

Intensivkurs Präeklampsie Antihypertensive Therapie

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Overview

- **Physiology**

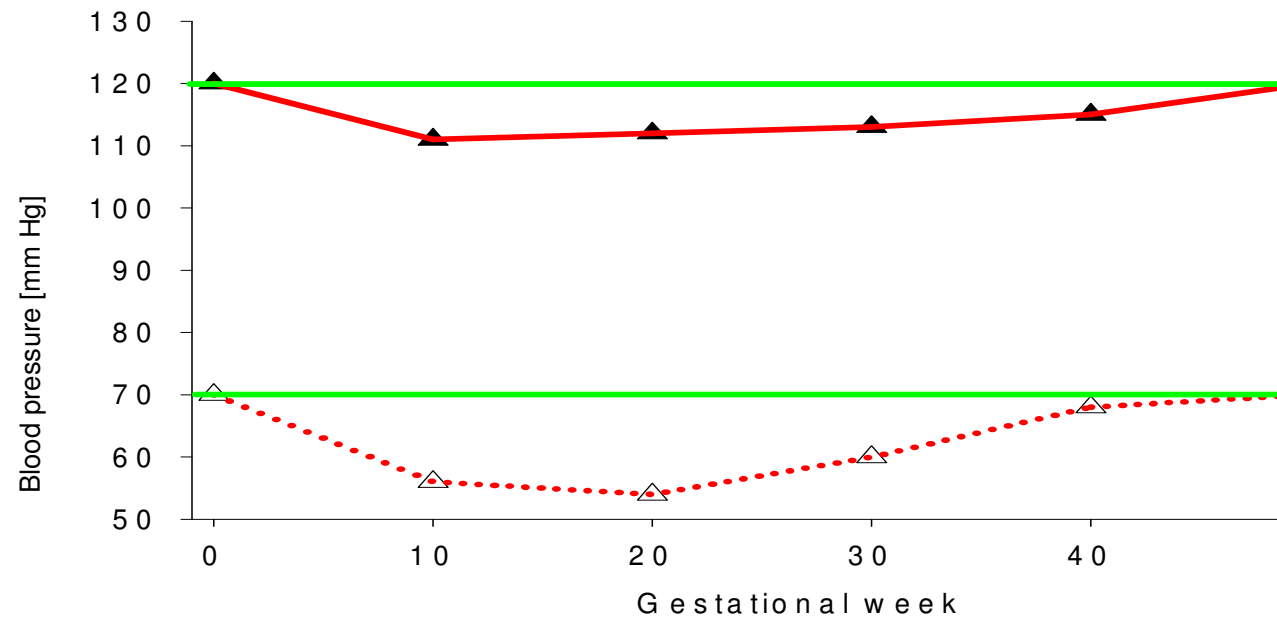
- Treatment – Behavioral adjustments

- Treatment – Drug therapy

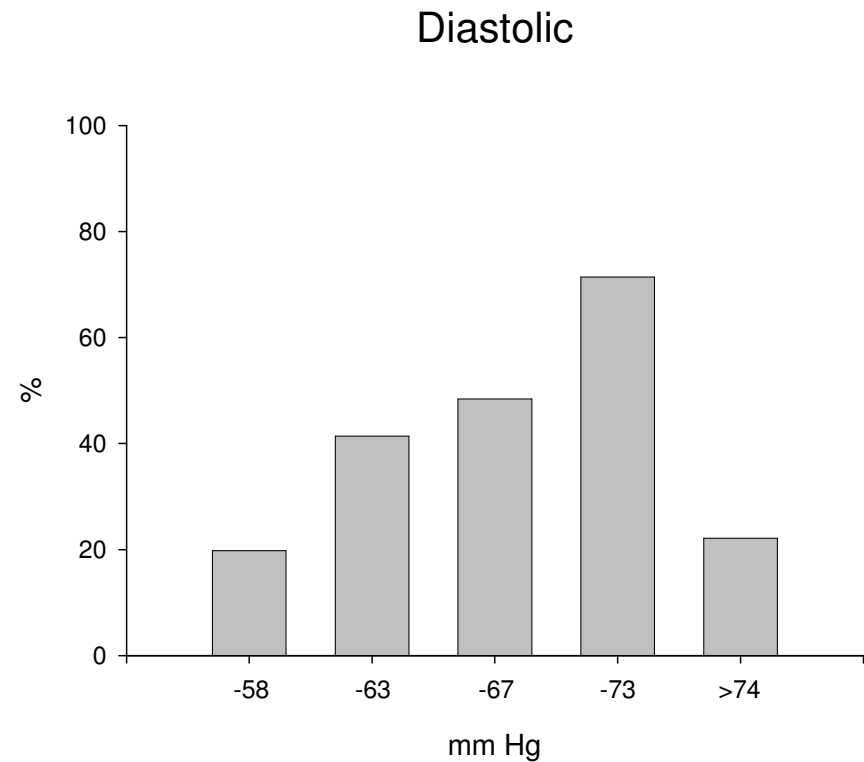
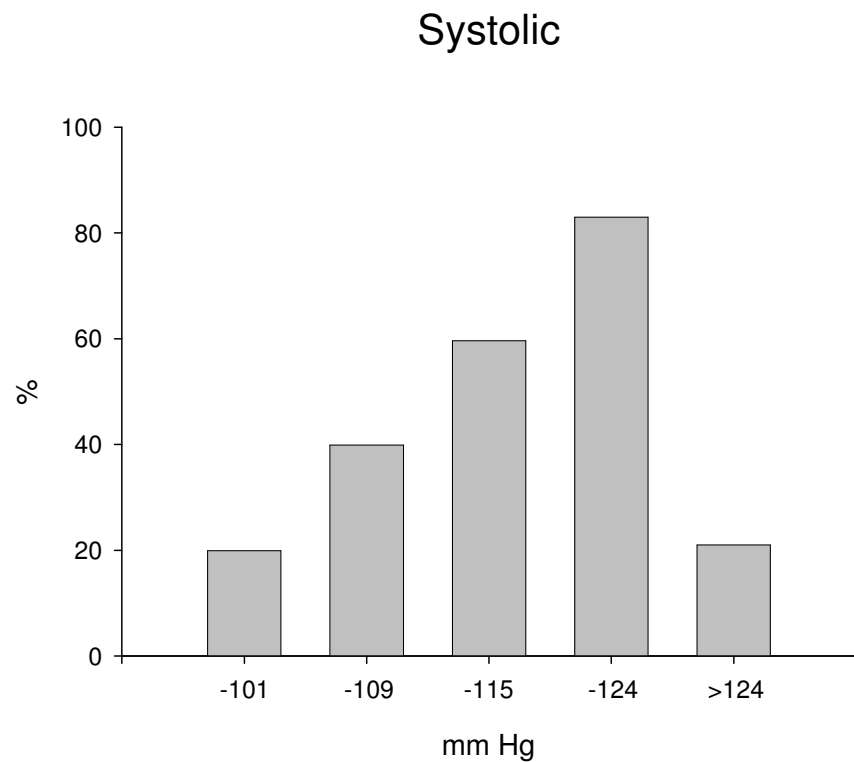
- Treatment – New developments

- Summary

Arterial Blood Pressure in Pregnancy



Blood Pressure in the 1th Trimenon of Pregnancy



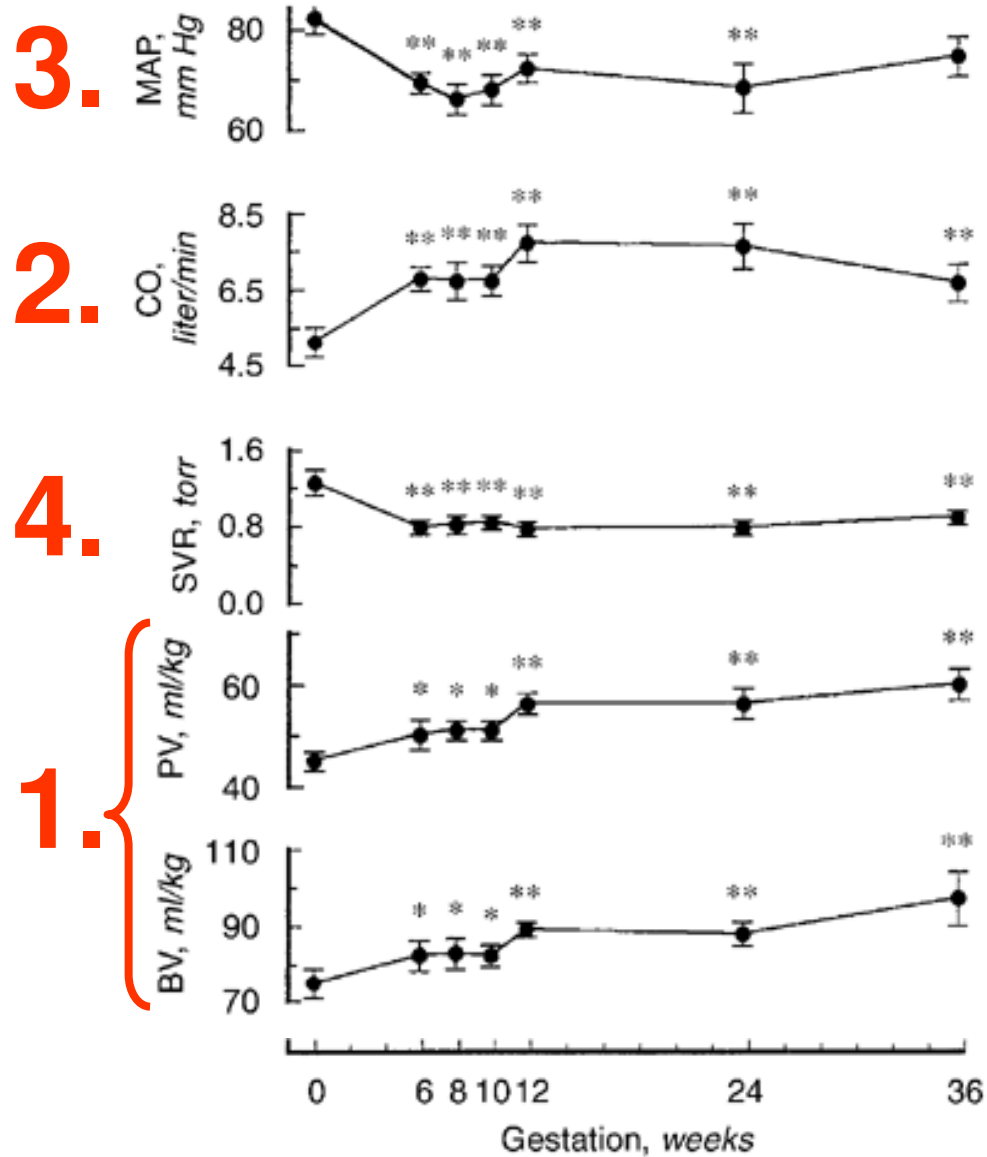
Blood pressure =

Cardiac output

X

Vascular resistance

Arterial Blood Pressure in Pregnancy



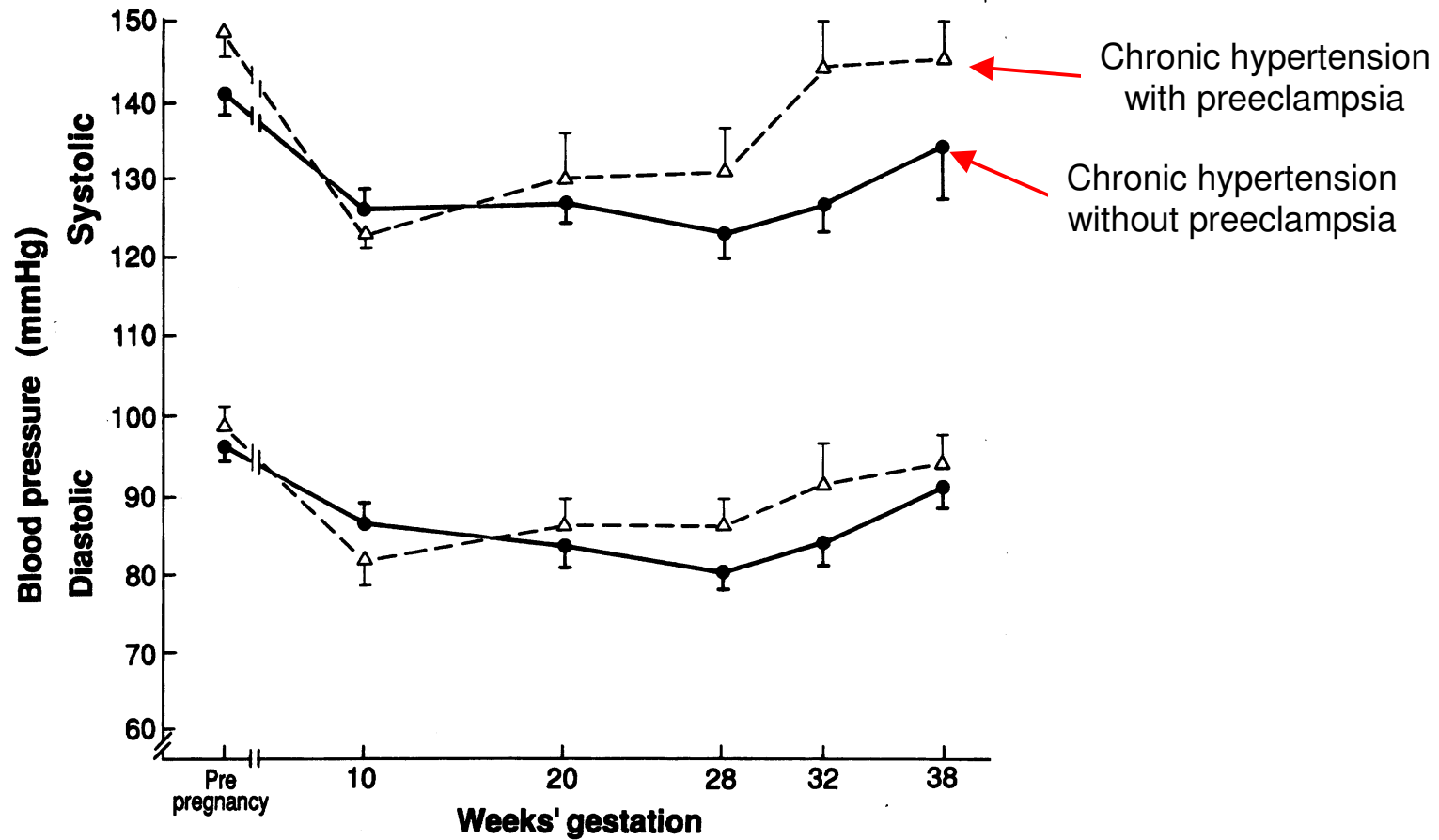
Chapman et al. *Kidney Int* 1998

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Hypertension in Pregnancy

Therapy?



August et al. *Am J Obstet Gynecol* 1990

Consequences of Arterial Hypertension in Pregnancy

Treatment absent

13 % mortality (*Yale J. Biol. Med.* '37)

Insufficient treatment

- 45 % maternal renal insufficiency
- 52 % preeclampsia (*Obstet Gynecol* '86)

Hypertension in Pregnancy

Behavioral Adjustments?

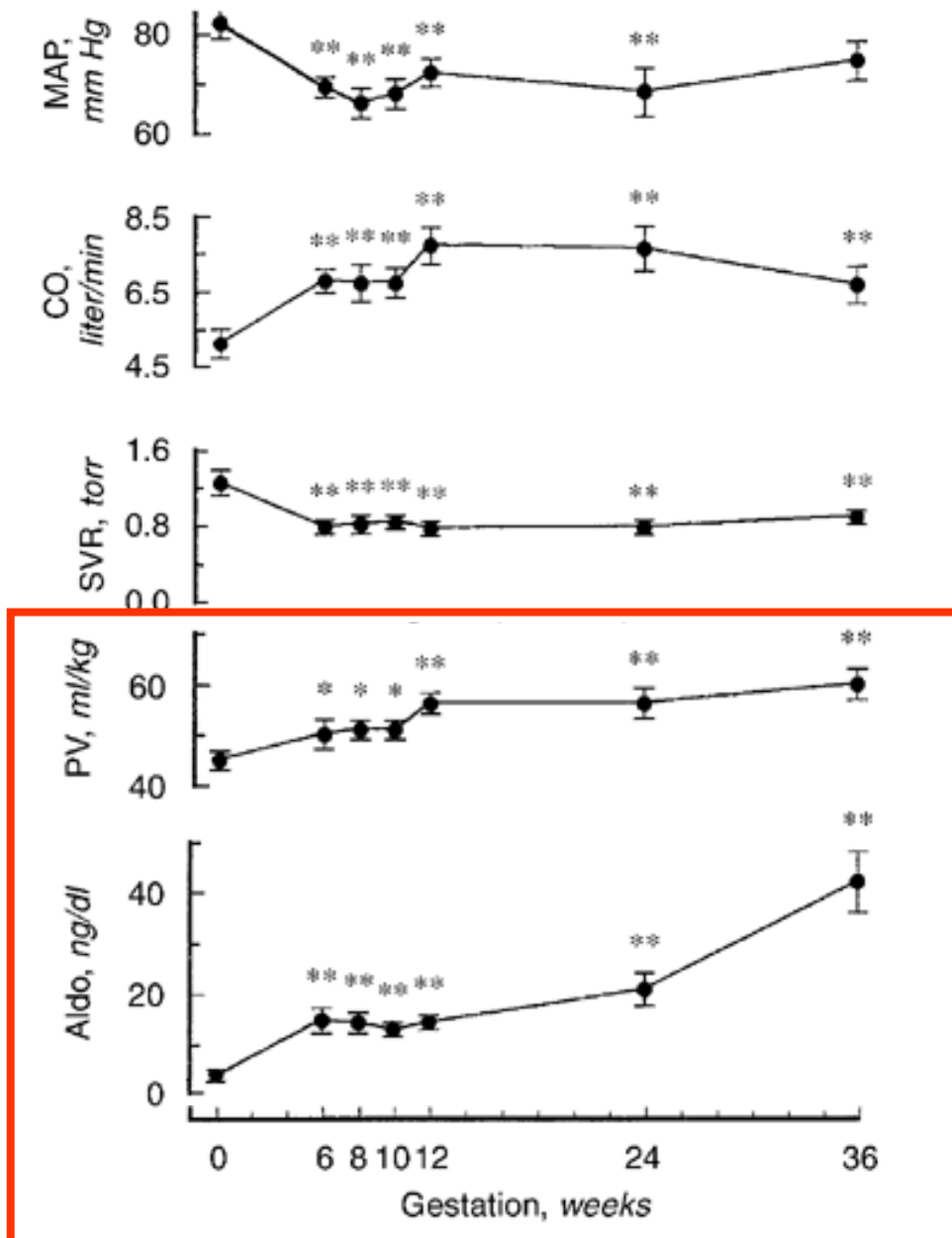
NO

- **Aerobic training**(no primary endpoint studies, theoretical considerations)
- **Weight reduction**(no impact on hypertension, fetal growth retardation)
- **Bed rest**(no benefit on metaanalysis)
- **Protein- and energie-enriched diet**(no benefit on metaanalysis)
- **Salt reduction**(inkonklusive studies, but diuretics counterproductive with reduced intravascular volume [preeclampsia, intrauterine growth retardation])

YES

- **Calzium supplementation**(with low Ca-diet antihypertensive acting)

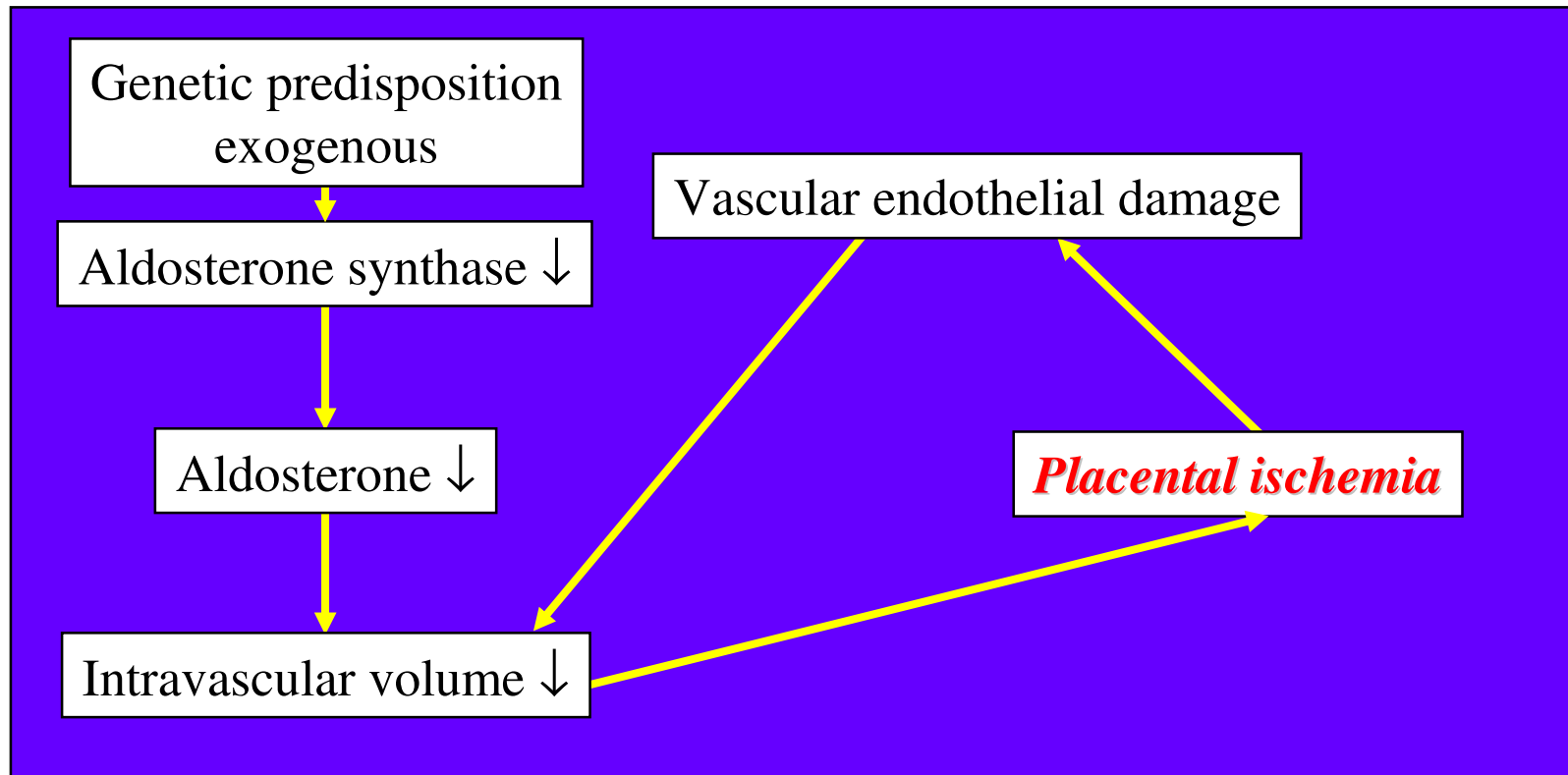
Arterial Blood Pressure in Pregnancy



Chapman et al. *Kidney Int* 1998

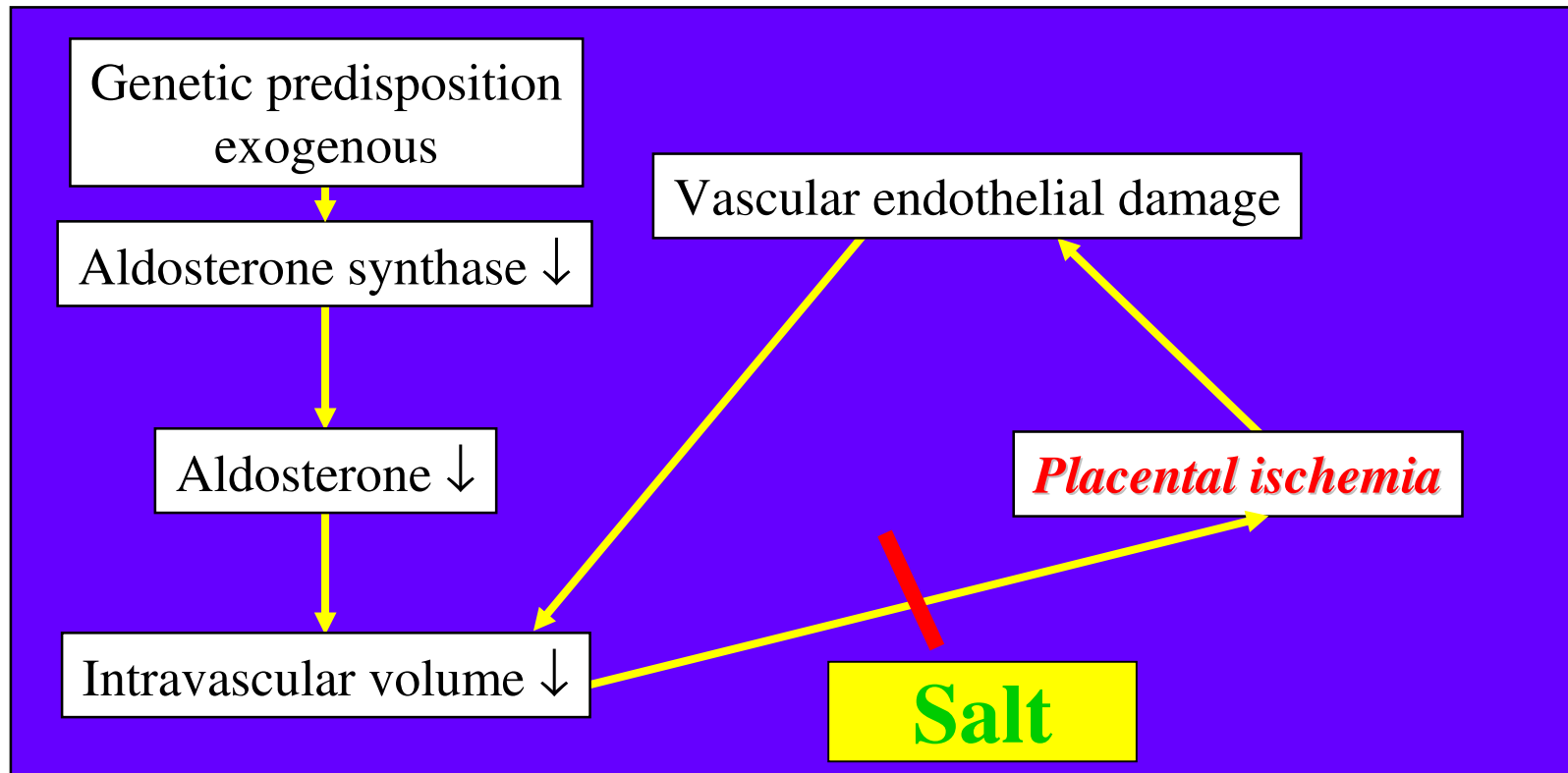
Hypothesis Related to Pregnancy-Induced Hypertension

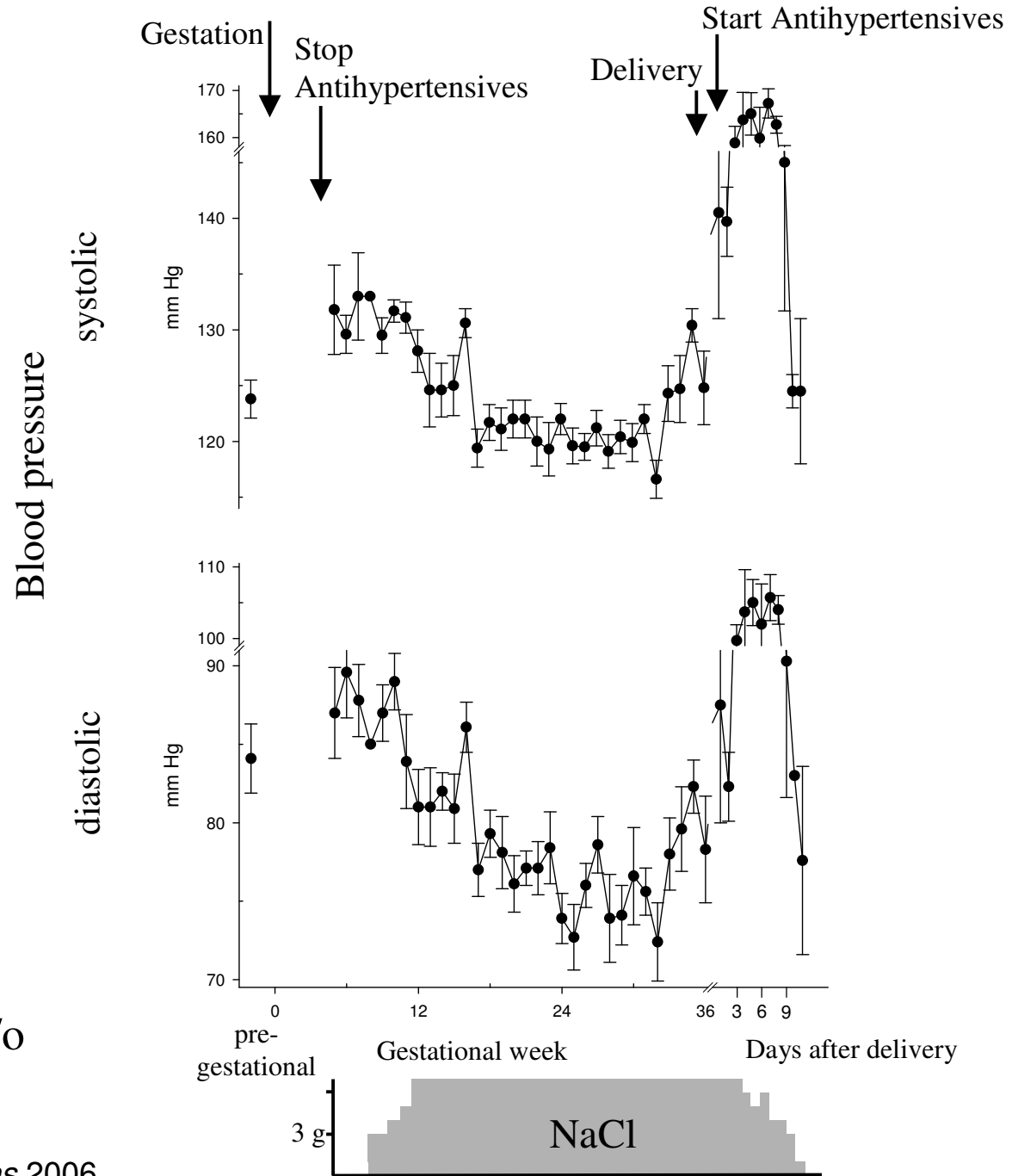
- Intravascular volume deficiency



Hypothesis Related to Pregnancy-Induced Hypertension

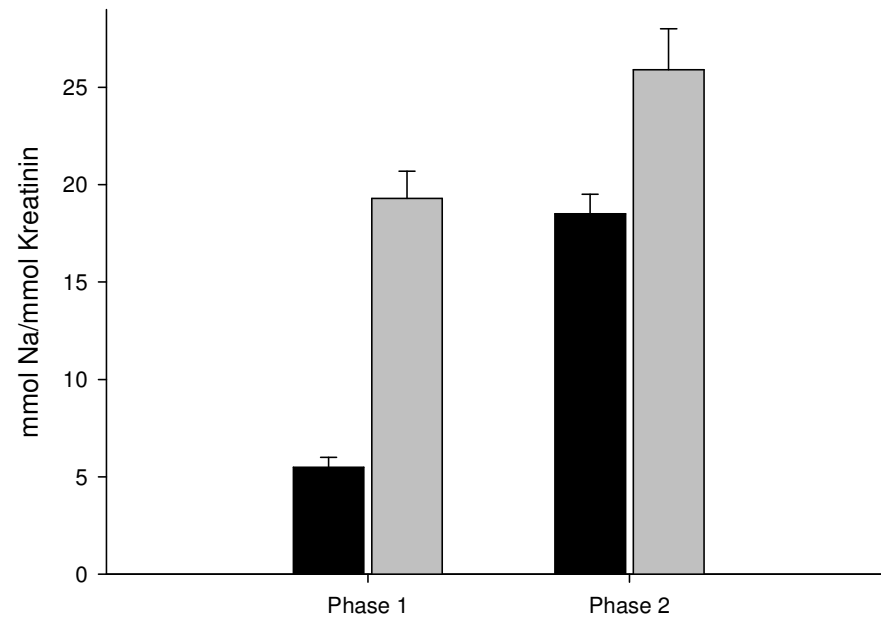
- Intravascular volume deficiency



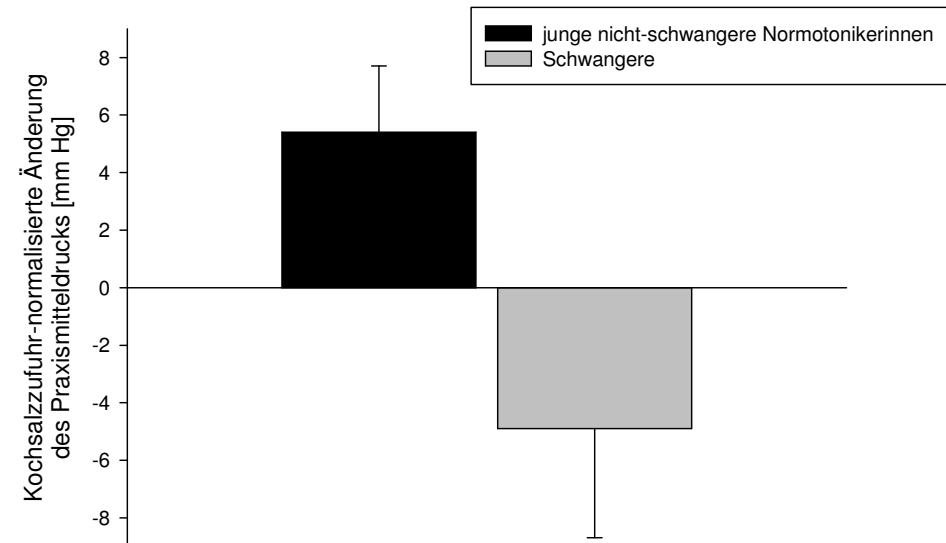


K.C., 35 y/o

Salt Supplementation



■ junge nicht-schwangere Normotonikerinnen, n=25
■ Schwangere, n=33



In 100% of non-pregnant women with increased salt intake MAP rose,
in 75 % of pregnant women with increased salt intake MAP decreased,
 $X^2=6,04$; $p<0.02$

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Hypertension in Pregnancy

Which Treatment?

- α -Methyldopa
- β -Blocker
- Labetalol
- Nifedipine

- Dihydralazine

- ?Thiazides

- No ACEI/ARB/Renin inhibitors

Hypertension in Pregnancy

α -Methyldopa vs. expectative?

- **diastolic >90 mm Hg**
 - 170 patients
 - unchanged incidence of preeclampsia (1/3)
 - unchanged incidence of 20 % fetal growth retardation
[Mabie et al. *Obstet Gynecol* 1986]

Hypertension in Pregnancy

Nifedipine vs. expectative?

- **diastolic 90-110 mm Hg**
 - 283 patients
 - Unchanged incidence of preeclampsia
 - Unchanged rate of preterm delivery
 - Unchanged fetal growth retardation [Gruppo di Studio Ipertensione in Gravidanza *Br J Obstet Gynaecol* 1998]

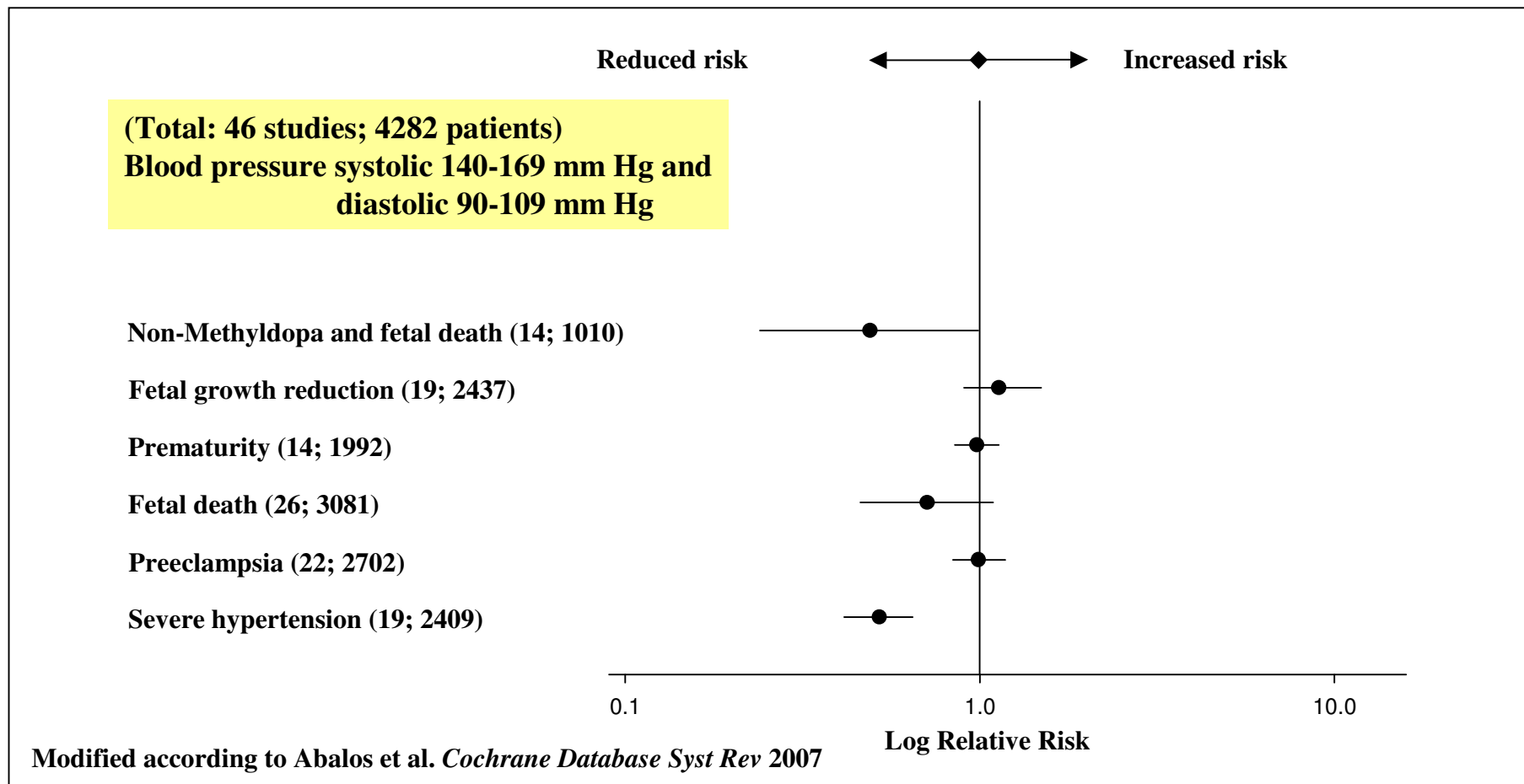
Hypertension in Pregnancy

α -Methyldopa+Labetalol vs. expectative?

- **systolic 140-150, diastolic 90-100 mm Hg**
 - 263 patients
 - Unchanged incidence of preeclampsia
 - Unchanged rate of preterm delivery
 - Unchanged rate of PROMs [Sibai et al. Am J Obstet Gynecol 1990]

Hypertension in Pregnancy

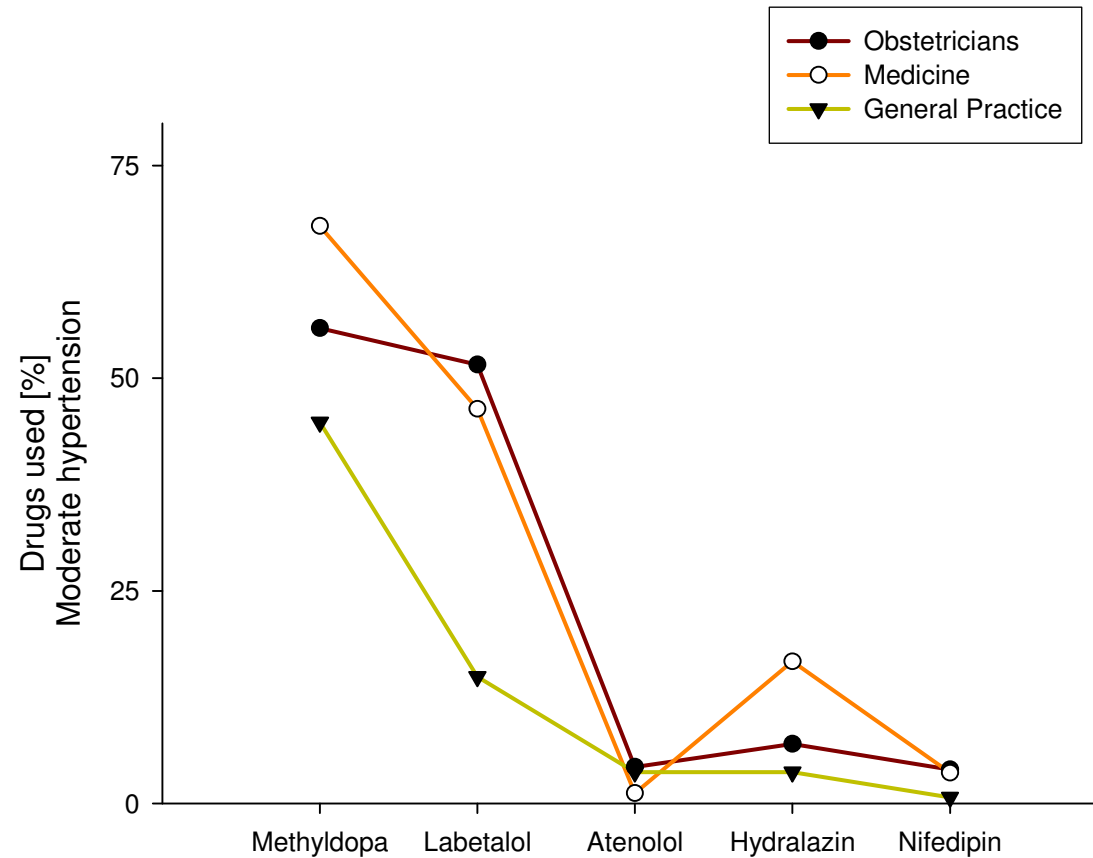
β -Blocker vs. alternative antihypertensive vs. expectative?



NEW: β -blocker better than α -methyldopa RR 0.75 for reducing the risk of severe hypertension

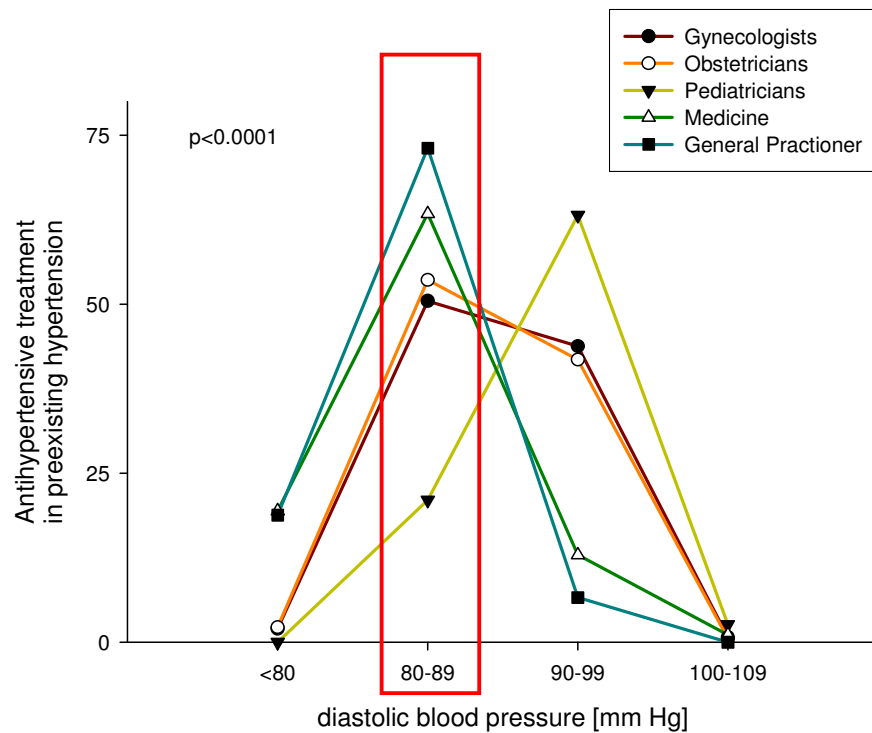
Hypertension in Pregnancy

Which Therapy?

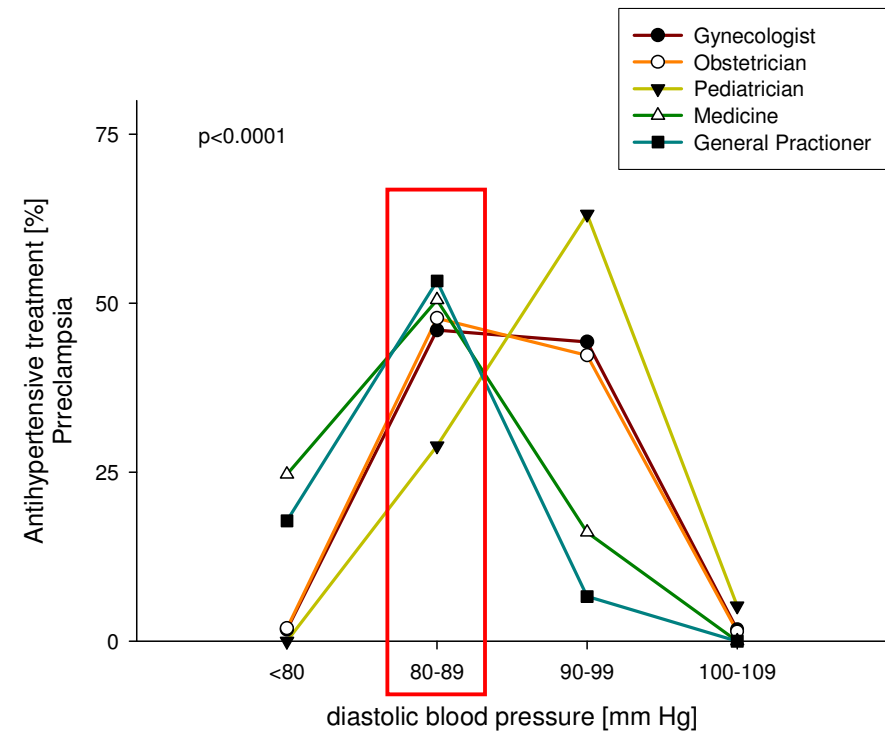


Hypertension in Pregnancy

Which Blood Pressure Goal?



Caetano et al. *Hypertens Pregnancy* 2004



Hypertension in Pregnancy

Why Wait?

- Metaanalysis of 27 studies including 2305 women
- MAP 107-129 mm Hg
- Each 10 mm Hg reduction in MAP → 145 g reduction of birth weight

Von Dadelszen et al. *Lancet* 2000

Hypertension in Pregnancy

When?

- In the presence of end organ damage (LVH, nephropathie) and/or symptoms if blood pressure < 170/110 mm Hg
- If blood pressure >170/110 mm Hg (no randomised studies)
- Beginn treatment latest at 160/100 mm Hg

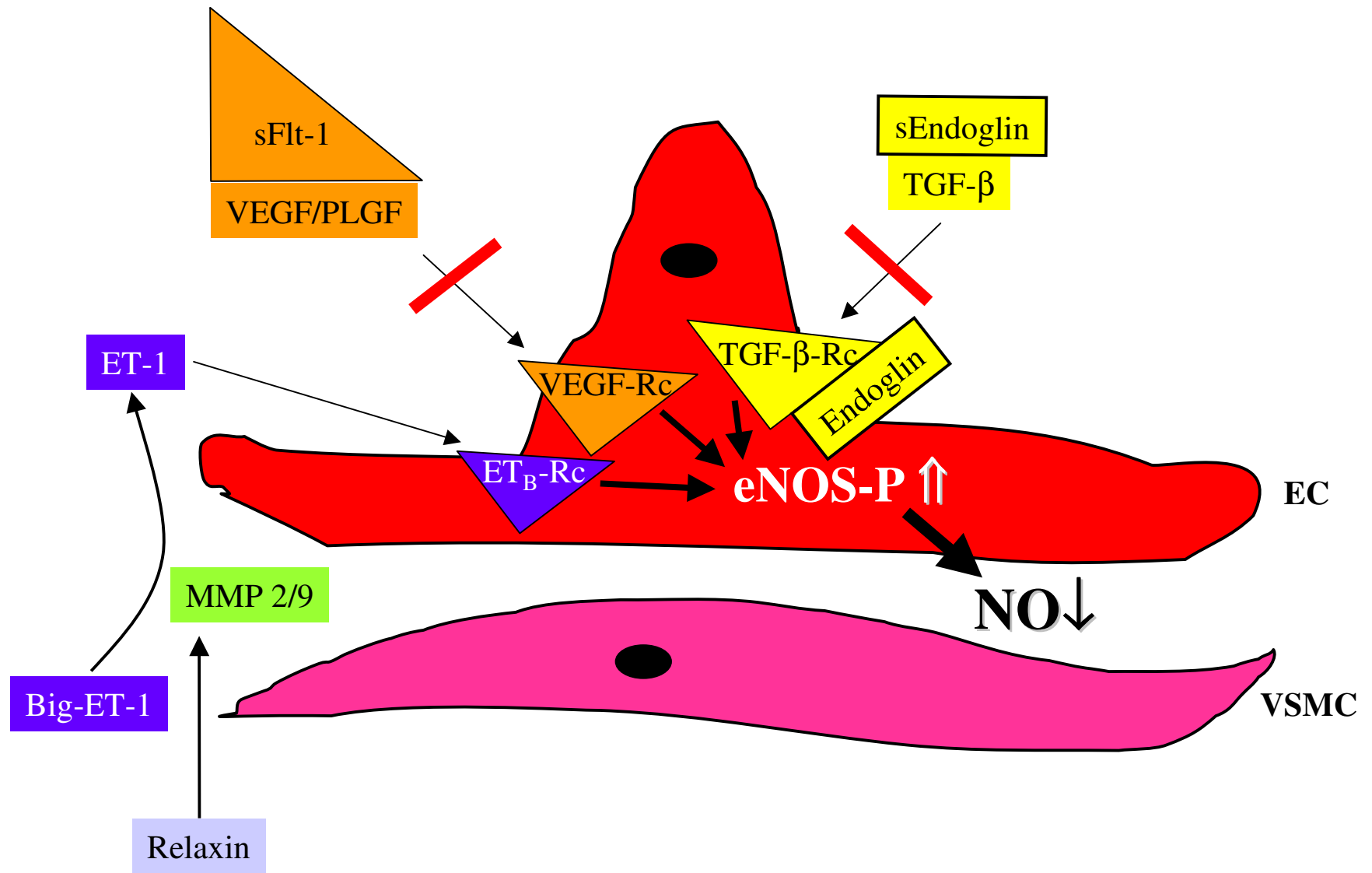
Aim

Maternal protection with drugs, which have been proven safe for the child

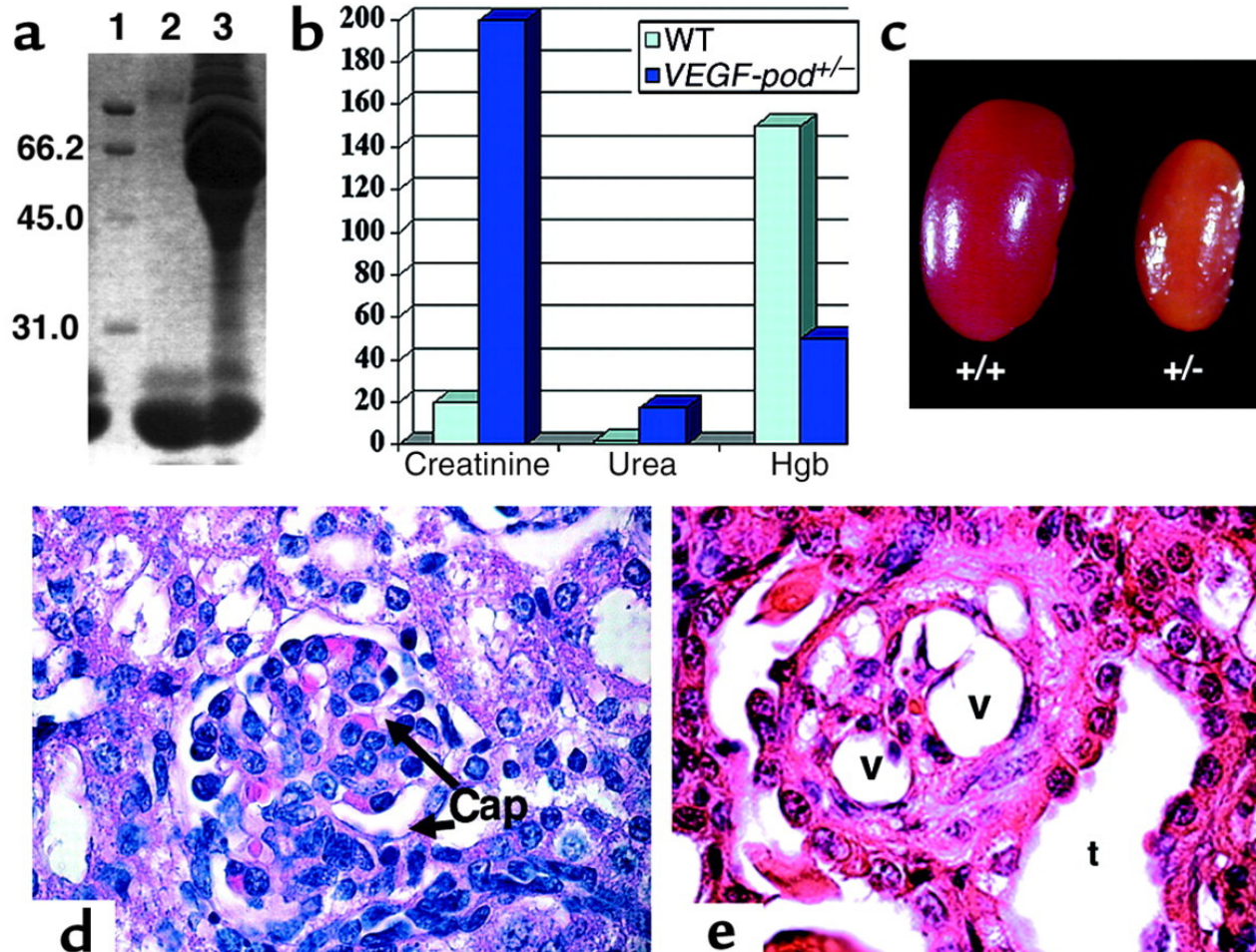
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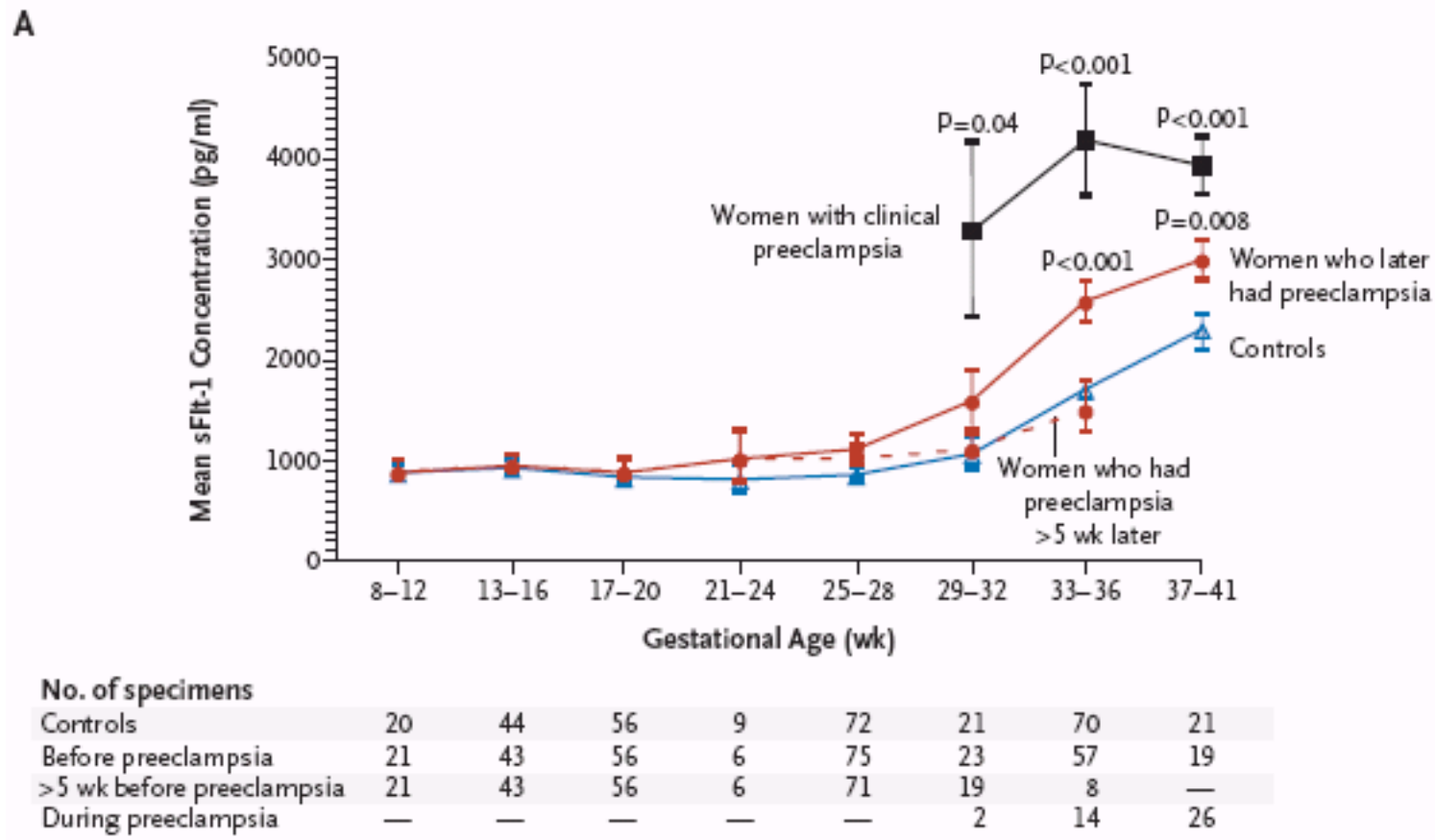
Actions on the Endothelial Layer



VEGF-Inhibition



VEGF-Inhibition by sFlt-1



Interaction Between Placenta and Endothelium

Placental Normoxia

- AT₁-agonists ↓
- 11β-HSD ↑
- Relaxin
- TGF-β
- VEGF/PLGF
- Flt-1

Placental Hypoxia

- AT₁-agonists ↑
- 11β-HSD ↓
- sFlt-1 (sVEGF-Rc)
- sEng (sTGF-β CoRc)
- NF-κB

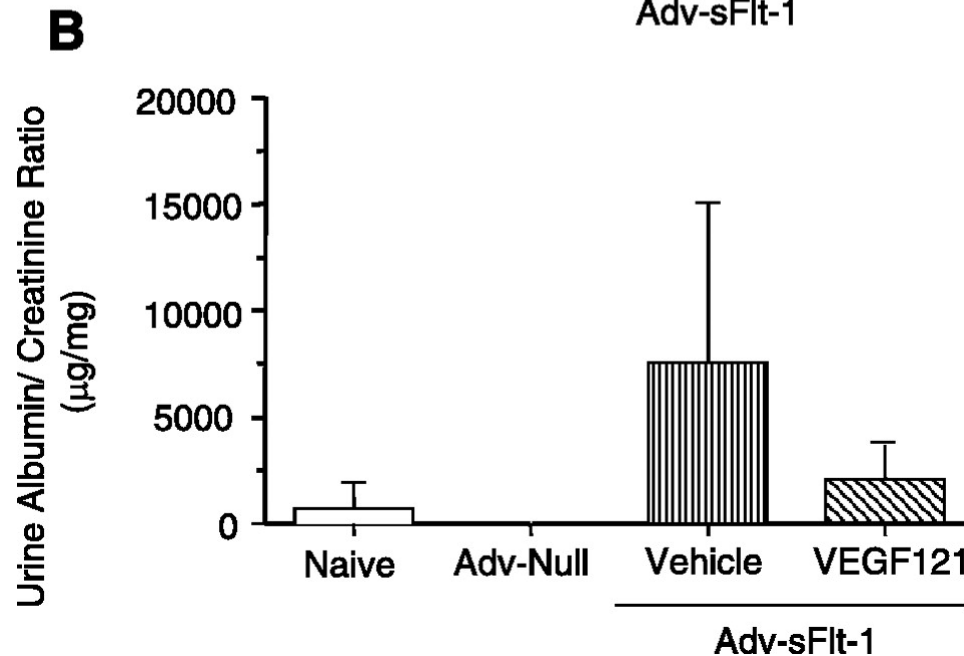
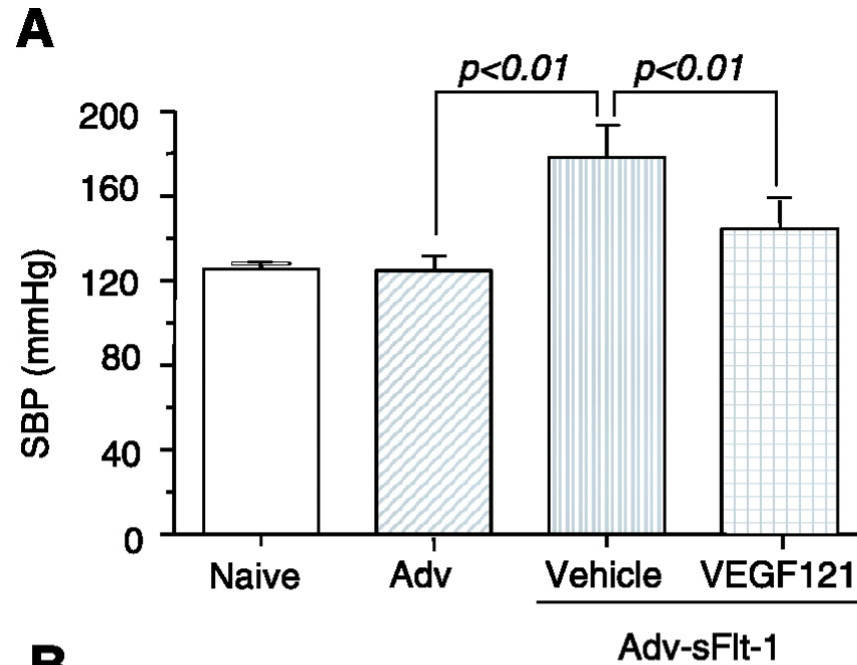
Vasoconstriction (AT-1 Rc) ↑
Vasodilatation (NO) ↓



Preeclampsia

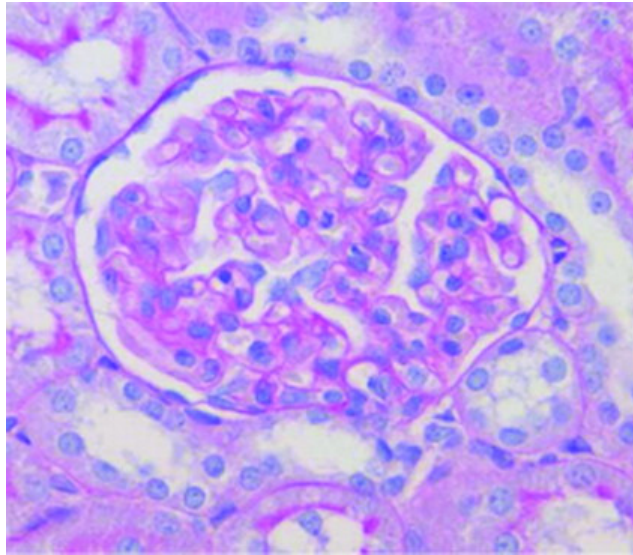
VEGF₁₂₁-Donation against sFlt-1

6 days of treatment

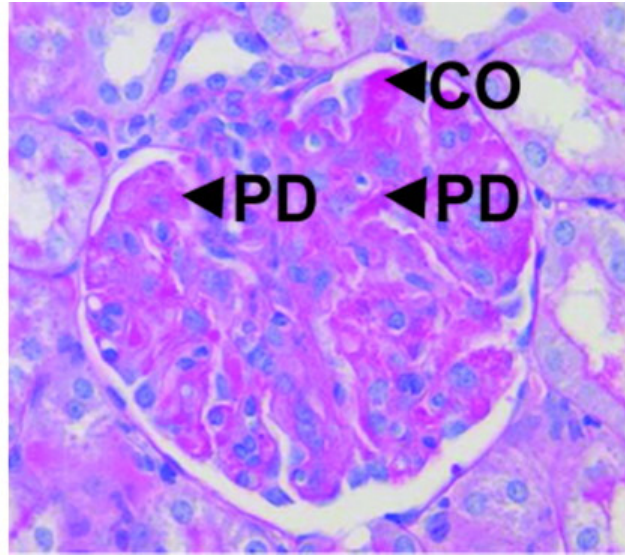


VEGF₁₂₁-Donation against sFlt-1

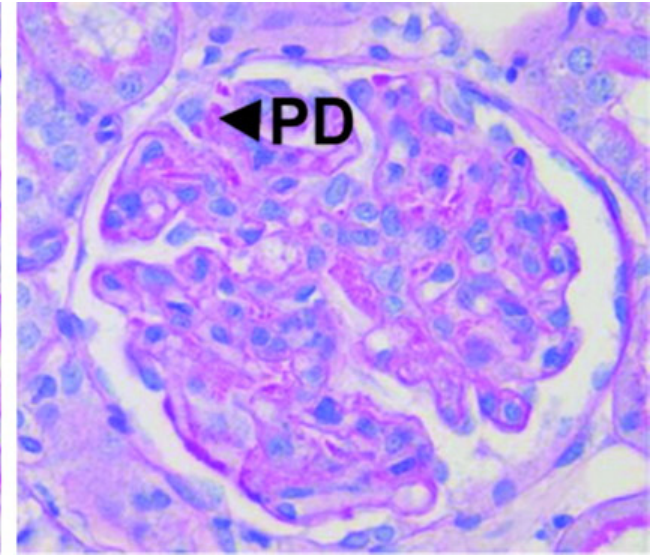
control



sFlt-1

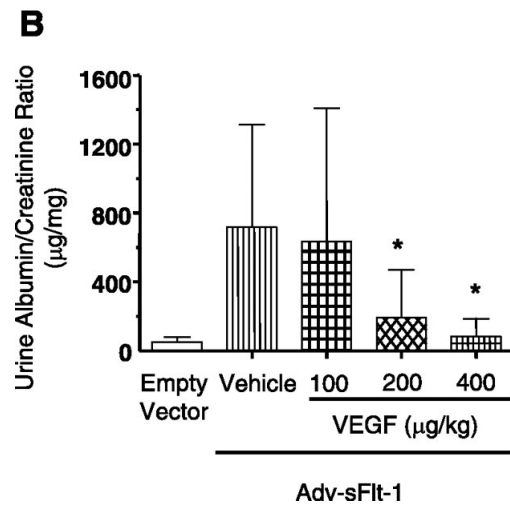
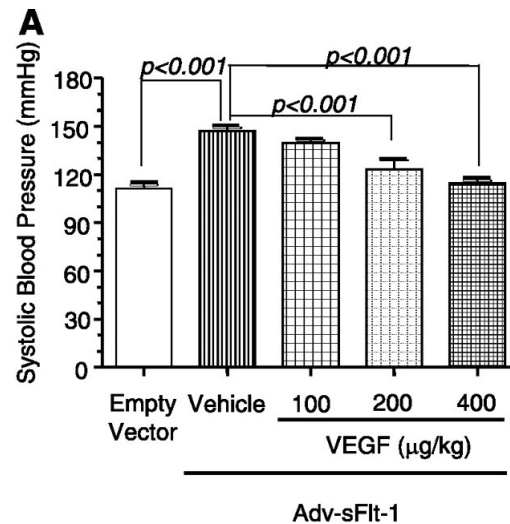


sFlt-1+VEGF₁₂₁

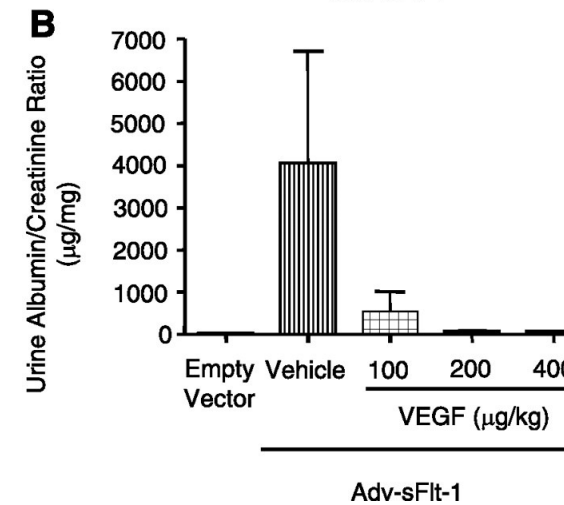
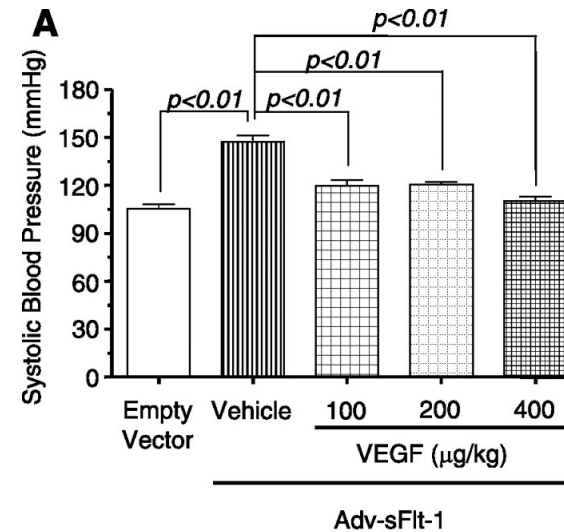


VEGF₁₂₁-Donation against sFlt-1

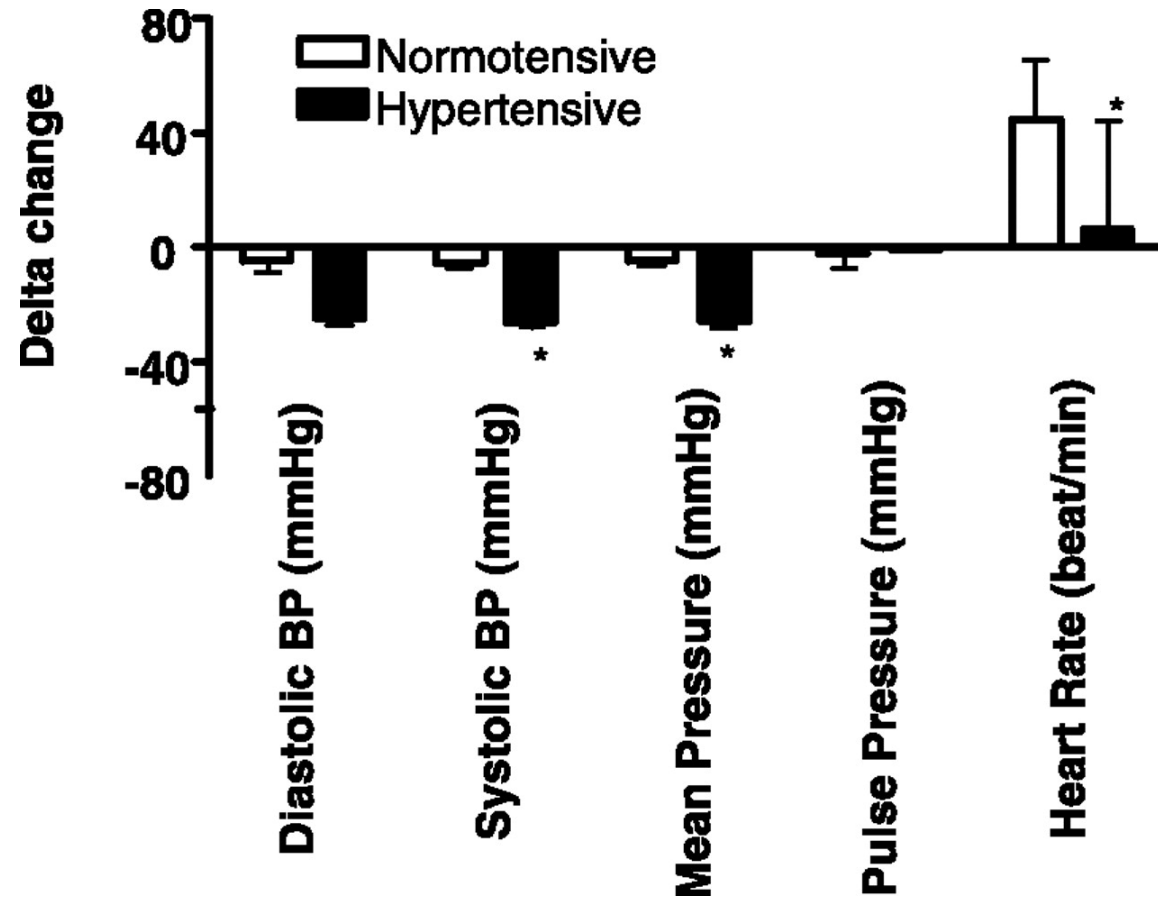
1x/day



2x/day



VEGF₁₂₁-Donation against sFlt-1



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Summary

- Treatment of arterial hypertension in pregnancy necessary, yet unsatisfactorily solved
- Behavioral adjustments in general useless, potentially salt
- Drug therapy
 - discontinuation should be considered
 - as little as possible, as much as necessary
- Treatment of preeclampsia – VEGF₁₂₁ in the pipeline