Effects of Oestrogen on Haemodynamic and Vascular Reactivity
A study in animal models and humans

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This thesis is based on the following papers:

I Brandin L, Gustafsson H. 17beta-estradiol relaxes precontracted mesenteric arteries from male and female rats; a transient effect which is lost after a short incubation period.
In manuscript

II Brandin L, Bergstrom G, Manhem K, Gustafsson H. Oestrogen modulates vascular adrenergic reactivity of the spontaneously hypertensive rat.
J Hypertension 2003;21:1695-1702

III Brandin L, Bergstrom G, Manhem K, Gustafsson H. Estrogen attenuates ambulatory pressure and heart rate in hypertensive rats with small effects on hemodynamic responses to stress.
Submitted

IV Manhem K, Brandin L, Ghanoum B, Rosengren A, Gustafsson H. Acute effects of transdermal estrogen on hemodynamic and vascular reactivity in elderly postmenopausal healthy women.
J Hypertension 2003;21:387-394

V Brandin L, Gustafsson H, Ghanoum B, Milsom I, Manhem K. Chronic effects of conjugated equine estrogen on hemodynamic and vascular reactivity in hypertensive postmenopausal women
Submitted
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Abstract

Previous studies have shown that oestrogen, the female sex hormone, plays a protective role in 
the cardiovascular system. However the site of action remains incompletely understood. Large 
clinical interventional trials have not proven that longer treatment with oestrogen plus 
progesterone yields lower incidence of cardiovascular outcomes, suggesting that hormone 
replacement therapy (HRT) might protect only a selective group of postmenopausal women.

The present study treated normo- and hypertensive female rats and postmenopausal women with 
oestrogen for short and longer time periods. We also investigated the acute effect of 17β-
estradiol on isolated small resistance arteries and the effects of oestrogen treatment on vascular 
reactivity and endothelial function in a wire-myograph. Further, we recorded haemodynamic 
parameters during daily life and stress, and evaluated the effect of HRT on the autonomic 
nervous systems of hypertensive women by evaluating heart rate variability (HRV) with 24 h 
alanalysis.

Blood pressure (BP) was attenuated after 24 hour treatment with 17β-estradiol in normotensive 
postmenopausal women and normo- and hypertensive rats. In hypertensive rats a lowered BP 
sustained after 10 days of treatment. Although we observed an attenuated heart rate (HR), 
haemodynamic responses to stress remained largely unaffected. Six months of HRT did not 
affect BP, HR, HRV, or haemodynamic responses to stress in hypertensive postmenopausal 
women but did result in reduced sensitivity to noradrenaline, a stress hormone, in subcutaneous 
arteries. Lower adrenergic response occurred in the resistance arteries of hypertensive rats but 
not in normotensive rats or women. 17β-estradiol relaxed precontracted mesenteric arteries, due 
mainly to endothelial release of nitric oxide. We also observed a modulated endothelial response 
to acetylcholine following 17β-estradiol treatment in normotensive women and hypertensive 
rats and HRT in hypertensive women.

In conclusion, the effects of oestrogen on vascular reactivity and haemodynamics differed 
between hypertensive and nonhypertensive subjects and also according to the type of oestrogen 
used. Decreased BP and HR with 17β-estradiol treatment but not with HRT suggests that 17β-
estradiol participates selectively in the haemodynamic system. However, the attenuated 
adrenergic vascular response observed in hypertensive subjects independent of oestrogen type 
may contribute to improved blood flow to peripheral tissue even though BP remains unchanged. 
The clinical importance of the reinforced acetylcholine induced response in normotensive and 
hypertensive women and rats after oestrogen treatment requires further evaluation.

Key words: adrenergic reactivity, endothelium, haemodynamic, hypertension, oestrogen, 
postmenopausal women, resistance arteries, spontaneously hypertensive rats, stress