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METHODS FOR THE SCREENING AND PREVENTION
OF PREECLAMPSIA AND ITS COMPLICATIONS

by

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To Nick and my parents. For their unconditional support.
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Abstract

Preeclampsia is a serious disorder of pregnancy. The syndrome is the leading cause of maternal mortality in the United Kingdom and it also contributes significantly to perinatal morbidity and mortality. Maternal mortality is primarily due to cerebral complications.

Despite continued research, the aetiology of preeclampsia remains unknown. This has limited the development of screening, preventive and therapeutic measures to control the syndrome.

Present management is based on basic screening to detect early signs of the syndrome, observation of its progress and occasionally therapeutic intervention to control hypertension. Delivery is timed to prevent maternal and fetal complications, while simultaneously aiming to gain fetal maturity. Unfortunately, in many situations this control is not possible.

Owing to an increasing understanding of the pathogenesis of the disease, a new option for prophylaxis - low-dose aspirin - may soon be available. If prevention of preeclampsia becomes a reality, a simple but sensitive screening test will be required to select those women who will benefit from treatment.

This thesis is focused on the prevention of preeclampsia and its complications. It will involve examination of screening tests, the preventive therapy low-dose aspirin, and the preliminary assessment of a new technique to detect women at risk for developing cerebral complications from the disease.
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Abbreviations

5HT  serotonin
ABP  ambulatory blood pressure
AII  angiotensin II
AC   abdominal circumference
ANOVA analysis of variance
AST  Angiotensin Sensitivity Test
AUK  active urinary kallikrein
BP   blood pressure
BPM  beats per minute
CLASP Collaborative Low-dose Aspirin Study in Pregnancy
CV   coefficient of variation
EPD  effective pressor dose
FVW  flow velocity waveform
HMWK high molecular weight kininogen
IUGR intrauterine growth retardation
IUK  inactive urinary kallikrein
IUK/Cr inactive urinary kallikrein / creatinine ratio
JRH  John Radcliffe Hospital
K5   Korotkoff Phase 5
MAP  mean arterial pressure
MAXA2 maximum angiotensin II dose
MCA  middle cerebral artery
NPV  negative predictive value
OD  405 optical density 405 nM
PGE1 prostaglandin E1
PGE2 prostaglandin E2
PGI2 prostacyclin
PI   pulsatility index
PPV  positive predictive value
QCH  Queen Charlotte's and Chelsea Hospital
SD   standard deviation
SENS sensitivity
SPEC specificity
TCD  transcranial Doppler ultrasound
TXA2 thromboxane A2