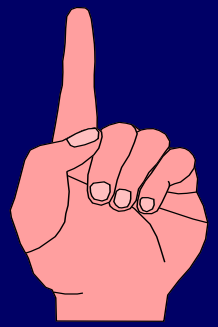
Salt intake and blood pressure:

is there a possibility of *programming* already in infants., toddlers and children?

A review of problems



Österreichische Arbeitsgruppe

für pädiatrische Nephrologie

Zwettl, 7. Juli 2006

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Department of Pediatrics,

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Is high salt/sodium intake significant for the later development of hypertension in adolescents and adults?

Initial thoughs:

1. **Salt intake presents a significant risk factor for blood pressure increase in adults** (well established, proven)
2. **Also small increase of BP in hypertonics increases risk of organ complications** (well established, proven)
3. **Adolescents presenting BP in the range of *„normal high“ BP= 90.-95. percentile* are a population at risk-tracking phenomena?** (speculation, but high probable)

Is a high salt intake in early infancy/ childhood connected with a risk of hypertension in adulthood?

Is there a possible imprinting? (Theories of Konrad Lorenz and David Barker)?

4. Essential hypertension does not start with the 18th birthday! (that is logical, partially proven)

5. Animal experiments (rats) showed increased sensitivity to „hypertensive stimuli“in early age (*critical periods*) when some physiological functions (including the salt intake) mature (proven)

May the salt intake in early life period influence the later blood pressure? Is there really any programming possible?

When this premise would be correct also in humans, the logical consequence would be an attempt to limit salt intake since the infancy and first years of life (in infants/toddlers) as a prevention of the essential hypertension and its organ complications later in adulthood.

Until now, this thoughs are rather a speculations, only partially proven data

Be carefull- following data are very often not percieved not only by laics, but also by MD!!

A. Borderline hypertension:

diastol. BP up 5 mmHg higher than 95.percentil

B. Significant hypertenison:

diastol. BP up 5-10 mmHg higher than 95.percentil

C. Severe hypertension:

diastol. BP more than 10 mmHg higher than 95.percentil

Effect of the blood pressure control

- **Decrease of diastolic blood pressure at 5-10 mm Hg decreases the morbidity/mortality for ischemic cardiac complication at 14% !!!,**

  but cerebral strokes even at 33-42% !!!!

  and mortality at 40% !!!!

  (in adults hypertonics)

  Therefore exact reading- e.g. 132/78 mmHg

Empirical data established in several human studies:

1. Yanomamo Indians (living on the boundary between Brasil/Venezuela
2. Native population living on Solomon Islands (Pacific- Polynesia)
3. Japanese fishermen (northern part of Honsu island)

Yanomamo Indians and their blood pressure

Even today there are populations living in practical separation from the „civilized word“. Yanamamo are probably the most primitive tribe in the world – a population of some 20.000 people living in South America in Amazonia scattered in rain forest in ca 200 separated villages

Basic nutrition: bananas, maniok, wild fruit, insects!, absolutely no or only limited access to salt, sugar, milk/milk products and alcohol

Yanomamo Indians and their blood pressure

Originally, there were thoughs, that this population is living in an arcadian existence, but psychological surveillance established a high level of stress situation (chronic warfare with violence and tension, wild animals, open hostility to neighbours)

Despite this facts, the blood pressure of this population is normal and there is no increase correlating with age

Yanomamo Indians
and their blood pressure

Field study:

206 persons aged 20-50 ys (adults from 3 villages), examinations showed extremely low salt intake (assesed as sodium excretion in urine), on the other side very high excretion of potassium

Na^+: K^+ urine excretion = 0.03/3.0 g/24 hrs. !!

The only source of sodium is that in ash, as addition to meals. Low blood pressure also in the old individuals. However, the body weight in men was some more than 50 kg!

Oliver WJ et al: Circulation, 1975, 52, 146-51,
Chagnon NA, Holt, Rinehart and Winston, New York, 1968
Costa E et al: Bulletin of PAHO, 1990, 24, 159-76

Native population in Solomon Islands

Different tribes living in different areas, but having similar nutrition (potato, vegetables, high potassium intake!):

1. in inland (salt intake lesser than 2g/day

rate of hypertension 1% of population

2. near to the sea (salt intake 3-8 g/day

rate of hypertension 3% of population

3. at the coast (salt intake as high as 9-15 g/day due to cooking in sea water!)

rate of hypertension 8% of population (despite very high salt intake, but balanced by extremely high potassium intake

Page LB et al: Circulation, 1974,49, 1132-46, Prior IAM et al: NEJM, 1968, 279, 515-20

Salt intake in Japanese population and its impact on the blood pressure

- **In the fifthies (last century) extremely high morbidity/mortality due to strokes in some regions of Japan**
- **Screening of urine salt excretion revealed average salt intake 15 gram/day, but differencies ranged up 60 g/day!!**
- **Salt-rich sauces (*Miso* 13% of salt, *Shoy* even 18% of salt)**

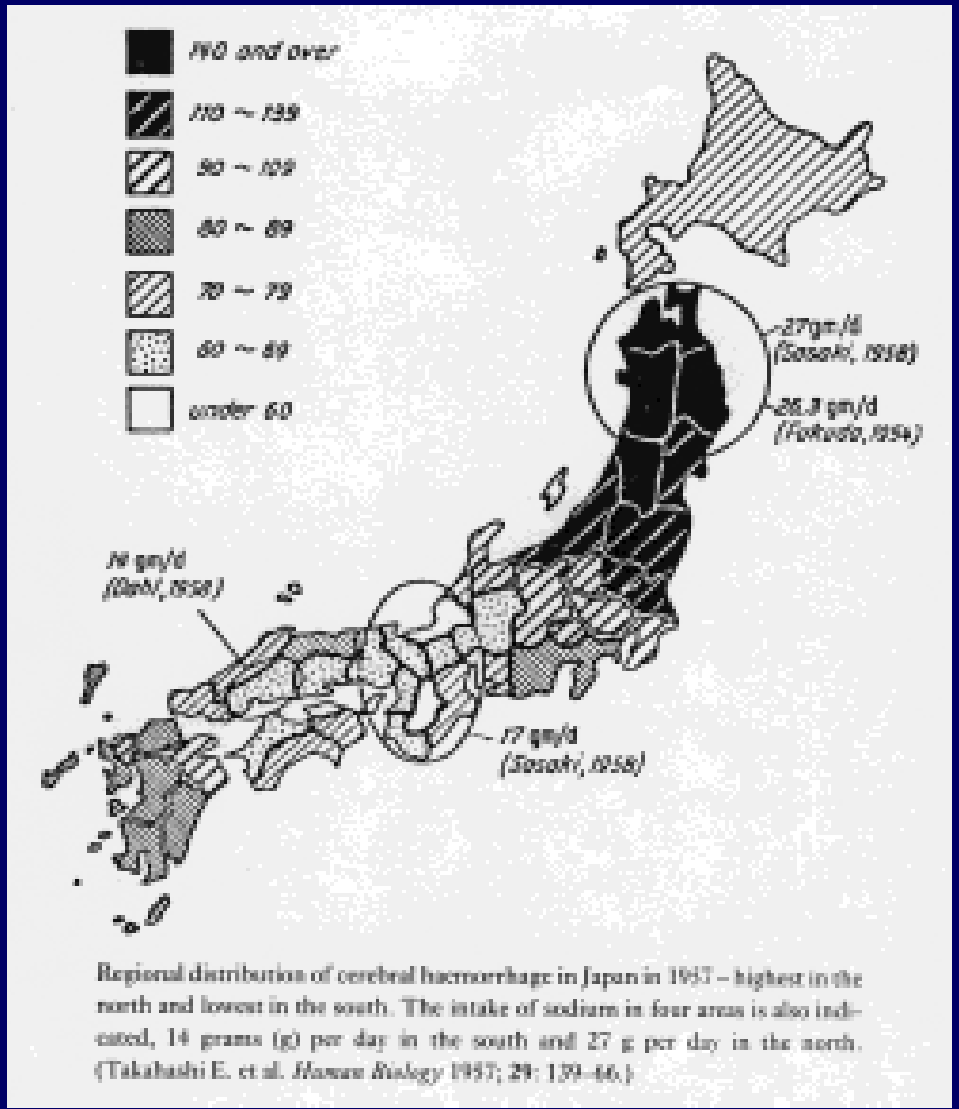
Sasaki N: Geriatrics, 1964, 19, 735-44

Salt intake in Japanese population and its impact on the blood pressure

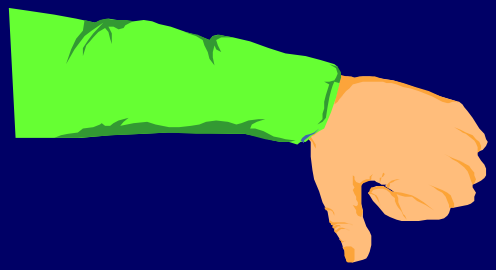
- **Nevertheless, this high salt intake was balanced by almost vegetarian nutrition (rice, vegetables, vegetable oils, no milk/milk products including the milk fat (practically no cattle breed)**
- **Since 1950-1964 the fat intake increased at 100%! That time the mortality due the cerebral strokes increased in the northern part of Honsu Island immensely and was the highest worldwide**

National Survey on circulatory Disorders- a summary 1989, Ministry of Health and welfare, Tokyo, Japan

Northern Japan- salt intake, hypertension and cerebral strokes



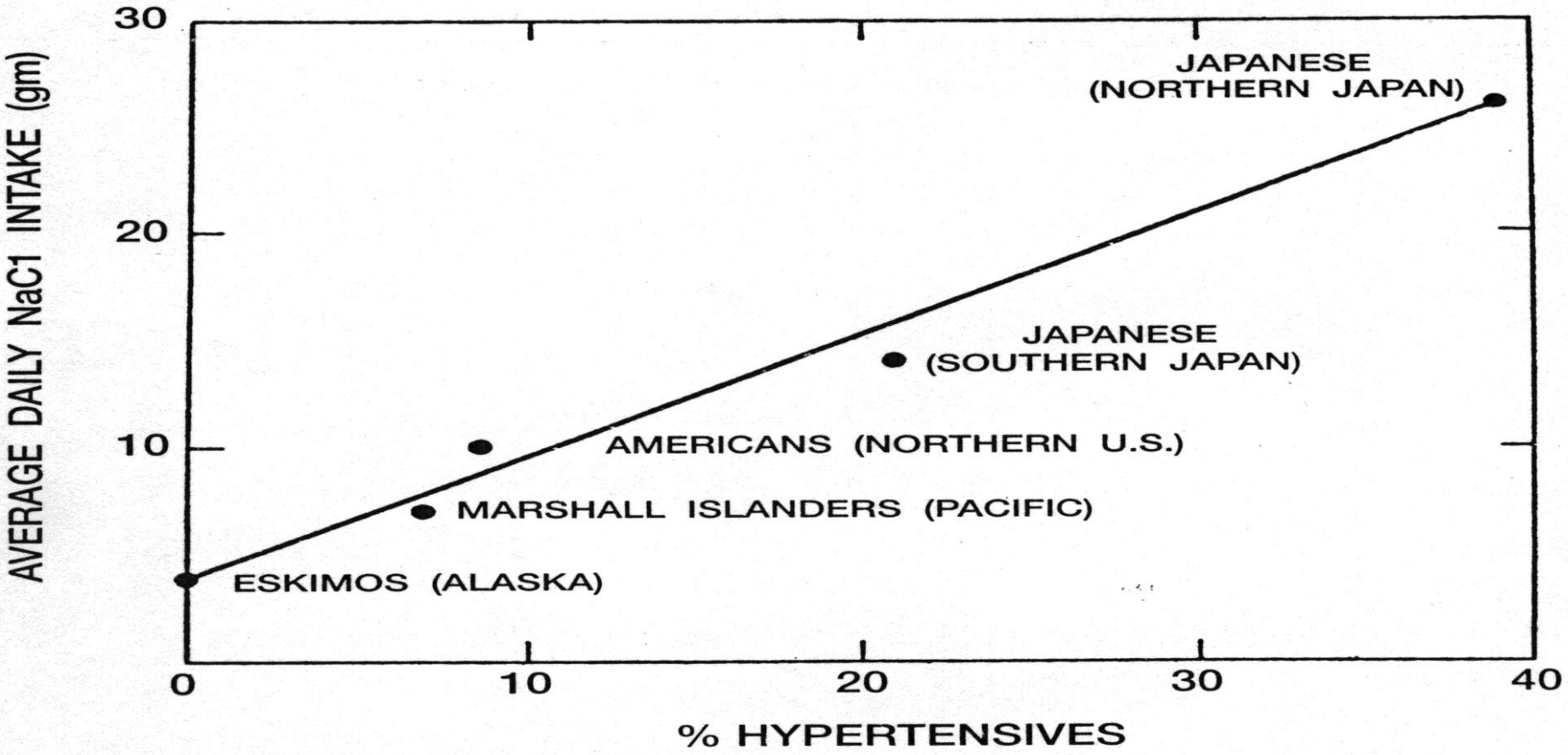
Regional distribution of cerebral haemorrhage in Japan in 1957 – highest in the north and lowest in the south. The intake of sodium in four areas is also indicated, 14 grams (g) per day in the south and 27 g per day in the north. (Takahashi E. et al. *Human Biology* 1957; 29: 139–66.)



Salt intake in the southern Japan 17g/day, but in northern Honsu 27 g/day!!
The black areas – mortality due strokes more than 140
Autopsies: no cerebral thrombosis, but hemorrhagies prevailed- due to severe hypertension

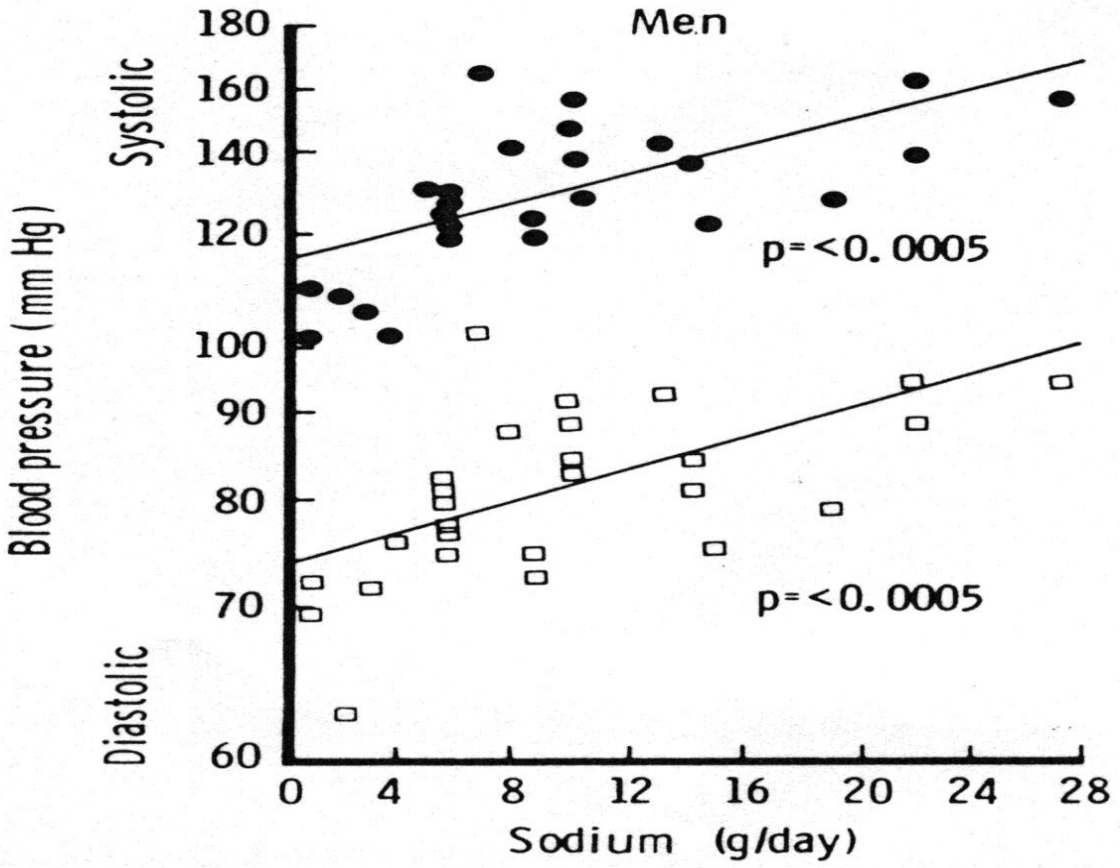
Takahashi E et al: Human Biology, 1957, 29, 139-66

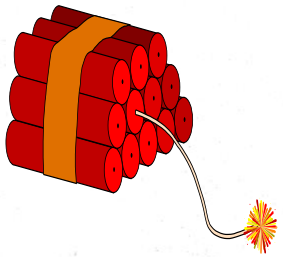
Correlation of NaCl intake and blood pressure in different world regions and populations



The first international population study of the relation of the salt intake to blood pressure. (From Meneely G.R. & Dahl L.K. *Medical Clinics of North America* 1961; 45: 271–83. Reprinted by permission of W.B. Saunders Company.)

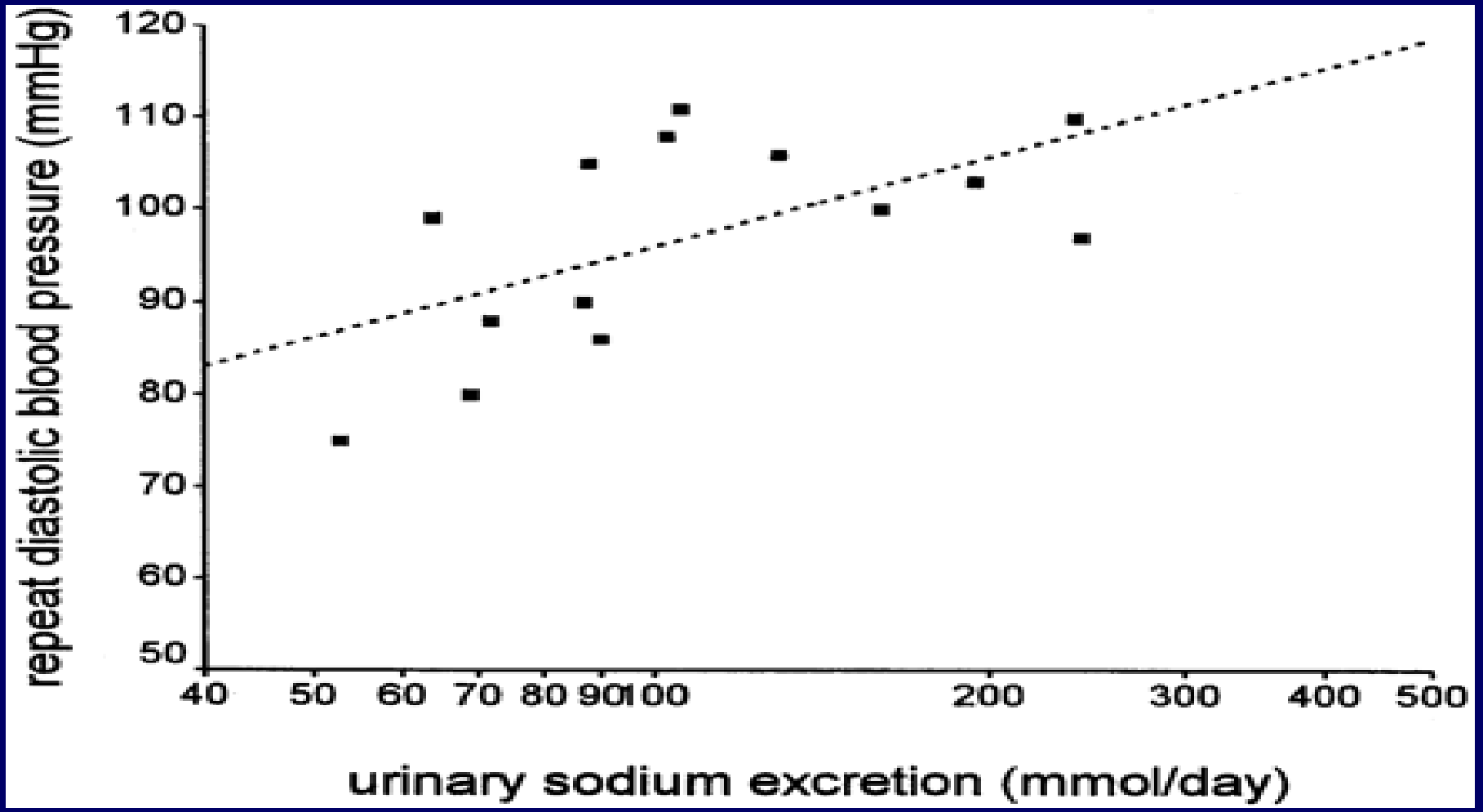
Correlation of NaCl intake and blood pressure in men aged 50-55 years in 27 different populations





The relation of the blood pressure of men aged 50–55 years to their salt intake in 27 populations according to Glieberman. (From Glieberman L. *Ecology of Food and Nutrition* 1973; 2: 143–56. Reprinted by permission of Gordon and Breach Publishers.)

Diastolic blood pressure is related to urinary sodium excretion in hypertensive Chinese patients (B.M.Y. Cheung, Q J Med 2000; 93: 163-168



Intersalt revisited: further analyses of 24 hour sodium excretion and blood pressure within and across populations (reported by Paul Elliott)

- **CONCLUSION**
- Data presented here indicate that a sodium intake lower by 100 mmol--for example, 70 instead of 170 mmol/day--could result, in adults (average age 40) in systolic pressure lower by 3-6 mm Hg and in slope in systolic pressure from age 25 to age 55 less by 10 mm Hg. Extensive data from prospective population studies indicate that such improvements in average systolic pressure levels could substantially reduce rates of major cardiovascular diseases and mortality from all causes. This potential underscores the value of current recommendations encouraging the general population to reduce salt intake

BMJ 1996;312:1249-1253 (18 May)

Links between dietary salt intake, renal salt handling, blood pressure, and cardiovascular diseases.

Epidemiological, migration and interventional studies showed a significant correlation between salt intake and blood pressure/hypertension

The main reason of high rate of hypertension in developed countries population is probably the failure of kidneys to excrete surplus of salt

During the human evolution the population was adapted to a salt intake lesser than 1 g/day!!

Gleiberman L: Ecology and Nutrition, 1973, 2, 143-56

Dyer AR et al: British Medical journal, 1996, 312, 1661-4

Brenner´s theory on low number of nephrons in preterm newborns

This author has postulated a theory, that the formation of fewer nephrons at birth (then favouring the sodium retention due to lower renal excretion) may present a risk factor for hypertension, which may partly explain the association between low birth weight later in life.

It fits with the David Barker´s theory – according that, low birth weight is statistically significantly connected with hypertension

Mackenzie HS, Brenner BM: Am J Kidney Dis, 1995, 26, 91-98

Hypertension in African- Americans:

a hypothesis supporting the role of kidneys preserving the sodium

- **The prevalence of hypertension is twice as high among African- Americans than in Caucasian Americans (38% vs 20%) and two to four times higher than in West Africans.**
- **The BP of African- Americans is also more sensitive to increases in salt intake comparing with Caucasians (longer sodium retention after i.v. salt load, better decrease of BP only after diuretics comparing with Caucasians).**

Wilson TW: Hypertension, 1991, 17, Suppl. 1, 122-8

Hypertension in African- Americans:

a slavery hypothesis

- **Between 1500-1800 some 12 million of black people were transported from the African West Coast to the western hemisphere, most went to South America, only 5.8. landed in Northern America.**
- **This population came mostly from the sub-Saharan savanna (low salt areas) having high ability to conserve salt with their kidneys. A selection of the slaves already before and during the shipping, only 60% captured survived 2 years, just those, who were able to conserve their sodium and to resist to vomitus and diarrhea.**
- **So, after that selection their descendends are more likely to develop hypertension, particularly following the increased salt intake living in a developed society**

- **Moscovitz DW: Clinical and Experimental Hypertension, 1996, 18, 1, 1-191**

A slave trader licking a slave- face
to assess his fitness for shipping him
across the Atlantic to South America.
Presumably the less salty, the better

Impact of the significant increase of salt intake and results on the blood pressure

The contemporary salt intake in developed countries is ca 10 times so high- resulting in hypertension, hypertrophy of the left heart ventricle, thickness of arteries wall and decrease of their elasticity. The physiological functions are rather rigid and do not follow up the social development

Meneton P et al: Physiol Rev. 2005 Apr;85(2):679-715.

Molecular genetics and BP: urinary sodium excretion in relation to the *A*-1984*G* adrenomedullin polymorphism

- **Adrenomedullin (ADM) is a vasodilator and inhibits salt appetite. An *A*-to-*G* substitution at position -1984 in the promoter region of the ADM gene likely increases transcription.**
- **Testing the gene polymorpismus in Chinese comparing with urinary sodium excretion G- allele carriers revealed lower BP and sodium urinary excretion**
- In conclusion, in Chinese, the ADM -1984*G* allele is associated with lower sodium excretion and in older subjects also with lower systolic pressure and narrower pulse pressure

- **Y Li, J A Staessen, L-H Li, P-J Gao, L Thijs, E Brand, S M Brand-Herrmann, D-L Zhu and J-G Wang: Blood pressure and urinary sodium excretion in relation to the *A*-1984*G* adrenomedullin polymorphism in a Chinese population, Kidney Int 69: 1153-1158**

Salt intake and imprinting of hypertension in early life period?

- **Increased salt intake during the weaning and prepuberty period- may it result in later disorders of the blood pressure regulation?**
- **These both periods are typical for important changes targeting circulation, electrolyte metabolism, neurohumoral regulations.**
- **A classical question- is it possible to applicate the animal experiments to a human population?**

Salt intake in early age – may it result in later increase of blood pressure?

- **Epidemiological study in Netherlands:**
- **476 newborns in NL**
- **a) group with low Na Cl-intake n= 231**
- **b) group with „normal“Na Cl-intake n=245**
- **after 6 monts systol. BP lower at 2.1 mmHg in a)**
- **167 probands examined even after 15 years!!**
- **Systol. BP lower at 3.6 mmHg and diastol.BP at 2.2 mmHg**

Geleijnse J M et al: Hypertension, 1997, 29, 913-917
Geleijnse J M et al: J of Hypertension, 2002, 20, 2121- 2124

Infuence of salt concentration in water for preparation of milk formulas

- **Randomized study in newborns (Israel)**
- **Water for formulas preparation:**
- **A. Spring water having only 1.4 mmol Na^+/L (n=25)**
- **B. Pipe line supply water: 8.5 mmol Na^+/L (n=33)**
- **After 8 weeks BP measurement and in A) systolic and diastolic BP lower at 5.3/11.1 mmHg resp.**
- **After 6 months BP controls, but only 50% of the former probands examined. Still a difference, but not more significant (1.9 vs 5.9 mmHg)**

- **Pomeranz Aet al: Increased sodium concentrations in drinking water increase blood pressure in neonates. J Hypertens 2002; 20:203–207**

Salt intake in infants

- **NaCl intake daily lower than 10 mmol/day, i.e. ca 0.58 g NaCl and 0.23 g of sodium in breastfed children during the first months**
- **In a Holland study in eighties sodium concentration in commercial formulas 3times higher than in breast milk.**
- **This changed in the last 2 decades, lowered sodium contnent in all formulas.**

Salt intake in infants

- **Pediatricians should know the concentration of sodium in water used for formula preparation**
- **Salt intake has to be adapted to the birth weight of newborns (paradoxically the preterm babies need higher sodium intake)**

Salt intake in pre- and school-children

- **Salt intake increases significantly after introducing of mixed nutrition**
- **e.g. in 5 years old up 95 mmol/day, i.e. 5-5.5 g soli/den**
- **In developed western countries increase up 150 mmol/den= cca 9 g/day (that is 1000 ml of normal saline!)**

Some examples of average salt levels that are found in foods per child serving

Chicken nuggets	1.75g
Pizza	1.25g
Can of beans and sausages	1.5g 1.2g
Doughnut	2g
Burger	2.0 !!
Milk shake	0.5g
Frosties cereal	1.5g
Cheese or ham Lunchable pack	2.4g !!!

High salt intake early in life: does it increase the risk of hypertension?

- **Conclusions: it remains unclear whether high sodium intake in infants and children increases their risk of hypertension later in life.**
- **However, there is biological plausibility for such an effect, and circumstantial empirical evidence to encourage further research in this field.**
- **If there is an independent effect of early sodium intake on lifetime development of blood pressure, a major question that remains to be resolved is the age until which such adverse effects can be reversed.**

Geleijnse JM, Grobbee DE.
J Hypertens. 2002 Nov;20(11):2121-4.

Salt intake in adolescents

- **A clinical study of adolescents aged 13 years with BP higher than 75th percentile**
- **Randomization according the NaCl and KC and placebo intake**
- **In girls with low sodium intake blood pressure moderate lower after 3 year of study**

Sinaiko AR: Hypertension 1993; 21:989–994.

There are some contraversion concerning the role of salt intake in hypertension

- The problem may has its roots in methodological approach:
- The blood pressure is influenced by a complex of different factors (family history- genetics (the ability of kidneys to conserve the sodium), caloric intake, obesity, body mass index, body fitness, family habits preparing meals, etc.
-

Recommendation for the salt intake according the age

- **Infants: max. 1 g NaCl/ day**
- **1-6 years max. 2 g NaCl/ day**
- **7-14 years max. 5 g NaCl/ day**
- **Adults max. 6 g NaCl/ day**
- **Reality: very often much higher intake, even in adults it would be 4 g/day enough!**

Cit.: Coma dietary reference value

Review of literature reveals that studies showing low correlation between salt intake and blood pressure prevail

- Nevertheless, these negative findings do not exclude this causality. There are no long term follow up studies, where in a large cohorts the significant correlation could be present despite minor blood presure changes (in range of 2-3 mmHg, which are already important)
- Furthermore, there are no epidemiological studies with long term prospective studies following in a „high normal“ blood pressure population

Evidence based medicine- metaanalytic studies-

Cochrane Database Syst Rev., 2003, 3, CD003656

Advice to reduce dietary salt for prevention of cardiovascular disease (Hooper L, Bartlett C, Davey SG, Ebrahim S.)

REVIEWER'S CONCLUSIONS::

- **Evidence from a large and small trial showed that a low sodium diet helps in maintenance of lower blood pressure following withdrawal of antihypertensives.**
- **If this is confirmed, with no increase in cardiovascular events, then targeting of comprehensive dietary and behavioural programmes in patients with elevated blood pressure requiring drug treatment would be justified.**

Evidence based medicine- metaanalytic studies-

- **Further reviews:**
- **Hooper L, Smith GD, Ebrahim S.Related Articles, Links**
  Cochrane reviews on dietary advice for reducing intakes of fat and salt. Eur J Clin Nutr. 2006 Jul;60(7):926-8.
- **Hooper L, Smith GD, Ebrahim S.Related Articles, Links**
  Cochrane reviews on dietary advice for reducing intakes of fat and salt.
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  Eur J Clin Nutr. 2006 Jul;60(7):926-8.

What pediatricians can recommend knowing the previous facts?

1. Stimulate the breastfeeding
2. Using appropriate water for preparation of formulas
3. Avoid meals with high salt content (fast food smoked foods, sausages, fankfurter, wienerwurst, etc
4. Increase the potassium intake (fruits, vegetables)
5. Decrease of fat intake
6. The best approach: combination of all factors- healthy lifestyle
7. Do not forget the obesity as a very important factor of hypertension

Potassium intake and blood pressure
(Bandolier net)

- **Potassium intake and blood pressure (Bandolier net) Results**
- **There were 33 trials conducted between 1981 and 1995, with a median of 32 participants (2,600 in total).**
- **Oral potassium high intake resulted in an average fall in BP of 3 mmHg and 2 mmHg in systolic and diastolic BP respectively**
- **Somewhat larger reductions were found in trials with more than 20 mmol/day increase in urinary potassium excretion and in trials where antihypertensive drugs were not used**
- **PK Whelton et al. Effects of oral potassium on blood pressure. JAMA 1997 277: 1624-1632**

Spreading information on the high salt intake and its adverse effects

An example from oversea:

Salt Awareness Day 2003 in USA:

CASH (Consensus Action on Salt and Health) are making the issue of salt and children's diets the main campaign thrust this year. We propose to work as much as we can by linking with other stakeholders and creating a 'groundswell'. This may mean that **we talk about the importance of reducing salt as part of an overall healthy eating message aimed at children.**

It will culminate with a media event at the House of Commons on National Salt Awareness Day (January 29, 2003.) under the sponsorship of MP Kerry Pollard. As last year we hope to work with a celebrity and involve all the major supermarkets. As mentioned we also hope to work with other charities and action groups that work with children, including those that target school children and the school meal system.

A proposal as a hyperbolic joke

- **When living in developed countries in a nutrient-rich society and our population is not able to decrease the salt intake:**
- **„… once-a day diuretics may be a better health dose than once-a-day vitamins!“**

Kuller LH, J clin Hypert, 2001, 3, 32-6

An what about the fairy tales ?

- **In Böhmen *„Sůl nad zlato“* (*Salt is more than the gold*)**
- **Is there a need to correct this myth and instruct our children?**

Proposal of the Czech Working Group for Pediatric Nephrology:

A prospective Study of Sodium Intake in Adolescents with „high normal“Blood Pressure

- **Cooperation with the Institute for Clinical and Experimental Medicine and South Bohemian University Budweis**

- **Using the previous epidemiological study in healthy children and adolescents- see the monograph presented to your working group and short summary in the Abstract book of our last Annual Meeting of our Working Group in Český Krumlov, October 2005.**

- **Proposal for the protocol of the study will be probably ready in October 2006, Slovak colleauges express a willingness to cooperate – a multicentric cooperative study**

Proposal of a prospective study in adolescents with „high normal“ blood pressure

To create a protocol is a rather complicated task:

1. The sodium urine excretion reflects the sodium intake (U_{Na+}:U_{cr}), (UK_{K+}:U_{cr}), C_{cr}
2. How many samples, mornings urine
3. Standardized accidental BP measurement
4. Design of the BP measurement as in previous study
5. Gender, weight, height, BMI estimation, dietary habits in the family (outside the family, familial history of high BP
6. Availabilty of fast food centers (cohorts from rural vs city areas)

Thanking the audience for your attention and attention listen to the data on salt intake in children and adolescents