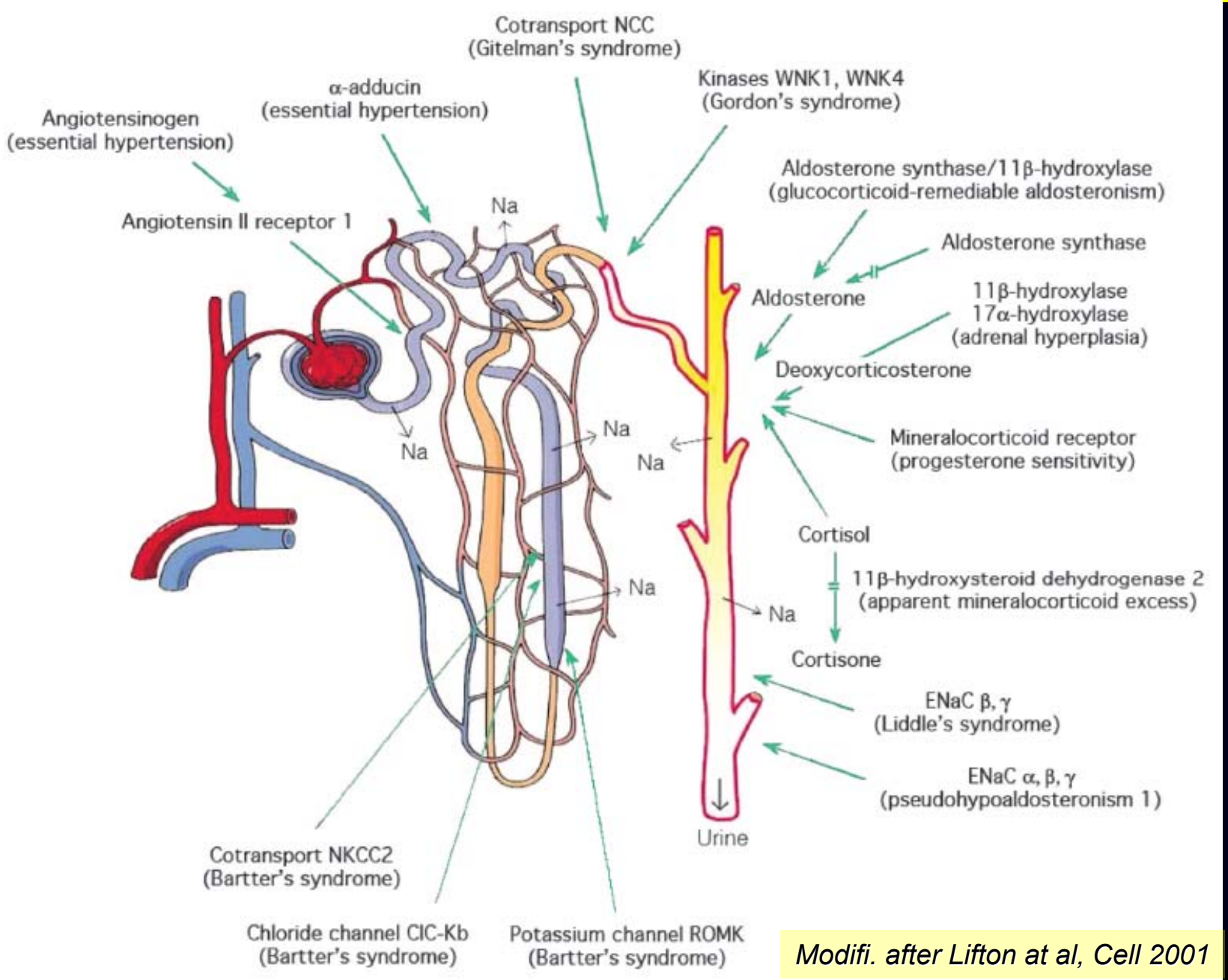


Figure 1. Photomicrograph of the Nephrectomy Specimen from a Patient Typical of Those Considered to Have Nephrosclerosis.

Table 2. Evidence of Resolution of Cardiac Hypertrophy from Electrocardiograms and Chest X-Ray Films before and after Renal Transplantation.

PATIENT NO.	SCORE FOR VENTRICULAR HYPERTROPHY *		DIAMETER OF HEART †	
	BEFORE	AFTER	BEFORE	AFTER
			centimeters	
1	4	0	16.8	13.2
2	6	0	17.0	13.0
3	6	0	16.2	13.5
4	3	0	17.3	14.2
5	6	0	16.8	14.8
6	7	2	18.0	14.0
Mean ±S.E.M.	5.3±0.6	0.3±0.3	17.0±0.2	13.8±0.3
	(P<0.001)		(P<0.001)	

Monogenic hypertensions & hypotensions



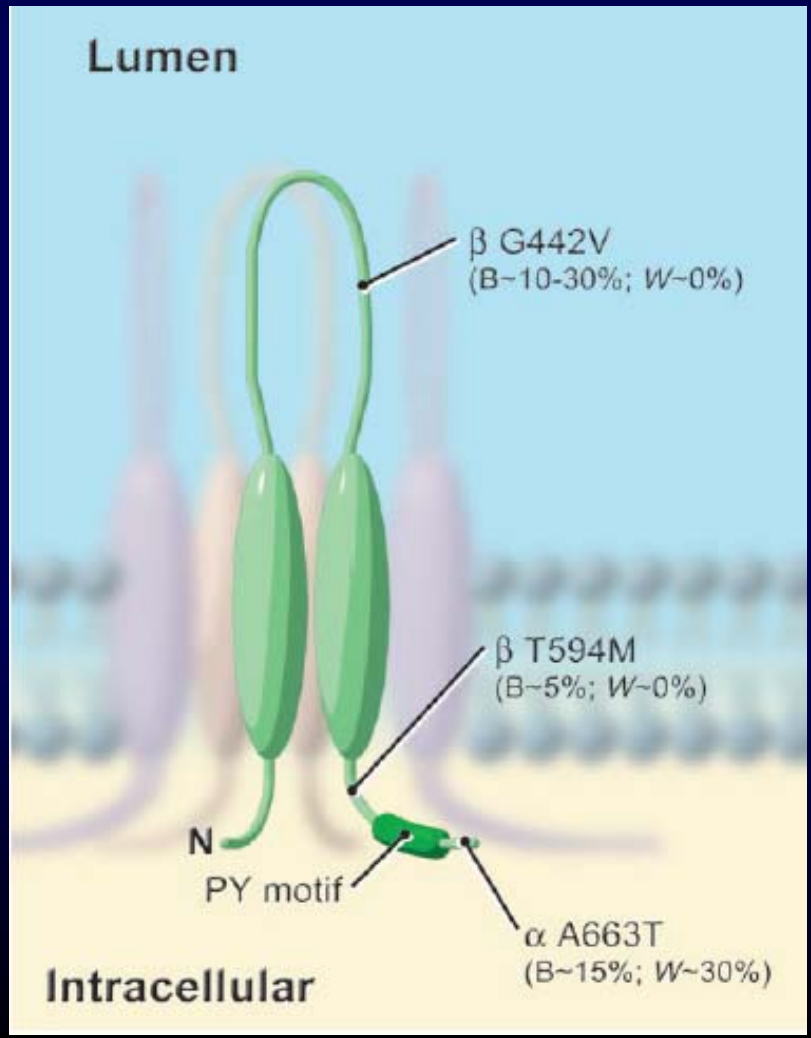
Modifi. after Lifton at al, Cell 2001

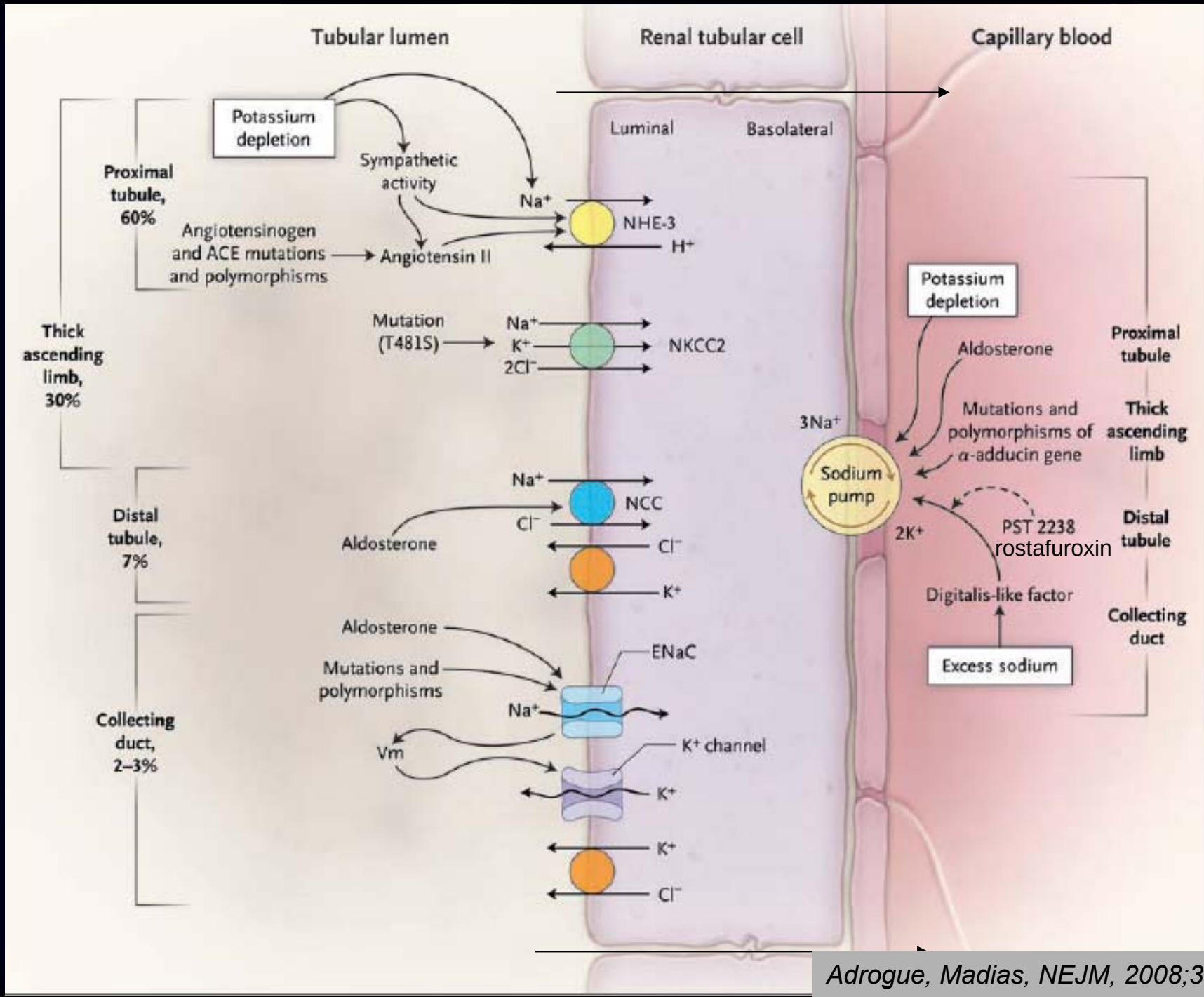
Frontiers in Nephrology

Central Role for ENaC in Development of Hypertension

J. Howard Pratt

J Am Soc Nephrol 16: 3154–3159, 2005.

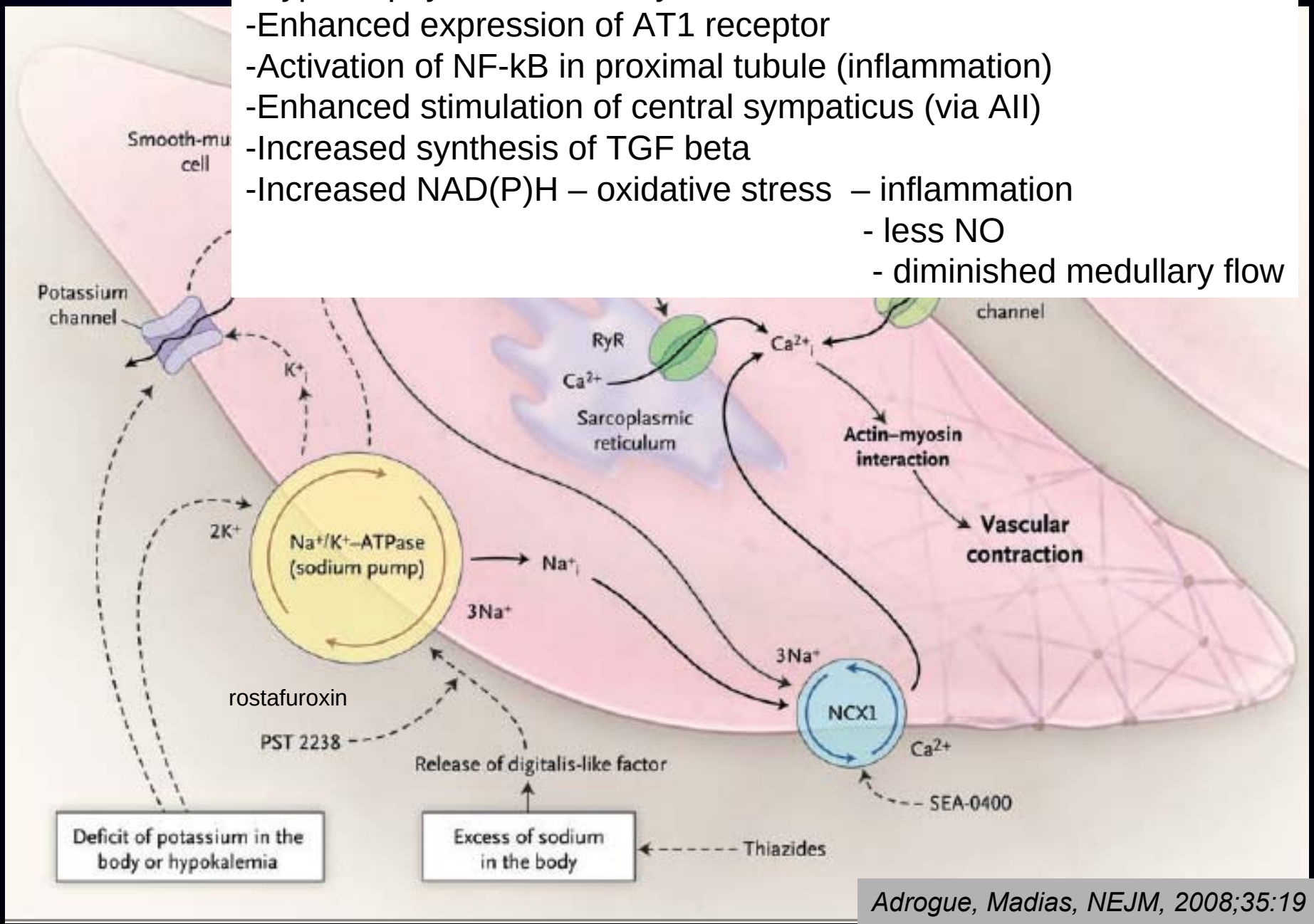




Adrogue, Madias, NEJM, 2008;35:19

Increased sodium absorption in renal tubules:

-Hypertrophy of cardiomiocytes and VSM in blood vessels
-Enhanced expression of AT1 receptor
-Activation of NF-kB in proximal tubule (inflammation)
-Enhanced stimulation of central sympaticus (via AII)
-Increased synthesis of TGF beta
-Increased NAD(P)H – oxidative stress – inflammation
- less NO
- diminished medullary flow



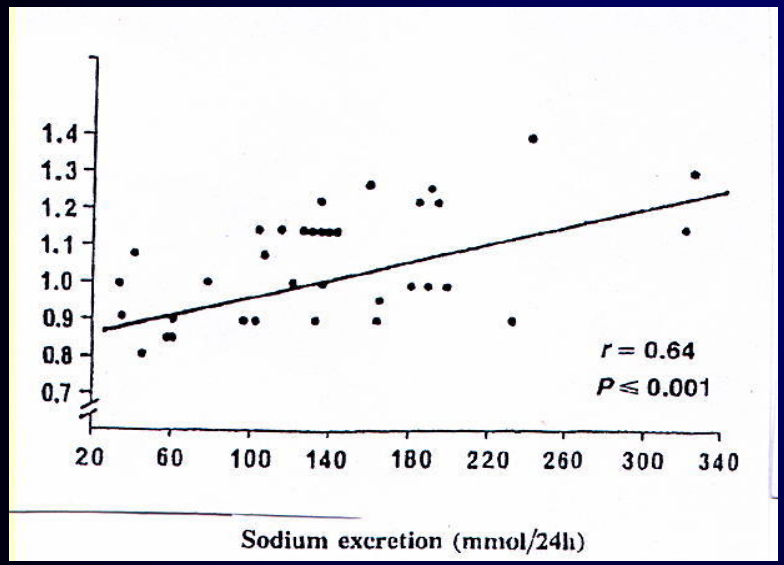
Adrogue, Madias, NEJM, 2008;35:19

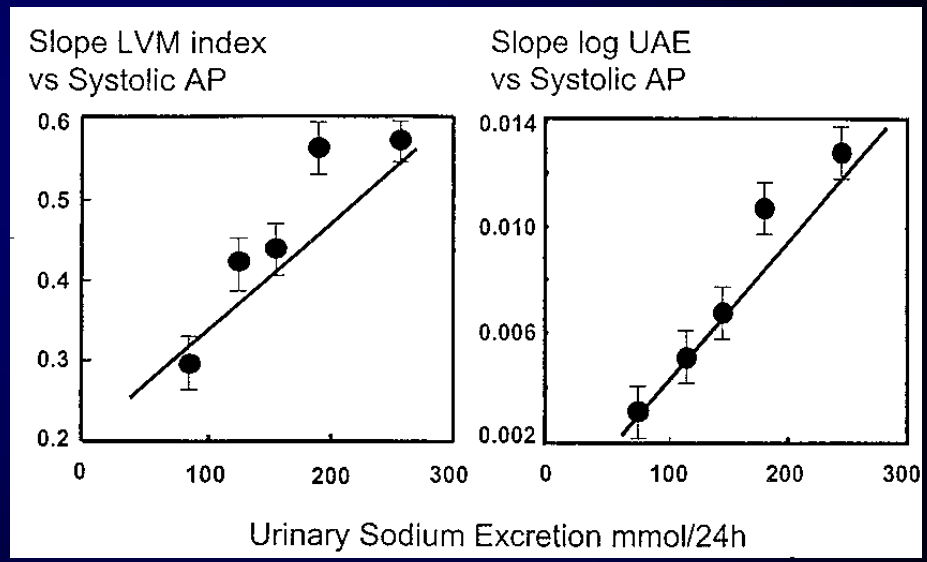
Increased sodium intake = increased total cardiovascular risk

- **increased reactivity of platelets**
  → *via* Na:Ca exchanger
  Gow, 1992, Nara, 1984
- **increased hypertrophy and fibrosis**
  → *via* TGF β
  Gu, 1998
- **↑ expression of AT1 R and ↓ AT2 R**
  → *via* local RAS
  Schmid, 1997
- **↑ ET 1**
  Ferri, 1997
- **endothelial dysfunction**
  → *via* NO, EDHF
  Miyoshi, 1997
- **↑ insulin resistance**
  Campese, 1994

Increased sodium intake = increased total cardiovascular risk, independently of blood pressure

Sodium excretion and left ventricle hypertrophy and albuminuria



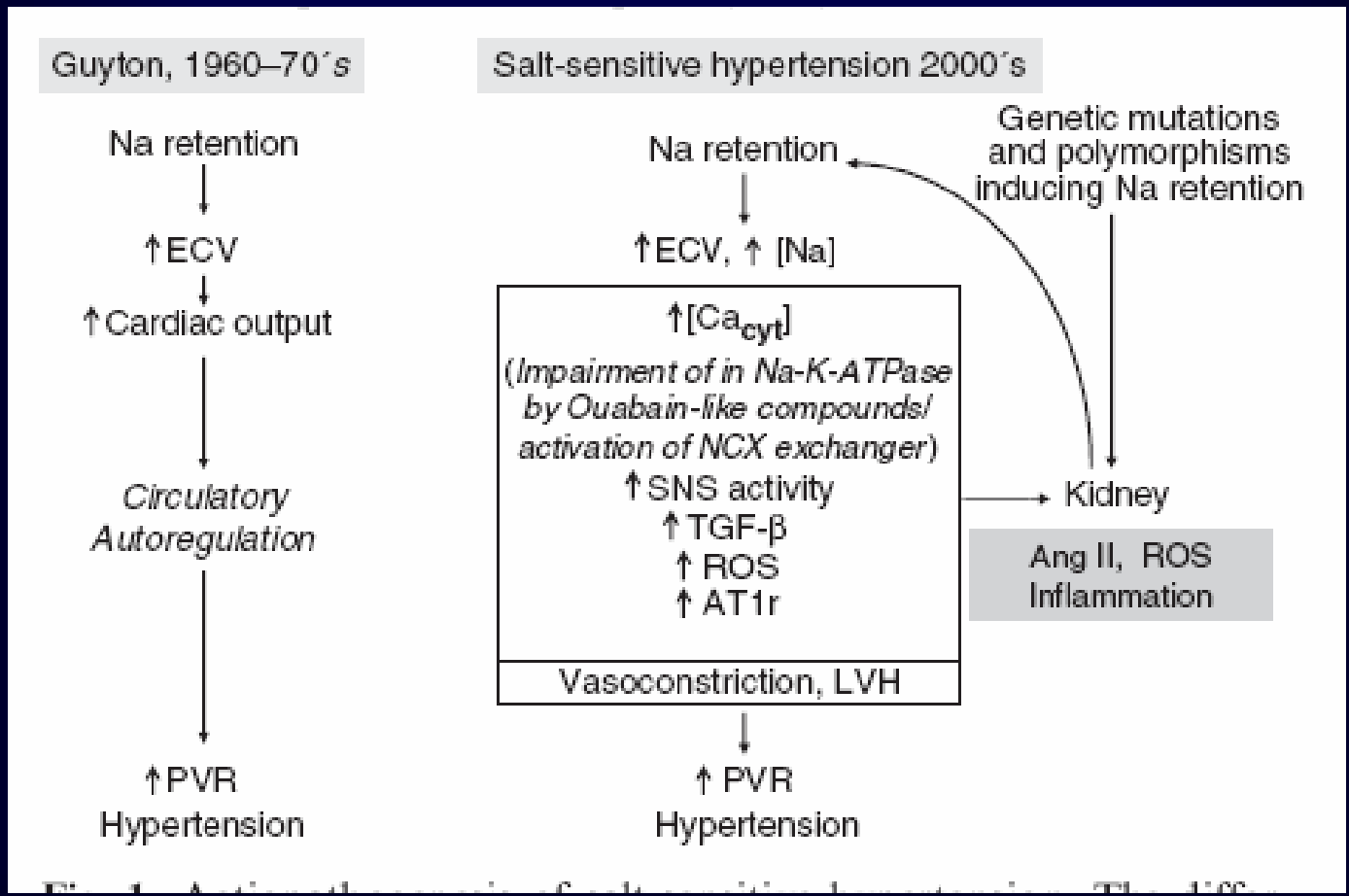


Schmieder, 1990 du Cailar, 2002

Salt-sensitive hypertension—update on novel findings

Bernardo Rodriguez-Iturbe[1] and Nosratola D. Vaziri[2]

Nephrol Dial Transplant (2007) 22: 992–995



Insulin resistance and salt-sensitive hypertension in metabolic syndrome

Toshiro Fujita

Nephrol Dial Transplant (2007) 22: 3102–3107

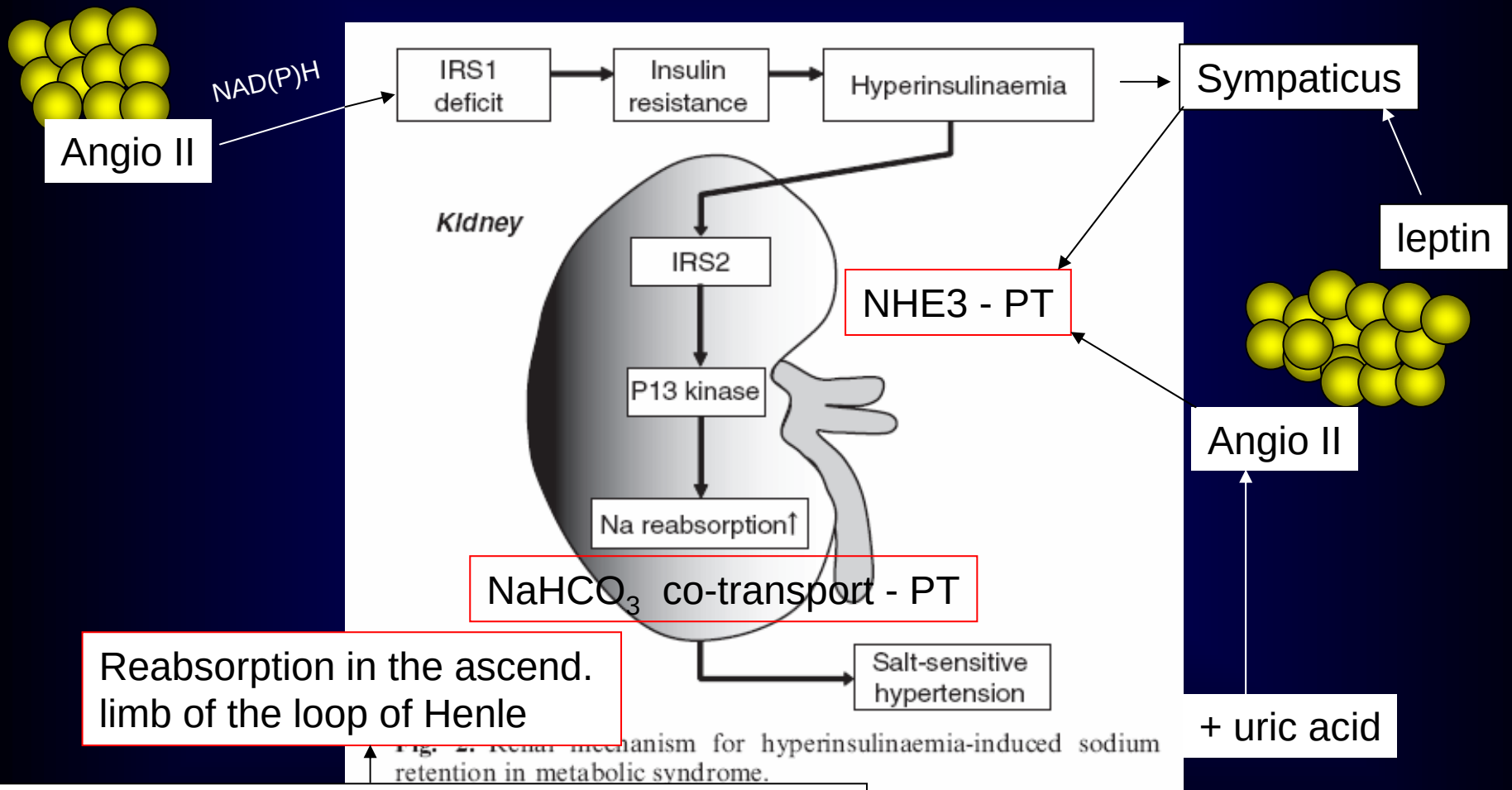


Fig. 2. Renal mechanism for hyperinsulinaemia-induced sodium retention in metabolic syndrome.

Reabsorption in the ascend. limb of the loop of Henle

Compression of the kidney by the abdominal fat
-Reduced medullary blood flow

No kidney,

No cry !

KEMPNER W, PESCHEL E, STARKE H. **Rice diet in malignant hypertension ; a case history**.

Am Pract Dig Treat. **1949** May;3(9):556-63.

KEMPNER W.

Treatment of heart and kidney disease and of hypertensive and arteriosclerotic vascular disease with the rice diet.

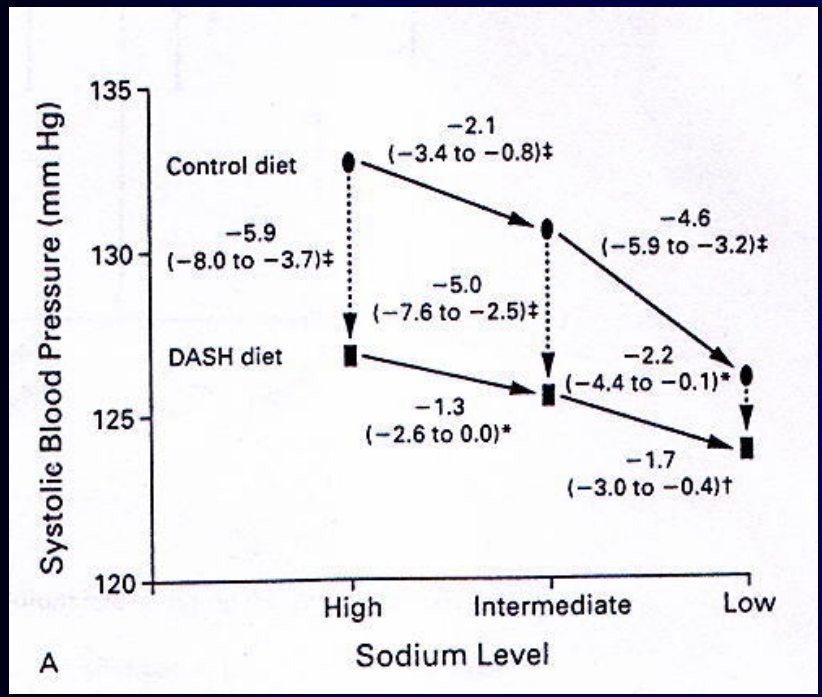
Ann Intern Med. **1949** Nov;31(5):821-56,

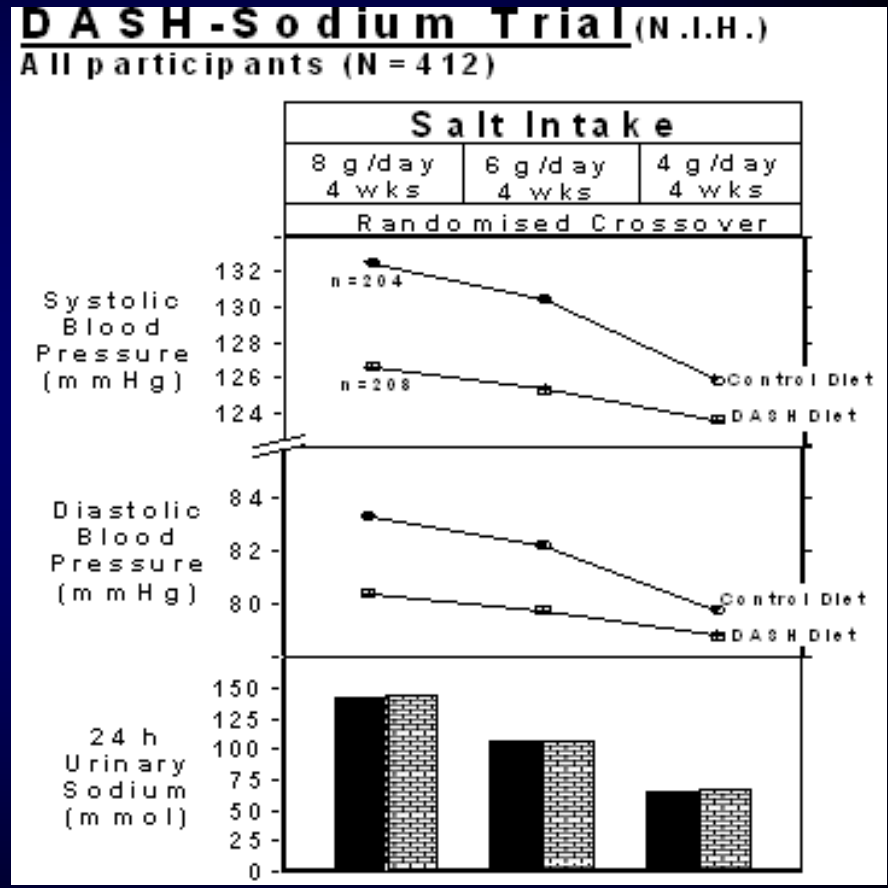
Since the 1930s, Kempner and his associates have employed the Rice Diet to treat more than 18,000 patients from all around the world.

Walter Kempner retired from Duke University in 1974 and from the Rice Diet program in 1994.

He died in 1997 at the age of 93.

DASH Sodium Trial





Sacks, 2001

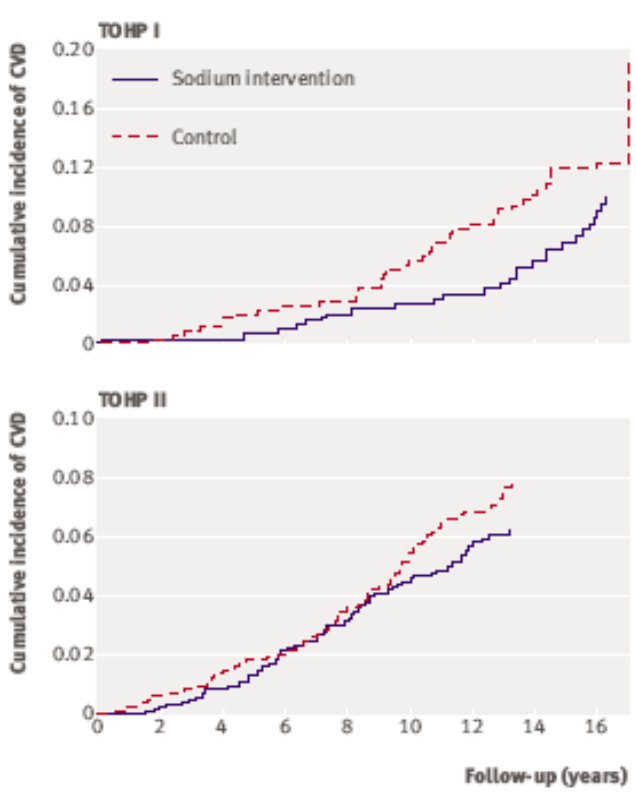
BMJ

RESEARCH

Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP)

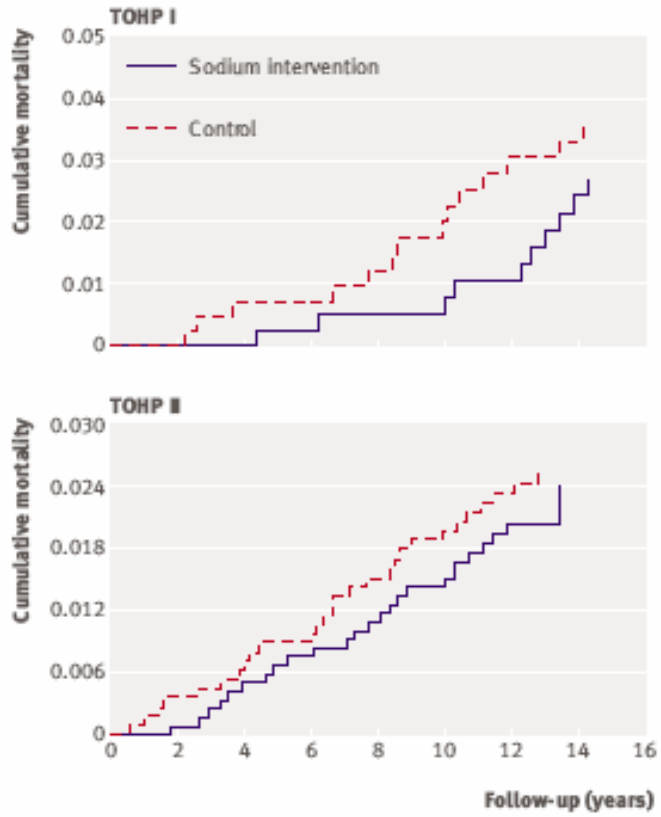
Nancy R Cook, associate professor,[1] Jeffrey A Cutler, former senior scientific adviser,[2] Eva Obarzanek, research nutritionist,[2] Julie E Buring, professor,[1] Kathryn M Rexrode, assistant professor of medicine,[1] Shiriki K Kumanyika, professor of epidemiology,[3] Lawrence J Appel, professor of medicine,[4] Paul K Whelton, president and chief executive officer,[5] for the Trials of Hypertension Prevention Collaborative Research Group

Long term effects (after 15 years) of 3 g lower salt intake



Cardiovascular risk 25%

sex, and clinic



Total mortality 20%

in TOHP I

Wisdom begins in wonder.

Socrates